DEPARTMENT OF MEDICAL MICROBIOLOGY
ROYAL WOLVERHAMPTON
HOSPITALS NHS
TRUST

ANTIMICROBIAL PRESCRIBING GUIDELINES

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Introduction

1.0 General Principles Guiding Antimicrobial Therapy

1.1 Establish Microbial Diagnosis

Collection of appropriate and adequate specimens **prior to** starting or changing antibiotic therapy is essential to maximise the chances of establishing the microbial aetiology of infections. If in doubt, please contact the laboratory or medical microbiologist for advice (see Section 28, page 48 for contact numbers).

Complete request cards with as much information as possible to enable the laboratory to make full use of specimens.

1.2 Choice of Antibiotic

Initial 'best guess' therapy will depend on consideration of:

- the most likely pathogen(s).
- the usual sensitivity pattern (local variations may occur).
- the site of infection - the ability of the antibiotic to penetrate in adequate concentrations to the site of infection.
- route of administration - the most appropriate route of administration depends on the antibiotic chosen, severity of illness (septicaemic patients should have initial i.v. therapy) and patient factors (e.g. ability to take oral medication).

Oral agents are generally much cheaper than parenteral preparations. Very few conditions require intravenous therapy to continue beyond the initial 48 hours of the antibiotic course. Therefore, with the exceptions of febrile neutropenia, infective endocarditis, septic arthritis, osteomyelitis, discitis, meningitis, other intracerebral infections, liver abscess, vascular graft infections, empyema, lung infections in patients with cystic fibrosis, severe pelvic inflammatory disease, line-associated sepsis, patients who are vomiting or patients not able to absorb oral intake, parenteral antibiotics will be questionned by the ward pharmacist after 48 hours and will usually therefore need to be substituted with an oral antibiotic.

Avoid topical antibiotics unless there is a clear indication for their use.

1.3 Duration of Therapy

Short courses of <5 days are often adequate to treat uncomplicated infections, such as simple UTIs.

Longer courses may be necessary to treat some specific infections, such as: febrile neutropenia, infective endocarditis, septic arthritis, osteomyelitis, discitis, meningitis, other intracerebral infections, liver abscess, vascular graft infections, empyema, lung infections in patients with cystic fibrosis, severe pelvic inflammatory disease, tuberculosis and *Clostridium difficile* infection.

The Pharmacist will challenge unnecessarily long duration of therapy, and will stop the antimicrobial if there is no indication for a prolonged course after discussion with medical staff.

1.4 Dose

Influenced by:

- sensitivity of infecting organism.
- route of excretion - accumulation may occur in renal or hepatic failure.
- site of infection - high doses may be required for CNS penetration. Many agents are highly concentrated in urine.
- toxicity.
- drug interactions.

It is advisable to review all clinical and microbiological information frequently (at least every 24 hours). The results of cultures are generally available within 48 (often within 24) hours, and antimicrobial therapy may be revised if necessary. If the patient is responding well to empirical therapy, however,

treatment should not necessarily be changed solely on the basis of the results of cultures and antibiotic sensitivities. Consideration should still be given, though, to change from broad spectrum to narrow spectrum agents if possible.

If the patient is failing to respond to apparently appropriate therapy (given by an appropriate route at the appropriate dose), a review of the diagnosis should be considered, e.g. is there an abscess which requires drainage, has a complication of the infection developed, or is a non-infectious condition responsible for the clinical presentation?

1.5 Documentation

Antibiotics are potent drugs with serious and potentially fatal side effects. Therefore it is important that all antimicrobial prescribing decisions are documented in the healthcare record. The use of the antimicrobial sticker is the ideal way of achieving this. The information recorded should include the antibiotic(s) prescribed, the indication, route, anticipated duration and means of monitoring the response to therapy. Patients on antibiotics should be reviewed daily and their need for continued antibiotics considered.

Antimicrobial Prescribing Sticker

Allergy Status:_____
Name of antimicrobial:_____
Indication:_____

Empirical treatment □ or based on sensitivities □

Was this Microbiologist approved? Yes □ No □

Route_____ (IV for a max. of 48 hours)
Anticipated duration:_ _____

Is antimicrobial high risk for c.diff? Yes □ No □

If yes has the patient been informed? Yes □ No □

Print name of Prescriber_____Contact no_____ 1668.30.09.09

1.6 Side Effects

It is advisable to warn patients of common or potentially serious side effects of antimicrobial therapy at the start of the course of treatment. If antibiotics that fall into the 'High Risk' category for causing or exacerbating *Clostridium difficile* infection are used (see below), this risk should be explained to the patient, along with the reasons why that antibiotic choice has been made. It should be documented in the healthcare record that this process has taken place.

Antibiotics – Risk Assessment for Developing / Exacerbating *C. difficile* Infection

High Risk	**Medium Risk**	**Low Risk**
Cefotaxime	Meropenem	Benzyl penicillin
Ceftriaxone	Ertapenem	Amoxicillin
Cefalexin	Co-amoxiclav	Flucloxacillin
Cefuroxime	Piperacillin/tazobactam	Tetracyclines
Ceftazidime	Erythromycin	Trimethoprim
Ciprofloxacin	Clarithromycin	Nitrofurantoin
Moxifloxacin	Clindamycin (high dose)	Rifampicin
Ofloxacin		Fusidic acid
Clindamycin (low dose)		Gentamicin
		Vancomycin
		Teicoplanin
		Metronidazole
		Synercid
		Linezolid
		Daptomycin
		Tigecycline

Notes on Some Antimicrobial Agents

To aid rational prescribing, all antimicrobials have been placed into one of three categories:

Category 1: open, unrestricted use. All antimicrobials prescribed according to the 'Antibiotic Card' are Category 1 for that indication

Category 2: use restricted to specific indications, with consultant approval, or following discussion with a medical microbiologist, unless being used according to the 'Antibiotic Card'

Category 3: not available except under exceptional circumstances, following discussion with the medical microbiologist. (i.e. not on Trust Formulary)

Numbers in parentheses after antibiotics denote category

These are intended to be guidelines only. For additional details of doses, drug interactions, contraindications etc., please refer to the current edition of the British National Formulary (BNF), or the electronic BNF on the Trust intranet site.

Abbreviations used in tables:

Route:

im	**intramuscular**
inj	**injected**
iv	**intravenous**
neb	**nebulised**
po	**oral**
pr	**rectal**
top	**topical**

Frequency:

od	**once daily**
bd	**twice daily**
tds	**three times daily**
qds	**four times daily**

2.0 Beta - lactams

2.1 Penicillins (BNF section 5.1.1)

AGENT (category)	MODE OF ADMIN.	COMMENTS / INDICATIONS
benzylpenicillin (pen G) (1)	inj	• remains drug of choice for many infections e.g. streptococci and meningococci • best given 4 - hourly in severe infection
phenoxymethyl-penicillin (pen V) (1)	po	• less active than penicillin G • use for mild infections only (amoxicillin better absorbed)
procaine penicillin (2)	inj	• long acting, for GUM clinic use only
flucloxacillin (1)	po/inj	• anti-staphylococcal activity only • monitor liver function on long-term therapy (>14 days)
amoxicillin (1)	po/inj	• ampicillin no longer available in Trust • resistance common in staphylococci, *E. coli*
co-amoxiclav (1)	po/inj	• amoxicillin and clavulanic acid • active against penicillinase producing organisms resistant to amoxicillin • additional anti-anaerobic activity (therefore no need to give metronidazole concurrently) • should **not** be considered a routine alternative to amoxicillin

2.2 Extended Spectrum Penicillins (BNF sections 5.1.1.4, 5.1.2)

AGENT (category)	MODE OF ADMIN.	COMMENTS / INDICATIONS
piperacillin / tazobactam (Tazocin®) (2)	inj	• broad spectrum activity, antipseudomonal • for empirical use (with gentamicin) in febrile neutropenia
ticarcillin / clavulanic acid (Timentin) (3)	inj	• for use against *Stenotrophomonas maltophilia* only
aztreonam (3)	inj	• activity limited to Gram negative organisms only • occasional use in patients with cystic fibrosis

Penicillin allergy is commonly reported, however, a full history is essential to establish a causal relationship between beta-lactam therapy and symptoms. It is wise to avoid penicillins where there is a clear history of anaphylaxis, angioedema, or urticaria. A history of rash or other symptoms however, is less reliable as an indicator of significant allergy.

2.3 Cephalosporins / Cephamycins (BNF section 5.1.2)

AGENT (category)	MODE OF ADMIN.	COMMENTS / INDICATIONS
cefalexin (2)	po	• useful for UTI only • not suitable for treatment of chest infections
cefuroxime (2)	inj	• high incidence of *C. difficile* associated with its use in adults • only use is orthopaedic prophylaxis for elective implant surgery plus some limited use in term pregnancy
cefuroxime axetil (3)	po	• oral cefuroxime **not** equivalent to i.v. preparation • oral cefuroxime is **not** suitable for treatment of respiratory tract or post operative infections
cefotaxime (2)	inj	• only to be used for treatment of meningitis, epiglottitis, neonatal sepsis and enteric fever • very strong association with symptomatic *C. difficile* infection in adults
ceftazidime (2)	inj	• has antipseudomonal activity • high incidence of *C. difficile* associated with its use in adults • only to be used when pathogen resistant to other antipseudomonal antibiotics, or allergies prevent the use of an alternative
ceftriaxone (3)	inj/im	• once daily administration - useful for home iv therapy • only to be used for treatment of meningitis and enteric fever on advice of Microbiologist • very strong association with symptomatic *C. difficile* infection in adults
cefixime (2)	po	• longer half life than other oral cephalosporins (once daily dosing) • 2nd line agent for paediatric and 1st line GUM for uncomplicated *Neisseria gonorrhoea.* (unlicensed indication)

Cephalosporin therapy is a common cause of *Clostridium difficile* associated diarrhoea; they should only be used when there is no suitable alternative antibiotic available.

The oral cephalosporins should **not** be assumed to have the same activity as parenteral preparations – in particular, oral cefalexin is not equivalent to i.v. cefuroxime.

Cephalosporins have **no** useful activity against MRSA, *Listeria* spp. or enterococci.

The cephalosporins must be used with caution in patients with penicillin allergy (10% risk of cross hypersensitivity).

2.4 Carbapenems (BNF section 5.1.2)

AGENT (category)	MODE OF ADMIN.	COMMENTS / INDICATIONS
ertapenem (2)	inj	• once daily dosage - useful for home iv therapy • useful for therapy of ESBL-producing organisms • useful for therapy of serious infections if anti-pseudomonal or anti-acinetobacter cover is not essential
meropenem (2)	inj	• broad spectrum • excellent anti-anaerobic activity (therefore no need to give metronidazole concurrently) • reserve for serious sepsis • expensive

The carbapenems must be used with caution in patients with penicillin allergy (10% risk of cross hypersensitivity). If there is a history of severe penicillin allergy or anaphylaxis with penicillin please discuss with microbiologist.

3.0 Aminoglycosides (BNF section 5.1.4)

AGENT (category)	MODE OF ADMIN.	COMMENTS / INDICATIONS
gentamicin (1) **tobramycin (2)** **amikacin (2)**	inj	• broad spectrum agents • good Gram negative activity • nephro- and oto-toxic (monitor levels) • synergy with penicillins • amikacin and tobramycin should be reserved for specific indications (e.g. cystic fibrosis)
streptomycin (2)	inj	• generally reserved for particular infections e.g. tuberculosis, brucellosis

Guidelines on Extended Dose Interval Gentamicin Regime

Giving aminoglycoside antibiotics (e.g. gentamicin) as a large single dose using the extended dose interval regime (also known as once daily dosing), rather than using the traditional two or three times per day regimes, offers several advantages. These include:

- reduced staff time in preparing and administering the drug
- reduced drug wastage
- timing of dose less critical (as giving the dose an hour or two early or late makes much less difference to potential toxicity than with a multiple daily dose regime)
- reduced likelihood of underdosing
- reduced staff time in taking blood for levels
- reduced laboratory costs in measuring levels

In addition, as this class of antibiotics has concentration-dependent activity (i.e. the higher the concentration of antibiotic, the more rapidly it kills bacteria), there is better bactericidal activity with a once daily dose, while the long dose interval allows almost total elimination of the drug between doses, and therefore reduced toxicity. The marked ‘post-antibiotic effect’ of aminoglycosides ensures that there is no significant bacterial regrowth between doses.

An extended interval, high-dose regimen **(5mg per kg)** of an aminoglycoside with subsequent nomogram interpretation **MUST be avoided** in the following situations:

- gross ascites
- burns > 20%
- haemodialysis
- haemofiltration
- pregnancy
- creatinine clearance < 20 ml/min **
- bacterial endocarditis
- treatment of chest infections in cystic fibrosis patients

**In patients with renal failure the creatinine clearance (CrCl) must be estimated using the Cockcroft Gault formula:

$$CrCl = F \times \frac{(140 - age) \times weight\ (kg)}{Serum\ creatinine}$$

F = 1.23 if male

F = 1.04 if female

Neonates and children may use a once daily dosing regime, but the nomogram used for adult serum level interpretation is not validated for use in children. Therefore a pre-dose level (i.e. a level taken 23 hours or more after the dose) should be taken and further doses given if this is <1 mg/L. If in doubt over the correct use of aminoglycosides discuss the dosage and monitoring with the duty microbiologist.

ICCU Patients

For some acutely unwell patients on the ICCU admitted with severe sepsis a 7 mg/kg dose of gentamicin may be used in conjunction with the Hartford Nomogram. Please refer to the separate ICCU policy or discuss with the duty microbiologist.

Patients in the ICCU receiving haemofiltration may be given a single dose of gentamicin of 3-5 mg/kg depending on the severity of the infection. The Urban and Craig nomogram must not be used in these patients. A pre-gentamicin level taken between 20 – 24 hours after the dose must be obtained. A repeat dose may be given when the level is < 1mg/l

Renal Patients

Patients with end-stage renal disease are usually receiving either haemodialysis or continuous ambulatory peritoneal dialysis. If these patients are receiving intra-venous gentamicin using the extended dose interval regime the use of the Urban and Craig nomogram is NOT appropriate. The trough gentamicin level must be measured , a further gentamicin dose may be given when the trough level is < 1mg/l. Please refer to the table below **"Quick guide to extended interval dosing of intra-venous gentamicin"**. For multiple daily dosing for endocarditis treatment please discuss with the on-call microbiologist. For use of intra-peritoneal gentamcin please refer to the Peritoneal Dialysis Peritonitis Protocol:

http://intranet/pdf/departments/Renal/CAPD_Peritonitis_Protocol.pdf

PRACTICAL STEPS FOR ADMINISTERING AND MONITORING EXTENDED DOSE INTERVAL GENTAMICIN REGIME IN ADULTS

If using the extended dose interval regime the clinical need for gentamicin must be reassessed on a daily basis. Most side-effects are dose related therefore care must be taken with dosage and duration. Whenever possible treatment must not exceed 7 days.

Once daily dosing of gentamicin is calculated according to the weight of the patient.

1. **Estimate the "dosing" weight of the patient**
   - Obtain weight of the patient in kilograms (Kg) and height
   - Refer to the ideal body weight table (IBW) below
   - If the patient is obese (ie. > 20% above **ideal body weight** – **IBW**) the dose should be calculated using the **obese dosing weight** – **ODW** . (see table below)

     ODW = IBW + 0.4 (actual body weight – ideal body weight)
   - If the patient is not obese calculate the gentamicin dose using the **ideal body weight** for the patient's height(see table below)
   - For very underweight patients these principles may not apply, please discuss with a microbiologist. (Use the patients actual body weight if less than ideal body weight)

2. **Calculate correct dose**
   - The optimal dosage for patients with creatinine clearance > 20 ml/min is 5 mg/kg.
   - Therefore multiply either ideal body weight or obese dosing weight by 5 to obtain approximate dose
   - Round the dose up or down to the nearest 20 mg, **TO A MAXIMUM DOSE OF 500 mg of gentamicin**
   - If creatinine clearance is < 40 ml/min please refer to the table below for correct dosing. A 5mg/kg dose must be avoided in these patients

Examples:

1) Mrs A, weighs 52 kg and is 5" 2 inches tall. She is not obese. Calculate treatment dose based on 5 mg/kg gentamicin.

5 x 52 = 210 mg (give 200 mg gentamicin)

2) Mr B, weighs 84 kg and is 5" 6 inches tall. Mr B is obese. Use obese dosing weight to calculate a treatment dose.

Obese dosing weight = IBW + 0.4 (actual body weight – IBW)
= 66.2 + 0.4 (84 – 66.2)
= 73 kg 5 x 73 = 360 mg (give 360 mg of gentamicin)

IDEAL BODY WEIGHT TABLE

This chart tabulates height against ideal body weight and gives the weight at which the patient is defined as obese.

		MEN		WOMEN	
HEIGHT (CM)	HEIGHT (FEET & INCHES)	IBW (KG)	OBESE IF >KG	IBW (KG)	OBESE IF >KG
150	4"11 1/10	50	60	45.5	54.6
152	4" 11 8/10	51.8	62.2	47.3	56.8
154	5" 0 6/10	53.6	64.3	49.1	58.9
156	5" 1 4/10	55.4	66.5	50.9	61.1
158	5" 2 2/10	57.2	68.7	52.7	63.2
160	5" 3	59	70.8	54.5	65.4
162	5" 3 8/10	60.8	73	56.3	67.6
164	5" 4 6/10	62.6	75.1	58.1	69.7
166	5" 5 4/10	64.4	77.3	59.9	71.9
168	5" 6 1/10	66.2	79.4	61.7	74
170	5" 6 9/10	68	81.6	63.5	76.2
172	5" 7 7/10	69.8	83.7	65.3	78.4
174	5" 8 5/10	71.6	85.9	67.1	80.5
176	5" 9 3/10	73.4	88.1	68.9	82.7
178	5" 10 1/10	75.2	90.2	70.7	84.8
180	5" 10 9/10	77	92.4	72.5	87
182	5" 11 7/10	78.8	94.6	74.3	89.2
184	6" 0 4/10	80.6	96.7	76.1	91.3
186	6" 1 2/10	82.4	98.9	77.9	93.5
188	6" 2	84.2	101	79.7	95.6
190	6" 2 8/10	86	103.2	81.5	97.8
192	6" 3 6/10	87.8	105.4	83.3	100
194	6" 4 4/10	89.6	107.5	85.1	102.1

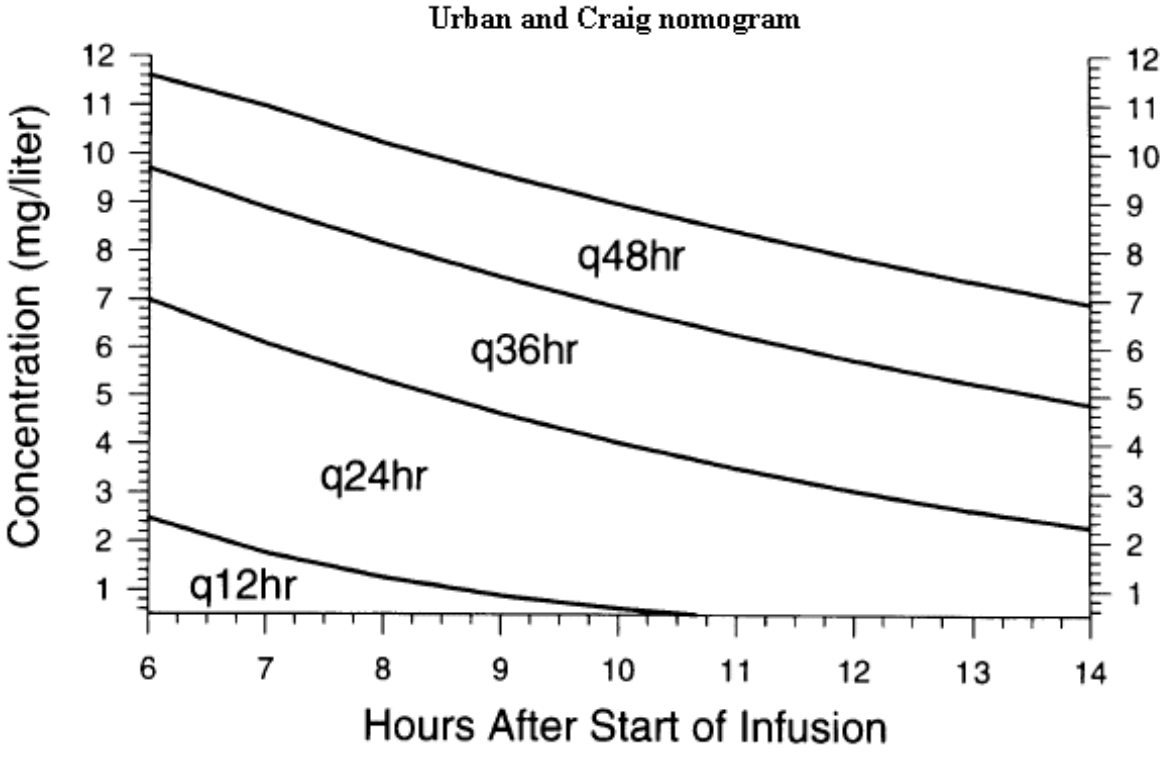
3. **Administration of gentamicin**

- IV administration
- Give in 100 mls of sodium chloride 0.9% over one hour

4. **Monitor gentamicin levels:**

- Record the time at which first dose is given (start of infusion)
- **A LEVEL MUST BE TAKEN AFTER THE FIRST DOSE TO ESTABLISH DOSE INTERVAL**
- Take a 5-10 ml blood sample into a brown-topped tube at a convenient time between **6 and 14 hours** after the start of the infusion. **Record the time at which this sample is taken**

- If the laboratory is not open, store the sample in a refrigerator until the next morning. The sample should be sent to microbiology using a microbiology request form, **stating the time at which the dose was given and the time at which the blood sample was taken**. Do not give any further gentamicin until this result is known. **(N.B. Interpretation of the level is impossible if the times requested as above are not known.)**
- When the result is obtained plot it on the Urban and Craig Nomogram (see below). This will tell you the optimal dose interval. If the value lies on the line, use the longer interval. A small number of patients with a very high creatinine clearance may be suitable for a bd regime of high dose gentamicin. If you are unsure please discuss with the duty microbiologist.
- If the renal function is stable and normal the level need only be checked twice per week. If the renal function deteriorates the level must be checked more frequently; if you are unsure please discuss with the duty microbiologist.
- **Document** clearly in the patient records advice relating to gentamicin dosing.



Quick guide to extended interval dosing of intra-venous gentamicin

Creatinine Clearance (ml/min)	**Total dose** (based on ideal body weight or obese dosing weight)	**Maximum daily dose**	**Expected dosing Interval**	**Initial drug level** To be taken after the first dose	**Frequency of therapeutic drug monitoring**
> 60	5 mg/kg	500 mg	Every 24 hours	6 – 14 hours post dose. Use the Urban and Craig nomogram to confirm or modify the dose interval.	Every three days if prolonged therapy and stable renal function. Monitor renal function daily.
40 - 59	5 mg/kg	500 mg	Every 36 hours		
20 - 39	5 mg/kg	500 mg	Every 48 hours		Every two days if prolonged therapy and stable renal function. Monitor renal function daily.
10 - 20	2-3 mg/kg	300 mg	Give repeat dose when trough < 1 mg/l.	Check levels 20 - 24 hours after the first dose. Await result and redose only when level is < 1mg/l	After each dose. Monitor renal function daily
< 10	2 mg/kg	200 mg			
Haemo-dialysis	2mg/kg after dialysis.	200 mg	Give repeat dose when trough level < 1 mg/l. Expected dose interval 48–72 hours	Check levels 48 hours after the first dose. Await result and repeat dose only when trough level is < 1mg/l	After each dose
Continuous Ambulatory Peritoneal Dialysis	2 mg/kg	200 mg			After each dose
Haemo-filtration	3-5 mg/kg depending on severity of infection	500 mg	Give repeat dose when trough level < 1mg/l	Check levels 20 - 24 hours after the first dose. Await result and redose only when level is < 1mg/l	After each dose

<u>Conventional</u> Multiple Daily Dosing and <u>Endocarditis</u> Multiple Daily dosing of Aminoglycosides

In clinical situations where extended interval (once daily) dosing is contraindicated (see previously: gross ascites, burns > 20%, treatment of chest infections in cystic fibrosis patients, pregnancy) conventional multiple daily dosing of aminoglycosides may still be used. In the treatment of endocarditis aminoglycosides are given for synergy and therefore at a reduced multiple daily dose. Multiple daily dosing is monitored differently to once daily gentamicin.

The pre-dose level must be taken immediately before a dose to obtain a trough concentration. This is to ensure that the patient is excreting the antibiotic and not accumulating toxic levels. The post-dose level must be taken one hour after administration of a dose to obtain a peak concentration. This is to ensure that therapeutic concentrations are being obtained. It is usual to send paired pre and post levels to the laboratory for testing.

If the patient has normal renal function and the level is taken as recommended above, the next dose may be given whilst awaiting the result. If there are any concerns regarding renal impairment please withhold the next dose whilst awaiting the result or discuss with the duty microbiologist.

The standard dose of gentamicin in <u>conventional</u> multiple daily dosing is 3-5 mg/kg in divided doses 8 hourly, assuming normal renal function.

The standard starting dose of gentamicin used in <u>endocarditis treatment</u> is 1mg/kg every 8 hours assuming normal renal function.

For the use of multiple daily dosing of aminoglycosides in patients with impaired renal function please discuss with the on-call microbiologist.

<u>Target serum concentrations for multiple daily dosing of aminoglycosides</u>:

Aminoglycoside		**Pre-dose level (mg/l)** Target concentration	**One hour post-dose level (mg/l)** Target concentration	**Timing of first level** (<u>normal</u> renal function)	**Recommended frequency of monitoring** (if <u>normal</u> renal function)
Gentamicin	Endocarditis	< 1	3 - 5	After 3-4 doses	2 -3 times week
	Conventional multiple daily dosing:	< 2	5 - 10	After 3 -4 doses	2 -3 times week
Tobramycin (CF patients)		< 2	8 - 12	After 3–4 doses	2 -3 times week
Amikacin		< 10	> 20	After 3– 4 doses	2 -3 times week
Streptomycin **(TB treatment)**		< 5	15 - 40	After 3 – 4 doses	**Liaise with microbiology and respiratory physicians**

.0 Macrolides/Lincosamines (BNF section 5.1.5)

AGENT (category)	MODE OF ADMIN.	COMMENTS / INDICATIONS
erythromycin (2) **erythromycin (3)**	po/Inj	• now only used in pregnancy, as a GI pro-motility agent, campylobacter and for occasional patients in Paediatrics, Dermatology and GUM
clarithromycin (1)	po/inj	• useful for penicillin allergic patients • indications include whooping cough, legionnaire's disease, campylobacter, mycoplasma and chlamydial infection.
azithromycin (2)	po	• once daily dosage • 3 days treatment only • for GUM and paediatric use only
clindamycin (2)	po/inj	• good anti-staphylococcal and anti-anaerobic activity • excellent skin and soft tissue penetration • risk of *Clostridium difficile* associated diarrhoea (safer in high dose)

5.0 Tetracyclines (BNF section 5.1.3)

AGENT (category)	MODE OF ADMIN.	COMMENTS / INDICATIONS
doxycycline (1)	po	• once daily dosage • recommended for chlamydial, rickettsial, mycoplasma, brucella and borrelial infections • also used for acne, exacerbations of COPD and pelvic inflammatory disease • should not be given to children aged <12 years or pregnant women
minocycline (2)	po	• for treatment of acne • for use by Dermatologists only

6.0 Glycopeptides (BNF section 5.1.7)

AGENT (category)	MODE OF ADMIN.	COMMENTS / INDICATIONS
vancomycin (1)	inj/po	• useful for serious infections with Gram positive organisms (including MRSA) or where organism is resistant, or there is patient allergy, to beta-lactams • nephro- and oto-toxic (monitor levels) • **not** effective by mouth for systemic infections • oral therapy reserved for *Clostridium difficile* associated diarrhoea only

teicoplanin (2)	inj	• for use in haematology and for surgical prophylaxis only • suitable for im administration • antibiotic assays not routinely requir

The glycopeptides should be used judiciously to prevent the emergence of resistant organisms, e.g. vancomycin resistant enterococci (VRE).

PRACTICAL STEPS FOR ADMINISTERING AND MONITORING VANCOMYCIN IN ADULTS

1) In patients with normal renal function the usual adult dose is 1g BD
2) Vancomycin is administered by a slow IV infusion (1g over 100 minutes) in 250 mls of either 0.9% saline or glucose 5% solution.
3) Vancomycin pre-dose levels must be monitored to minimise the effects of toxicity and to ensure that therapeutic levels are being achieved.
4) There is NO indication to take post dose levels for vancomycin.
5) In patients with normal renal function the initial pre-dose level should be taken before the 3rd or 4th dose. This level must be taken immediately before the dose in a brown topped tube. The form must state clearly the time and date at which the last dose was given and the time the sample was taken. The sample must be sent to microbiology. In patients with impaired renal function the level will need to be checked earlier, please liaise with microbiology
6) That dose may then be given.
7) No further doses should be given until the vancomycin level is known and has been interpreted.
8) **The pre-dose level must be maintained between 10-15 mg/l.** Levels below 10 mg/l are sub therapeutic and levels > 15 mg/l may result in toxicity.
9) If the pre-dose level is high the overall vancomycin dosage will need to be reduced (either dose reduction or increase dose interval, and possible dose omission) after discussion with microbiology.
10) If the pre-dose level is normal and the patient has stable renal function the pre-dose level should be checked twice weekly.

Creatinine clearance **CrCl (ml/min)**	**Initial Vancomycin Dose Regime** *(The dose and/or interval may need to be modified when the results of levels are obtained)*
> 50 ml/min	1g BD
20 -50 ml/min	1g OD Check level before the 2nd dose
10 – 20 ml/min	1g every 48 hours Check pre-dose level before the second dose is given. Give repeat dose when level < 15 mg/l
< 10 ml/min	1g stat Check levels before next dose. Give repeat dose when level < 15 mg/l.

7.0 Quinolones (BNF section 5.1.12)

AGENT (category)	MODE OF ADMIN.	COMMENTS / INDICATIONS
ciprofloxacin **(2)** **(2)**	po inj	• all quinolones strongly associated with *C. difficile* infection • oral bioavailability excellent, parenteral therapy **rarely** indicated • poor activity against pneumococcus
ofloxacin (2)	po	• oral treatment of pelvic inflammatory disease by GUM and the Gynaecologists and epididymitis and prostatitis by the Urologists
moxifloxacin (2)	po	• third line use for chronic chest infections by Respiratory Physicians only

Fluoroquinolone therapy is a common cause of *Clostridium difficile* associated diarrhoea; they should only be used when there is no suitable alternative antibiotic available, usually after discussion with the duty microbiologist.

8.0 Miscellaneous (BNF sections 5.1.7, 5.1.8, 5.1.11, 5.1.13)

AGENT (category)	MODE OF ADMIN.	COMMENTS / INDICATIONS
metronidazole (1)	po/inj/ pr/ top	• anti-anaerobic and anti-protozoal activity • antabuse like effect (avoid alcohol) • iv form very expensive (70 x cost of oral) • administration by suppository is as effective • do not use in high dosage during first trimester of pregnancy
trimethoprim (1)	po	• useful broad spectrum oral agent • do not use in first trimester of pregnancy
co-trimoxazole (2)	po/inj	• only indications - prophylaxis and treatment of *Pneumocystis jiroveci*, *Stenotrophomonas maltophilia* infections and prophylaxis for spontaneous bacterial peritonitis (unlicensed indication) • high incidence of blood dyscrasias
sodium fusidate (1)	po/top	• antistaphylococcal agent - good tissue penetration • should not be used alone (resistance develops rapidly)
sodium fusidate (2)	inj	• excellent oral absorption, i.v. administration rarely indicated and poorly tolerated • monitor liver function on therapy
nitrofurantoin (1)	p.o.	• active only in the urinary tract • licensed for long-term prophylactic use • do not use in patients with renal failure
chloramphenicol (3)	po/inj	• broad spectrum agent - bacteriostatic • potentially serious side effects - agranulocytosis, grey baby syndrome

		• systemic therapy should be reserved for life threatening infections
chloramphenicol (1)	top	• topical preparation available for eye infections
linezolid (2)	po/inj	• active against Gram positive organisms only • reserved for oral treatment of multi-resistant pathogens (e.g. MRSA, VRE) • regular monitoring of blood counts is essential • do not use in patients on MAOIs and caution with multiple other drugs, please refer to BNF prior to use • use only as directed by microbiologist
colistin (2)	inj/neb	• active against Gram negative organisms only • nephro- and neuro-toxicity
tigecycline (2)	inj	• active against multi-resistant Gram positives and Gram negatives, including *Acinetobacter* spp. and ESBL-producing organisms • is not active against organisms in the urinary tract and is not active against *Pseudomonas* spp. • use only as directed by microbiologist
Synercid® (2)	inj	• reserved for treatment of glycopeptide-resistant enterococci • use only as directed by microbiologist
dapsone (2)	po	• for treatment of leprosy and second-line treatment of *Pneumocystis jiroveci* imfection
Daptomycin (2)	iv	• once daily dosage • for complicated skin and sift tissue infections caused by gram positive baceria • use only as directed by microbiologist

9.0 Antituberculosis Agents (BNF Section 5.1.9)

AGENT (category)	MODE OF ADMIN.	COMMENTS/INDICATIONS
rifampicin (1)	po/inj	• always use in combination with other drugs – resistance arises very easily • hepatotoxic

isoniazid (2)	po	• hepatotoxic • always give with pyridoxine to reduce the likelihood of peripheral neuropathy
ethambutol (2)	po	• test visual acuity before starting therapy
pyrazinamide (2)	po	• hepatotoxic
streptomycin (2)	im	• see Section 3 - Aminoglycosides

Other antituberculous drugs may be used at the discretion of the Chest Physicians. Antituberculous therapy should not be commenced without the involvement of the Chest Physicians (or Paediatrician with an interest in TB).

10.0 Antifungal Agents (BNF section 5.2)

AGENT (category)	MODE OF ADMIN.	COMMENTS/INDICATIONS
nystatin (1)	top	• used for mucosal, cutaneous and intestinal candidiasis
griseofulvin (1)	po	• used for dermatophyte infections if topical treatment inappropriate or has failed.
terbinafine (2)	po	• used for nail dermatophyte infections • not licensed for use in children
clotrimazole (1)	top	• useful local treatment for vaginal and skin fungal infections
ketoconazole (1)	top	• local treatment for skin and scalp infections
ketoconazole (2)	po	• associated with fatal **hepatotoxicity** (monitor liver function carefully on treatment) • should **not** be used for superficial fungal infections
fluconazole (1) **fluconazole (2)**	po inj	• systemic therapy for Candida and other fungal infections • oral absorption excellent, i.v. therapy rarely indicated • non- *Candida albicans* organisms may be resistant • reduce dose if renal impairment
itraconazole (2) **itraconazole (3)**	po inj	• similar to fluconazole, but should be reserved for infections with non- albicans *Candida* spp. • additional anti - *Aspergillus* activity • used for prophylaxis in Haematology
voriconazole (3)	po/inj	• reserved for treatment of fungal infections in heavily immunosupressed patients • monitor renal and liver function regularly
Posaconazole (3)	po	• broad spectrum azole anti-fungal • restricted use • seconday prophylaxis in haematology patients after a proven fungal infection • treatment of a probable/proven mucormycosis
5-flucytosine (3)	inj	• second line therapy for severe Candida and

		other yeast infections only in combination with other antifungal agents • toxic - serum drug level monitoring required
caspofungin (2)	inj	• first line therapy for serious fungal infections, if *Candida* spp.or *Aspergillus* spp. likely pathogen • no activity against other fungi.
amphotericin (3)	inj	• only use is intra-vitreal injection/instillation by the Ophthalmic Surgeons
Ambisome (liposomal amphotericin) (2)	inj	• very expensive • test dose required

Intravenous antifungals, with the exception of fluconazole, must only be used after discussion with the microbiologists.

11.0 Antiviral Agents (BNF section 5.3)

AGENT (category)	MODE OF ADMIN.	COMMENTS/INDICATIONS
aciclovir (1)	po/iv/ top	• used to treat Herpes virus (zoster, simplex) infections • should be given early in infection for maximum effect • check correct dose regime in BNF prior to administration
famciclovir (2)	po	• similar to aciclovir • not licensed for prophylaxis • od, bd and tds treatment regimen – check dose regime when prescribing
ganciclovir (2)	iv	• for treatment of life threatening or sight threatening CMV disease only • toxicity (haematological, hepatic, GI, rashes etc) • personnel must be adequately protected during handling and administration
valganciclovir (2)	po	• for follow-on treatment and secondary prophylaxis of CMV disease
Foscarnet (2)	iv	2nd line treatment for CMV disease only

Anti-retroviral agents are used as combination therapy for HIV disease and for post-exposure prophylaxis following needlestick injury from known HIV positives.
The Trust policy for management of Exposure to Blood and Body Fluids can be found at:
http://intranet/pdf/Policies/HS_03_attachment1.pdf

Advice on the use of anti-retrovirals is available from the GUM physicians or Physician with a special interest in HIV.

12.0 Antiprotozoal Agents (BNF Section 5.4)

12.1 Antimalarials (BNF Section 5.4.1)

AGENT (category)	MODE OF ADMIN.	COMMENTS/INDICATIONS
quinine sulphate (1) **quinine dihydro-chloride (1)**	po iv	• very toxic in overdosage – always check dosage carefully before administration • always give parenteral therapy as an infusion • monitor ECG during parenteral therapy
atovaquone / proguanil - Malarone® (1)	po	• for treatment of uncomplicated malaria • do not use for treatment if patient used it for prophylaxis
doxycycline (2)	po	• given in combination with quinine • do not use in pregnancy / children aged <12 years
clindamycin (2)	po/iv	• given in combination with quinine • alternative to doxycycline in pregnancy / children aged <12 years
pyrimethamine / sulfadoxine - Fansidar® (2)	po	• given in combination with quinine • alternative to doxycycline and clindamycin for children

For advice on the prevention and treatment of malaria, the duty microbiologist can be contacted. Advice on specific problems can also be obtained from the national malaria centres – phone number of regional centre 0121 242 0357.

12.2 Other Antiprotozoal Agents (BNF Sections 5.4.2 – 5.4.8)

AGENT (category)	MODE OF ADMIN.	COMMENTS/INDICATIONS
metronidazole (1)	po/inj/ pr/ top	• anti-anaerobic and anti-protozoal activity • antabuse like effect • i.v. form very expensive (70 x cost of oral) • administration by suppository is effective • do not use in first trimester of pregnancy
co-trimoxazole (2)	po/inj	• prophylaxis and treatment of *Pneumocystis jiroveci* pneumonia • treatment of *Stenotrophomonas maltophilia* infections
pentamidine (2)	inj/neb	• toxic – personnel must be adequately protected during handling and administration

In addition to the above, other drugs may be used on the basis of expert advice for the treatment of protozoal disease.

13.0 Antihelmintic Agents (BNF Sections 5.5)

AGENT (category)	MODE OF ADMIN.	COMMENTS/INDICATIONS
mebendazole (1)	po	• for the treatment of threadworm, roundworm, whipworm and hookworm infections • not to be used in pregnancy
piperazine (1)	po	• for the treatment of threadworm and roundworm, infections • not to be used in pregnancy

In addition to the above, other drugs may be used on the basis of expert advice for the treatment of helmintic disease. These drugs are often available on a named-patient basis only.

Antibiotic Prophylaxis

14.0 General Principles

Guidelines for antibiotic prophylaxis will vary for different procedures and between different units. However there are some general principles common to all prophylactic therapy:

- prophylaxis should aim to reduce the risk of infection with specific micro-organisms over an identified high risk period.
- the prophylactic regimen should be as simple, non-toxic, easy to administer and as cheap as practicable.
- administration of prophylactic antibiotics should be timed so that adequate tissue/serum levels are achieved to cover the period of greatest risk of infection, e.g. the perioperative period. Ideally it is administered immediately prior to the first incision; if metronidazole is given pr, however, it must be given 2 hours prior to the first incision.
- additional doses of surgical prophylaxis are not generally indicated unless there is blood loss >1500 mls or haemodilution up to 15 ml/kg or for prolonged procedures e.g. > 3 hours. The frequency of repeat dosing will depend on the half life of the antibiotic.

Antimicrobial agent	**Prophylactic dose**	**For prolonged surgery, interval after which to give repeat dose of antibiotic**
Cefuroxime	750 mg – 1.5g IV	After 4 hours
Co-amoxyclav	1.2 g IV	After 4 hours
Flucloxacillin	1 g IV	After 3 hours
Gentamicin	5 mg/kg IV	Redosing not recommended
Meropenem	1g IV	After 4 hours
Metronidazole	500 mg IV	After 8 hours
Teicoplanin	400 - 600 mg IV	Redosing not recommended

The doses and intervals above are intended for adult patients with normal renal and liver function.

- antibiotic cover should be maintained for as short a time as possible, and should rarely exceed one or two doses.
- surgical antibiotic prophylaxis is indicated when:
  a) the operation carries a significant risk of post-operative infection.
  b) pre-existing medical conditions increase the risk of infection, e.g. diabetes mellitus, malnourishment, immune deficiency.
  c) although a 'clean' surgical procedure, the consequences of infection could be disastrous, e.g. surgery that involves the insertion of prosthetic implants.
- if infection subsequently occurs, an alternative antimicrobial agent to that used for prophylaxis should be given (as infection may be caused by resistant organisms).
- if a patient has an infection pre-operatively and the surgery is non-urgent, the operation should be postponed until the infection has been successfully treated if possible. The decision whether or not to delay surgery must be taken by the consultant in charge of the case.
- MRSA colonised or infected patients must be commenced on decolonisation therapy (chlorhexidine body washes once daily and mupirocin nasal ointment to both nostrils tds). If prophylaxis is required for their procedure, cover against MRSA must be used. If the surgery is non-urgent attempts must be made to clear the patient of MRSA prior to their operation. Individual cases can be discussed with the duty microbiologist.

The following regimes are guidelines only. Consultants may choose alternative regimens as the clinical situation requires. Patients who are colonised or infected with multi-resistant organisms or who have complex conditions should be discussed with the duty microbiologist.

All regimes are single dose unless otherwise stated.

With the exception of pr metronidazole, induction is usually the optimal time to administer antimicrobial prophylaxis.

14.1 Antibiotic Prophylaxis for General and Vascular Surgery

Upper Gastrointestinal Surgery: prophylaxis recommended for: oesophageal surgery, gastro-duodenal surgery, endoscopic gastrostomy, small bowel surgery, open biliary surgery
Co-amoxiclav 1.2 g iv
Penicillin allergic patients: single dose gentamicin 5 mg/kg iv infusion plus metronidazole 500 mg iv

Splenectomy
Benzylpenicillin 1.2 g iv at induction then benzylpenicillin 600 mg iv 6 hourly until able to take penicillin V 250-500 mg bd orally
Penicillin allergic patients: clarithromycin 500 mg iv infusion then 500 mg iv 12 hourly until able to take oral clarithromycin 250 mg bd po or erythromycin 500 mg bd po

Lower Gastrointestinal Surgery: prophylaxis recommended for: colorectal surgery and appendicectomy
Colorectal Surgery:
Co-amoxiclav 1.2 g iv
Penicillin allergic patients: gentamicin 5 mg/kg iv infusion plus metronidazole 500 mg iv

Appendicitis:
Co-amoxiclav 1.2 g iv
Penicillin allergic patients: gentamicin 5 mg/kg iv infusion plus metronidazole 500 mg iv or 1 g pr

If there is evidence of perforation or peritonitis, antibiotics should be continued as per a therapeutic regime (refer to treatment guidelines)

General Laparoscopic Surgery and Laparotomy
Antibiotic prophylaxis is not indicated unless a viscus is perforated, if there is spillage of the contents of a viscus during the procedure or if pre-existing infection is present or suspected
Co-amoxiclav 1.2 g iv
Penicillin allergic patients: gentamicin 5 mg/kg iv infusion and metronidazole 500 mg iv

Hernia Surgery
Antibiotic prophylaxis is not required for routine hernia repair, unless a mesh is to be inserted. If mesh used:
Co-amoxiclav 1.2 g iv
Penicillin allergic patients: gentamicin 5 mg/kg infusion iv plus either metronidazole 500 mg iv or clindamycin 600mg iv infusion

Vascular Surgery
Recommended for: lower limb amputations, abdominal and lower limb surgery.

Co-amoxiclav 1.2 g iv
Penicillin allergic patients: gentamicin 5 mg/kg iv infusion plus metronidazole 500 mg iv at induction
MRSA colonised patients / redo Vascular Surgery: teicoplanin 400 mg iv

Prevention of gas gangrene (high lower limb amputation or following major trauma):
Benzyl penicillin 600 mg iv qds for 5 days
Penicillin allergic patients: metronidazole 500 mg iv / 400 mg po tds for 5 days

14.2 Antibiotic Prophylaxis in Urology

Patients who are colonised/infected with multiple-resistant organisms or who have complex urological conditions should be discussed with the duty microbiologist.

Diagnostic cystoscopy
Antibiotics are only required if there is an indication e.g. urine infection.

Endoscopic Surgery
Gentamicin 5 mg/kg iv infusion on induction
Patients with a previous history of infection / colonisation with an ESBL producing bacteria should receive meropenem 1 g iv on induction
Patients with a previous history of MRSA in their urine should receive teicoplanin 400 mg iv plus either gentamicin 5 mg/kg iv infusion or meropenem 1 g iv

Percutaneous Nephrostomy Insertion and Antegrade Stenting
Gentamicin 160 mg iv plus co-amoxiclav 1.2 g iv
Penicillin allergic patients and patients with a previous history of infection/colonisation with an ESBL producing bacteria: meropenem 1 g iv
Patients with a previous history of MRSA in their urine: teicoplanin 400 mg iv plus meropenem 1 g iv

Major Open Surgery - Radical Cystectomy / Radical Prostatectomy
Gentamicin 5 mg/kg iv infusion plus metronidazole 500 mg iv on induction
Patients with a previous history of infection/colonisation with an ESBL producing bacteria should receive meropenem 1 g iv on induction
Patients with a previous history of MRSA should receive teicoplanin 400 mg iv plus either gentamicin 5 mg/kg iv infusion or meropenem 1 g iv

Post-operative treatment to be given only at request of operating surgeon for treatment if viscus perforated, pre or peri-operative intraperitoneal faecal or urinary contamination or other indication. Indication and plan for duration of therapy should be clearly stated in the operation note. The antimicrobial of choice for this indication is meropenem unless there are any specific contraindications.

Urological Laparoscopic Surgery
Gentamicin 5 mg/kg iv infusion and metronidazole 500 mg iv on induction
Patients with a previous history of infection/colonisation with an ESBL producing bacteria should receive meropenem 1 g iv on induction
Patients with a previous history of MRSA should receive teicoplanin 400 mg iv plus either gentamicin 5 mg/kg iv or meropenem 1 g iv

Transrectal Biopsy of the Prostate
Gentamicin 5 mg/kg iv infusion plus metronidazole 400 mg po no more than 1 hour before the procedure followed by ciprofloxacin 500 mg po bd for 2 days post procedure
Patients with a previous history of infection/colonisation with an ESBL producing bacteria should receive meropenem 1 g iv 1 hour before the procedure

Trial Without Catheter
Patients undergoing trial without catheter following recent endoscopic procedures:
In-patients: gentamicin 5 mg/kg iv infusion 1 hour before catheter removal
Hospital at Home: ciprofloxacin 500 mg po 1 hour before catheter removal

Patients undergoing trial without catheter who have not had a recent endoscopic procedure do not require antibiotics

External Shock Wave Lithotripsy
Ciprofloxacin 500 mg po on arrival in department followed by trimethoprim 200 mg bd po for 3 doses.

14.3 Antibiotic Prophylaxis in Cardiac and Thoracic Surgery

Open Thoracic Procedures
Gentamicin 5 mg/kg iv infusion (single dose) plus flucloxacillin 1 g iv
Alternative: co-amoxiclav 1.2 g iv
Penicillin allergic patients, or if known to be colonised/infected with MRSA: teicoplanin 400 mg iv

Single dose only except for prolonged procedures or excessive blood loss

Cardiac Surgery
Gentamicin 5 mg/kg iv infusion (single dose) plus flucloxacillin 1 g 6 hourly for 24 hours
Penicillin allergic patient, return to theatre within 1 week of last operation or known to be colonised or infected with MRSA: teicoplanin 400 mg iv

14.4 Antibiotic Prophylaxis in Trauma and Orthopaedics

Elective and Emergency Surgery Without Implants
No prophylaxis recommended unless major trauma

Major Trauma (gas gangrene prophylaxis)
Benzyl penicillin 600 mg iv qds for 5 days
Penicillin allergic patients: metronidazole 500 mg iv / 400 mg po tds for 5 days

Elective Surgery Involving Implants
Cefuroxime 1.5 g iv on induction plus three further doses of 750 mg iv at 8 hourly intervals
Penicillin allergic: teicoplanin 400 mg iv

MRSA positive patients: teicoplanin 400 mg iv

Emergency Surgery Involving Implants

Flucloxacillin 1 g iv plus gentamicin 5 mg/kg iv infusion on induction followed by four further doses of flucloxacillin 1 g iv/po at six-hourly intervals
Penicillin allergic: teicoplanin 400 mg iv

MRSA positive patients: teicoplanin 400 mg iv

14.5 Antibiotic Prophylaxis in Obstetrics and Gynaecology

Caesarean Section
Co-amoxiclav 1.2 g iv
Penicillin allergic: cefuroxime 1.5 g iv or clindamycin 900 mg iv infusion (if penicillin allergy severe / life threatening)

Retained Placenta
Co-amoxiclav 1.2 g iv continued for 5 days (change to 625 mg tds po at earliest opportunity)
Penicillin allergic: cefuroxime 750 mg iv plus metronidazole 500 mg iv
If penicillin allergy severe / life threatening: gentamicin 5 mg/kg iv infusion (dose interval determined by level taken 6-14 hours post first dose – see Section 3.0 page 8-10) plus clindamycin 600 mg iv infusion / po for 5 days

Third or Fourth Degree Tear / Uterine Inversion
Co-amoxiclav 1.2 g iv (625 mg tds po for follow-on therapy)
Penicillin allergic: cefuroxime 750 mg tds iv plus metronidazole 500 mg tds iv (clindamycin 600 mg qds po plus trimethoprim 200 mg bd po for follow-on therapy) for 5 days total
If penicillin allergy severe / life threatening: gentamicin 5 mg/kg iv infusion (dose interval determined by level taken 6-14 hours post first dose – see Section 3.0) **plus** clindamycin 600 mg iv infusion / po. Oral follow-on therapy as above for penicillin allergy.
(Oral antibiotics may need to be continued for up to 7 days)

Group B Streptococcal Carriage / Infection

Specific prophylaxis is only necessary if the mother has had a previous infant with group B streptococcus infection or the mother has had a group B streptococcus UTI during the current pregnancy or there is incidental vaginal carriage found after 35 weeks gestation. Please refer to full guidelines at http://intranet/pdf/GROUP%20B%20SRTEPTOCOCCUS.pdf Women with prolonged rupture of membranes or who are in pre-term labour must be offered antibiotics as described in the 'Pyrexia in Labour' section below, whether or not they are known to be carriers of group B streptococcus.

Benzyl penicillin 3 g iv at onset of labour followed by 1.5 g iv every 4 hours until delivery

Penicillin allergic: clindamycin 900 mg iv infusion at onset of labour followed by 900 mg iv every 8 hours until delivery

Pyrexia in Labour

Cefuroxime 750 mg iv plus metronidazole 500 mg iv

Severe penicillin allergy: discuss with duty microbiologist

Hysterectomy

Co-amoxiclav 1.2 g iv

Penicillin allergic: gentamicin 5 mg/kg infusion plus metronidazole 500 mg iv

Termination of Pregnancy

Metronidazole 400 mg po

If genital chlamydial infection cannot be ruled out, also give: doxycycline 100 mg bd for 7 days (also recommended in early pregnancy failure if instrumentation of the uterus is undertaken)

14.6 Head and Neck Surgery

Co-amoxiclav 1.2 g iv

Penicillin allergic patients: clindamycin 600mg iv infusion

If patient known to be colonised or infected with MRSA: add teicoplanin 400 mg iv to one of the above antibiotics.

15.0 Endocarditis Prophylaxis

Adults and children with structural cardiac defects at risk of developing infective endocarditis

Healthcare professionals should regard people with the following cardiac conditions as being at risk of developing infective endocarditis:

- acquired valvular heart disease with stenosis or regurgitation
- valve replacement
- structural congenital heart disease, including surgically corrected or palliated structural conditions, but excluding isolated atrial septal defect, fully repaired ventricular septal defect or fully repaired patent ductus arteriosus, and closure devices that are judged to be endothelialised
- previous infective endocarditis
- hypertrophic cardiomyopathy

Antibiotic prophylaxis against infective endocarditis is not recommended:

- for people undergoing dental procedures
- for people undergoing non-dental procedures at the following sites:
  - upper and lower gastrointestinal tract
  - genitourinary tract; this includes urological, gynaecological and obstetric procedures, and childbirth
  - upper and lower respiratory tract; this includes ear, nose and throat procedures and bronchoscopy

Chlorhexidine mouthwash should not be offered as prophylaxis against infective endocarditis to people at risk of infective endocarditis undergoing dental procedures.

Patient advice

Healthcare professionals should offer people at risk of infective endocarditis clear and consistent information about prevention, including:

- the benefits and risks of antibiotic prophylaxis, and an explanation of why antibiotic prophylaxis is no longer routinely recommended
- the importance of maintaining good oral health
- symptoms that may indicate infective endocarditis and when to seek expert advice
- the risks of undergoing invasive procedures, including non-medical procedures such as body piercing or tattooing

Infection

Any episodes of infection in people at risk of infective endocarditis should be investigated and treated promptly to reduce the risk of endocarditis developing.

If a person at risk of infective endocarditis is receiving antimicrobial therapy because they are undergoing a gastrointestinal or genitourinary procedure at a site where there is a suspected infection, the person should receive an antibiotic that covers organisms that cause infective endocarditis. Such a patient should be discussed with the duty Microbiologist when a decision is made that the procedure will take place, to allow adequate time for prophylaxis, should it be deemed necessary, to be given.

To see the latest NICE guidance go to: http://www.nice.org.uk/CG64

Guidelines on the treatment of specific infections

These guidelines are for **empirical therapy**. It may be necessary to amend treatment when the results of microbiological investigations become available. Dose adjustments may be necessary for patients with renal impairment – see BNF Appendix 3 or discuss with a Pharmacist.

16.0 Urinary Tract Infections (U.T.I.)

16.1 Uncomplicated U.T.I.

common causative organisms: *E. Coli*, enterococci, streptococci, other coliform organisms, staphylococci

Recommended agents	Route	Dose / Duration	Comments
first line			
trimethoprim	po	200 mg bd 3 days	should not be used in 1st trimester of pregnancy
nitrofurantoin	po	50 mg qds 7 days	not effective in alkaline urine should not be used in 3rd trimester of pregnancy
second line			
co-amoxiclav	po	625 mg tds 3 days	no advantage over amoxicillin for sensitive organisms
meropenem / ertapenem	inj	500 mg tds / 1 g od for 7 days	for treatment of ESBL producing organisms resistant to oral agents, need to check sensitivities

Amoxicillin is no longer recommended for empirical therapy. It is suitable for use if the pathogen is known to be sensitive.

16.2 U.T.I in pregnancy

Causative organisms: as above. Up to 10% of pregnancies are complicated by symptomatic urinary tract infection. If untreated, UTI has a greater propensity to develop into pyelonephritis in pregnancy. In addition 4 – 10% of women will have asymptomatic bacteriuria in pregnancy, this is defined as persistent bacterial colonisation of the urinary tract in the absence of symptoms. If untreated this may be associated with pyelonephritis. For further details see “Urinary tract infection in pregnancy” in the ante-natal guidelines.

Recommended agents	Route	Dose / Duration	Comments
trimethoprim	po	200 mg bd 7 days	should not be used in 1st trimester of pregnancy
nitrofurantoin	po	50 mg qds 7 days	should not be used in 3rd trimester of pregnancy . Not effective in alkaline urine
cefalexin	po	500 mg bd 7 days	
co-amoxiclav	po	625 mg tds 7 days	no advantage over amoxicillin for sensitive organisms. Co-amoxiclav is associated with an increased risk of necrotising enterocolitis in the newborn if used in late pregnancy.

16.3 Hospital Acquired U.T.I.

Causative organisms: as above, but infection may be caused by more resistant organisms e.g. *Pseudomonas aeruginosa*.

Choice of treatment should be guided by urine culture and sensitivity tests

16.4 Pyelonephritis / Complicated U.T.I.

Causative organisms: as above. Treatment of hospital acquired infection should include agents with activity against more resistant organisms.

Please send urine and blood culture prior to commencing antibiotics

Recommended agent	Route	Dose / Duration	Comments
first line			
trimethoprim	po	200 mg bd 14 days	For outpatient use should not be used in 1st trimester of pregnancy
co-amoxiclav	po/inj	625 mg / 1.2 g tds 14 days	parenteral administration rarely indicated
second line			
amoxicillin plus gentamicin	inj	500 mg tds / 5 mg/kg dose interval according to levels 14 days	gentamicin levels require monitoring
piperacillin/tazobactam	inj	4.5g tds	
meropenem / ertapenem	inj	500 mg tds / 1 g od for 7 days	for treatment of ESBL producing organisms resistant to oral agents, need to check sensitivities

note:

initial iv treatment may be changed to oral therapy when a satisfactory clinical response has occurred.

Therapy should be modified if necessary when the results of sensitivity tests are available (particularly a switch from gentamicin to a less toxic agent).

16.5 Catheterised Patients

Bacteriuria in catheterised patients is inevitable. C.S.U. samples should only be sent and antibiotics given if systemic symptoms are present.

Antibiotics usually fail to eradicate bacteriuria and unnecessary antibiotic treatment encourages emergence of resistant organisms and the development of *C. difficile* infection

17.0 Respiratory Tract Infections

17.1 Pharyngitis / Tonsillitis

Common causative organisms: viral (most common, do not require antibiotic therapy)
streptococci, particularly group A streptococcus
Vincent's organisms
anaerobes

Recommended agent	Route	Dose / Duration	Comments
Phenoxymethylpenicillin (penicillin V)	po	500 mg qds 10 days	iv/im penicillin if severe infection
amoxicillin	po	500 mg tds 7 days	avoid if glandular fever likely
clarithromycin	po	500 mg bd 7 days	if penicillin allergic

17.2 Acute Epiglottitis

Common causative organism: *Haemophilus influenzae*

Recommended agents	Route	Dose / Duration	Comments
cefotaxime	inj	2 g tds 10 days	activity against β-lactamase producing organisms
chloramphenicol	po/inj	50 – 100 mg/kg/day in 4 divided doses	if history of severe penicillin allergy levels require monitoring

17.3 Otitis Media

Common causative organisms*:* *Streptococcus pneumoniae* *H.influenzae*
*G*roup A *streptococcus* *Staphylococcus aureus*
Moraxella catarrhalis

Recommended agents	Route	Dose / Duration	Comments
amoxicillin	po	500 mg tds 5 days	
co-amoxiclav	po	625 mg tds 5 days	second line – if not responded to amoxicillin
clarithromycin	po	500 mg bd 5 days	if allergic to penicillins

17.4 Otitis Externa

Common causative organisms: *Pseudomonas aeruginosa*
Staphylococcus aureus

Recommended agents	Route	Dose / Duration	Comments
Sofradex©	topical	2-3 drops 3-4 times per day	if systemic treatment not required
piperacillin/tazobactam	inj	4.5 g tds 5 days	Choice will depend upon culture results. Malignant otitis externa requires up to 6 weeks therapy and may require surgical debridement. Gentamicin toxicity is very common if used for >14 days
ciprofloxacin	po	500 mg bd 5 days	
gentamicin	inj	5 mg/kg, dose interval according to levels	

17.5 Acute sinusitis

common causative organisms: *Streptococcus pneumoniae* *H. influenzae* anaerobes

Recommended agents	Route	Dose / Duration	Comments
co-amoxiclav	po/inj	625 mg / 1.2 g tds 5 days	
clarithromycin	po/inj	500 mg bd 5 days	if allergic to penicillins
trimethoprim	po	200 mg bd 5 days	
doxycycline	po	200mg on day one then 100 mg od for 4 further days	do not use in pregnancy, children. Use with caution in renal failure

17.6 Acute Exacerbation of Chronic Bronchitis

Common causative organisms: *H. influenzae* *S.pneumoniae* *S. pneumoniae* *M.catarrhalis* mixed organisms

Recommended agents	Route	Dose / Duration	Comments
first line			
amoxicillin	p.o./inj	500 mg tds 5 days	
clarithromycin	po	500 mg bd 5 days	if allergic to penicillin
doxycycline	po	200mg on day one then 100 mg od for 4 further days	if allergic to penicillin
second line			
co-amoxiclav	po/inj	625 mg / 1.2 g tds 5 days	

17.7 Acute Community Acquired Pneumonia

Common causative organisms:	**Atypical pneumonia:**
S.pneumoniae	*Mycoplasma pneumoniae*
H.influenzae	*Coxiella burnetti* (Q fever)
S.aureus (post influenza A)	*Chlamydia spp. (*Psittacosis)
	Legionella spp. (Legionnaires disease)

Diagnosis of Pneumonia is based on:

- Clinical features
  - Fever
  - Cough
  - Pleuritic pain
  - New focal chest signs
- Consolidation on CXR

Severity assessment of pneumonia using the **CURB-65 Score**:

- **C**onfusion (Mental Test Score of 8 or less, or new disorientation in person, place or time)
- **U**rea > 7 mmol/l
- **R**espiratory rate ≥ 30/min
- **B**lood pressure (SBP < 90mmHg or DBP ≤ 60mmHg)
- **A**ge **≥** 65 years

Score 1 for each positive answer. A score of >2 represents a severe pneumonia.

Recommended agents	Route	Dose / Duration	Comments

Mild to Moderate (CURB-65 score 0-2) **first line**:			
amoxicillin	po/inj	500 mg tds 5 days	
clarithromycin	po/inj	500 mg bd 5 days	if penicillin allergy or atypical infection suspected
benzylpenicillin	inj	1.2 g qds 5 days	if pneumococcus isolated
second line:			
co-amoxiclav	po/inj	625 mg / 1.2 g tds 5 days	
clarithromycin	po/inj	500 mg bd 5days	if not used first line

Recommended agents	Route	Dose / Duration	Comments
Severe (CURB-65 score >2) **first line:**			
co-amoxiclav plus clarithromycin)	inj inj	1.2 g tds 5 days 500 mg bd 5 days	provides broad spectrum cover against the common pathogens, including atypical pathogens
second line (penicillin allergy):			
ertapenem plus clarithromycin	inj inj	1 g od 5 days 500 mg bd 5 days	consult microbiologists if patient has severe hypersensitivity to β-lactam antibiotics

notes:

If pneumonia is severe and atypical infection is suspected, clarithromycin should be used in addition to other first or second line therapy. Specific therapy for legionnaire's disease includes clarithromycin plus rifampicin (if severe infection). **Tetracycline** is the treatment of choice for psittacosis and Q fever.

If sputum, blood cultures, or antibody studies yield evidence of infection with a specific organism, a switch to narrow spectrum therapy should be considered, e.g. benzylpenicillin for pneumococcal infection. Pulmonary infection due to pneumococci with reduced sensitivity to penicillin should still respond to high dose penicillin therapy.

A switch to oral therapy should be made when a satisfactory clinical response has occurred (usually after 48 hr parenteral therapy). Choice of agent should take into consideration results of microbiological investigations and the likely organism responsible for infection, e.g. lobar pneumonia is commonly caused by *Streptococcus pneumoniae*, for which amoxicillin po would be appropriate follow on therapy. If beta-lactamase producing organisms have been isolated or are suspected, co-amoxiclav should be used. (Beta-lactamase negative strains of *H. influenzae* which are resistant to amoxicillin should also be considered resistant to co-amoxiclav.)

17.8 Hospital Acquired Pneumonia

Recommended agents	Route	Dose / Duration	Comments
first line:			
co-amoxiclav	po/inj	625 mg / 1.2 g tds 5 days	
piperacilllin/tazobactam	inj	4.5 g tds 5 days	if severe or pre-treatment with co-amoxiclav in same admission
second line:			
meropenem	inj	1 g tds 5 days	consult microbiologists if patient has severe hypersensitivity to β-lactam antibiotics

notes:

Nosocomial pneumonia is more likely than community acquired disease to be caused by Gram negative organisms, particularly if there has been prior treatment with broad spectrum antibiotics.

MRSA may be the cause of both community and hospital acquired pneumonia and is a common cause of ventilator associated pneumonia. Section 18.2 and 26.0 gives details on the treatment of MRSA infections, but advice from the Microbiologists should be sought when treating suspected or proven MRSA pneumonia.

17.9 Aspiration Pneumonia

Recommended agents	Route	Dose / Duration	Comments
Moderate:			
co-amoxiclav	po/inj	625 mg / 1.2 g tds 5 days	
doxycycline plus	po	100 mg bd 5 days	penicillin allergic patients
metronidazole	po/inj	400 mg / 500 mg tds 5 days	
Severe:			
Tazocin	inj	4.5 g tds 5 days	
meropenem	inj	1 g tds 5 days	if penicillin allergic - consult microbiologists if patient has severe hypersensitivity to β-lactam antibiotics

17.10 Pulmonary Exacerbation of Cystic Fibrosis and Bronchiecstasis

The management of pulmonary infections in cystic fibrosis patients or patients with bronchiecstasis is a specialised area. The choice and duration of antibiotic will depend on many factors including:

- Pathogen isolated and relevant sensitivities
- Patient drug allergies
- New acquisition versus chronic infection
- Treatment of acute infection versus eradication therapy

Antibiotics may be intravenous, oral or nebulised. Each case must be discussed with the appropriate respiratory physician.

18.0 Skin and Soft Tissue Infections

18.1 Surgical Wound Infections

Common causative organisms: (depends on site of infection)
Staphylococcus aureus
streptococci
coliforms
anaerobes

Recommended agents	Route	Dose / Duration	Comments
flucloxacillin	po/inj	500 mg–1 g qds 5 days	
co-amoxiclav	po/inj	625 mg / 1.2 g tds 5 days	Useful for 'dirty' or contaminated wounds
gentamicin	inj	5 mg/kg dose interval according to levels 5 days	particularly if resistant Gram negative organisms likely

note: Antibiotics are **not** always necessary - a distinction should be made between colonisation (which does NOT require antibiotic therapy) and infection. Duration of therapy depends on site and severity of infection.

18.2 Cellulitis / Erysipelas / Cutaneous Abscesses

Common causative organisms: (depends on site of infection)
Streptococcus. pyogenes
Staphylococcus aureus (including MRSA)
mixed infections

Recommended agents	Route	Dose / Duration	Comments
benzyl penicillin or amoxicillin plus	inj po	1.2 g qds 500 mg tds	route depends on severity of infection. Give for 5- 10 days
flucloxacillin	po/inj	1g qds 5–10 days	
clarithromycin	po/inj	500 mg bd 5–10 days	if penicillin allergic
co-amoxiclav	po/inj	625 mg / 1.2 g tds 5-10 days	useful 'out-patient' therapy
clindamycin	po/iv	600 mg-1.2 g qds 5-10 days	synergy with penicillins in cellulitis warn patient of potential for antibiotic associated diarrhoea and *C. difficile* infection
trimethoprim plus rifampicin	po po	200 mg bd 5-10 days 300-600 mg bd 5-10 days	for treatment of MRSA infection. Use sensitivity data – alternatives include doxycycline and fusidic acid in combination. Monitor liver function in patients on rifampicin or fusidic acid (do not use these two drugs together unless on Microbiologist advice)

vancomycin plus rifampicin **or** sodium fusidate	iv po	1 g bd 5-14 days 300-600 mg bd / 500 mg tds	severe MRSA infection - monitor levels (see Section 6.0) depending on sensitivity data
linezolid	iv/po	600 mg bd 10-14 days	only to be used on Microbiologist advice

note: surgical drainage is an important aspect of the management of abscesses

18.3 Leg Ulcers

Bacterial colonisation of leg ulcers is inevitable, particularly with staphylococci, streptococci, coliform organisms and anaerobes. Antibiotic treatment is not indicated unless there is good evidence of active infection e.g. cellulitis. Topical care is another important aspect of leg ulcer management. Advice should be sought from the Tissue Viability Nurse.

18.4 Acne

Systemic therapy not always necessary in mild to moderate acne. However if topical preparations prove inadequate oral antibiotics may be needed.

Recommended agents	**Route**	**Dose / Duration**	**Comments**
Oxytetracycline	po	500 mg bd	
doxycycline	po	100 mg od	Minocycline can cause irreversible pigmentation and SLE-type symptoms. Only to be used under dermatology supervision
minocycline	po	100 mg od or 50 mg bd	
trimethoprim	po	300 mg bd	unlicensed indication, may be used for acne resistant to other antibacterials. Use under dermatology supervision only

note:

Duration of therapy is usually months, but should be determined by a specialist who must monitor the patient for response to therapy and adverse effects during therapy.

19.0 Bone and Joint Infections

19.1 Osteomyelitis

Common causative organisms:

acute:	*Staphylococcus aureus* streptococci *Salmonella* spp.
chronic:	*Staphylococcus aureus* streptococci coliform organisms tuberculosis

Recommended agents	Route	Dose / (for Duration see notes below)	Comments
flucloxacillin **plus**	inj	1-2 g qds	>80% of infections due to *St. aureus*
sodium fusidate	po	500 mg tds	monitor liver function
clindamycin	inj	600 mg-1.2 g qds	if penicillin allergic
cefotaxime	inj	100-150 mg/kg day in 2-4 doses	children <5 yr (?*Haemophilus influenzae*)
vancomycin **plus** sodium fusidate	inj po	1 g bd 500 mg tds	if staphylococcus resistant to flucloxacillin (e.g. MRSA) monitor pre-dose vancomycin levels(see section 6.0) monitor liver function
ciprofloxacin **or**	po	500-750 mg bd	for *Salmonella* spp only. Must check sensitivities
cefotaxime	inj	1-2 g tds	

note:

Every effort should be made to make a microbiological diagnosis before commencing treatment. Prolonged therapy is required (usually a minimum of 4 or 6 weeks, but often 3-6 months is necessary); duration of therapy should be guided by clinical response combined with reduction of inflammatory markers e.g. CRP, ESR. Initial combination therapy using two agents with activity against the causative organism is recommended.

19.2 Septic Arthritis

Common causative organisms: *Staphylococcus aureus*
H. influenzae
streptococci
coliforms (rare)
coagulase negative staphylococci (post surgery)
Neisseria gonorrhoea (rare)

Recommended agents and duration: as for osteomyelitis

note: a gram stain of joint fluid may help guide empirical therapy, which should be amended if necessary once culture results are available.

20.0 Central Nervous System Infections

20.1 Meningitis

Causative organisms: many organisms may cause meningitis, particularly in immunocompromised patients, however more commonly isolated organisms include:
Group B β-haemolytic streptococcus (neonates)
E. coli (neonates)
Neisseria meningitidis
S. pneumoniae
H. influenzae (now rare)
Listeria monocytogenes

Recommended agents	Route	Dose / Duration	Comments

cefotaxime	inj	2 g qds 5-14 days (Duration will depend on clinical response and pathogen isolated)	drug of choice for penicillin resistant pneumococci, *H. influenzae* and neonatal infection. **Add amoxicillin 2 g 4 hourly if listeria infection is a possibility** (immuno-compromised, aged >50, alcoholic)
chloramphenicol	inj	50-100 mg/kg daily in 4 divided dose 5-14 days	if severe hypersensitivity reactions to β-lactam antibiotics. monitor levels in children (toxicity)

notes:

Urgent Gram stain of CSF may direct initial therapy.

If meningococcal disease is likely give parenteral cefotaxime **immediately**, before the results of investigations are available.

Consider other atypical organisms if the patient is immunosuppressed or history of recent trauma or neurosurgery (e.g. *Cryptococcus neoformans*, staphylococci).

Antibiotic prophylaxis (with rifampicin, ceftriaxone, or ciprofloxacin) should be offered to **household contacts** of patients with meningococcal meningitis or septicaemia, and will be co-ordinated via the Health Protection Unit, who should be informed of any cases of suspected meningitis (this is a notifiable disease). The patient should also receive antibiotic prophylaxis (usually ciprofloxacin or rifampicin) prior to discharge from hospital.

N.B. although recommended as alternative agents, ceftriaxone and ciprofloxacin are not currently licensed for meningococcal prophylaxis.

Pneumococcal meningitis requires treatment for at least 10 days.

Confirmed listeria meningitis should be treated with amoxicillin and gentamicin.

20.2 Viral Meningitis / Encephalitis

Many organisms may cause this disease. Anti-viral therapy with high dose aciclovir (10 mg/kg tds) recommended for Herpes Simplex Encephalitis, for 14 – 21 days.

20.3 Brain Abscess

Common causative organisms: often mixed including:

Streptococcus milleri — other streptococci
Anaerobes — coliform organisms
Haemophilus spp.

In the appropriate clinical setting consider also:

Mycobacterial infection
Actinomycetes
Aspergillus spp.

Recommended agents	Route	Dose / Duration	Comment
cefotaxime	inj	2 g qds	adjust therapy when Gram stain/ culture results are available
plus			
metronidazole	inj	500 mg tds	duration will depend on clinical progress

21.0 Abdominal Infections

21.1 Infectious Gastroenteritis

There are many causes of infectious gastroenteritis including bacteria, viruses and protozoa. The common bacterial pathogens include:

Salmonella spp.
Campylobacter spp.
Shigella spp.
E. coli 0157
Salmonella typhi

Most uncomplicated infections (except *Salmonella typhi* and *paratyphi*) do not require specific antimicrobial therapy - supportive treatment with fluids only is required.

Antibiotics should be reserved for specific circumstances:

- *Salmonella typhi* and *paratyphi* infection
- severe illness e.g. septicaemia, the elderly or very young, immunodeficiency
- prolonged debilitating disease

Recommended agents	Route	Dose / Duration	Comments
ciprofloxacin	po	750 mg bd 14 days	should be given for at least 14 days to prevent long term salmonella carriage
cefotaxime / ceftriaxone	inj	1-2 g bd / 1 g od 14 days	1st line therapy for suspected *Salmonella typhi/paratyphi* in returning travellers
erythromycin	po	500 mg qds 5 days	*Campylobacter* infection only

21.2 Cholecystitis / Cholangitis / Pancreatitis

Common causative organisms:

coliforms
enterococci
anaerobes

Recommended agents	Route	Dose / Duration	Comments
co-amoxiclav	po/inj	625 mg / 1.2 g tds 5 days	
amoxicillin	inj	1 g tds 5 days	
plus			
gentamicin	inj	5 mg/kg 5 days	dose interval according to levels
plus			
metronidazole	inj/po	500 / 400 mg tds 5 days	
piperacilllin/tazobactam	inj	4.5 g tds 5 days	
meropenem	inj	1 g tds 5 days	if penicillin allergic - discuss with microbiologist if patient has severe β-lactam hypersensitivity

21.3 Intra-abdominal Infection

Common causative organisms: coliforms
enterococci
streptococci esp. *Streptococcus milleri*
anaerobes

Recommended agents	Route	Dose / Duration	Comments
first line:			
amoxicillin	inj	1 g tds 5 days	
plus			
gentamicin	inj	5 mg/kg 5 days	dose interval according to levels
plus			
metronidazole	inj/pr	500 mg / 1 g tds 5 days	
second line:			
Piperacillin/tazobactam	inj	4.5 g tds	
meropenem	inj	1 g tds 5 days	if penicillin allergic - discuss with microbiologist if patient has severe β-lactam hypersensitivity

notes:

Drainage of intra-abdominal collections is essential. Antibiotics alone are unlikely to resolve infections if collections of pus are present.

21.4 Spontaneous Bacterial Peritonitis

Recommended agents	Route	Dose / Duration	Comments
Piperacillin/tazobactam	inj	4.5 g tds 5 days	
meropenem	inj	1 g tds 5 days	if penicillin allergic- discuss with microbiologist if patient has severe β-lactam hypersensitivity
co-trimoxazole	po	960 mg od	prophylaxis only

21.5 *Clostridium difficile* Associated Diarrhoea / Pseudomembraneous Colitis

Causative organism: *Clostridium difficile*

Recommended agents	Route	Dose / Duration	Comments
Moderate disease:			
metronidazole (1st line)	po/inj	400 / 500 mg tds	assess response to therapy after 5 days - if responding, continue for a total of 14 days if not responding, add vancomycin 500 mg po qds for 14 days and continue metronidazole until had 14 days

Severe disease:			early assessment by a colorectal surgeon is essential in severe disease
vancomycin	po	500 mg qds	
plus metronidazole	po/inj	400 / 500 mg tds	requires 14 days of combination therapy
			there is **no** role for iv vancomycin
			serum vancomycin levels do NOT need to be monitored with oral therapy

The assessment of the severity of the disease should be made using the *C. difficile* management guidelines on the intranet.

http://intranet/pdf/Clostridium%20Difficle%20Treatment%20Guidelines.pdf

22.0 Infective Endocarditis

It is important that all reasonable steps are taken to make a microbiological diagnosis before starting antibiotics. The Cardiologists should always be involved in the management of patients with proven or suspected infective endocarditis.

Causative organisms: viridans streptococci
enterococci
S. aureus
coagulase negative staphylococci (prosthetic valves)
Candida spp.

For advice on specific antimicrobial therapy, please see 'Guidelines for the Antibiotic Treatment of Endocarditis in Adults: Report of the Working Party of the British Society for Antimicrobial Chemotherapy (2004)'. These guidelines are on the Trust Intranet site.

Gentamicin and vancomycin levels must be monitored. Gentamicin, when it is used, should not be used in the high dose / extended dose interval regime. Pre-dose and 1-hour post-dose gentamicin levels are therefore necessary (just pre-dose level for vancomycin); the pre-dose gentamicin level must be maintained below <1 mg/l, the post-dose level (taken one hour post dose) between 3 and 5 mg/L.

Response to treatment should be monitored using serial CRP measurements.

Close liaison with the microbiologist is essential.

23.0 Infections in Haematology and Oncology patients

It is important to distinguish between those patients who are severely immuno-compromised as a result of disease or chemotherapy and those with haematological disorders who do not have significantly impaired immunity.

23.1 Neutropenic Patients

Those patients with an absolute neutrophil count of < 1 x 10^9/L with fever (single reading of 38.5^0 C or > 38^0 C for more than 2 hours) should receive empirical antibiotics with predictably good cover against Gram negative aerobes, as infection with these organisms may be rapidly fatal in this group of patients.

Recommended agent	Route	Dose / Duration	Comment
Tazocin	inj	4.5 g tds	
plus			
gentamicin	inj	5 mg/kg	dose interval according to levels
If no response after 48 hours, or if penicillin allergic:			
Meropenem	inj	1 g tds	if penicillin allergic - consult microbiologists if patient has severe hypersensitivity to β-lactam antibiotics
plus			
teicoplanin (Haematology)	inj	400 mg od	if Gram positive infection suspected (e.g. line infection)
or			
vancomycin (Oncology)	inj	1 g bd	if Gram positive infection suspected (e.g. line infection)

notes:

If there is no improvement in 48 hr review any microbiological results, repeat cultures, consider switching to second-line agents and also consider infection with the following:

a) fungi e.g.	*Candida* spp.,
	Aspergillus spp.
b) viruses e.g.	Herpes simplex,
	CMV
c) other atypical organisms e.g.	*Pneumocystis jiroveci*
	Mycoplasma pneumoniae
	Mycobacteria

23.2 Non-neutropenic Patients

These may not be at increased risk of Gram negative sepsis, and those with fever should be investigated along conventional lines: **empirical therapy** should reflect the probable source and **likely pathogen(s)** causing the infection.

24.0 Tuberculosis

24.1 Pulmonary Tuberculosis

Causative organisms: *Mycobacterium tuberculosis* complex

Recommended agent	Route	Dose / Duration	Comment
first line:			side effects:
rifampicin	po	Dose and duration of all myco-bacterial treatment must be determined by a Respiratory Physician or Paediatrician with an interest in TB	rash, hepatitis, G.I. upset, 'flu syndrome'
isoniazid	po		peripheral neuropathy (pyridoxine prophylaxis), hepatitis, cutaneous hypersensitivity
ethambutol	p.o.		optic neuropathy
pyrazinamide	p.o.		rash, nausea, ↑ serum uric acid, hepatitis, arthralgia
second line:			
streptomycin	inj		
cycloserine	p.o.		
thiacetazone	p.o.		
capreomycin	inj.		
kanamycin	inj.		
moxifloxacin	p.o.		

notes:

Tuberculosis is a notifiable disease.

In uncomplicated cases a total of six months therapy is sufficient, two months with quadruple therapy, followed by four months with rifampicin and isoniazid alone if the isolate is sensitive to these. All agents have the potential for drug interactions.

24.2 Non-pulmonary Tuberculosis

As above (24.1)

pericarditis	6 months therapy
bone and joint infection	6 months therapy
lymph node infection	6 months therapy
meningitis	12 months therapy (10 months rifampicin and isoniazid)

These are guidelines only and **it is recommended that the management of all tuberculosis is co-ordinated via the respiratory physicians.**

25.0 Genital Tract Infections

25.1 Post-operative Infection

If post-operative infection occurs an **alternative** antimicrobial agent to that used for prophylaxis should be given (as infection may be caused by resistant organisms).

Common causative organisms: haemolytic streptococci anaerobes
Staphylococci Gram negative aerobes

Recommended agents	Route	Dose / Duration	Comment
co-amoxiclav	po/iv	625 mg / 1.2 g tds 5 days	amend therapy if necessary when culture results available.
or			
amoxicillin	iv	1 g tds 5 days	
plus			
gentamicin	iv	5 mg/kg 5 days	dose interval according to levels
plus			
metronidazole	iv / po / pr	500 mg / 400 mg / 1g tds 5 days	
gentamicin	iv	5 mg/kg 5 days	dose interval according to levels
plus			
clindamycin	po/iv	600 mg qds 5 days	if penicillin allergic

25.2 Pelvic Inflammatory Disease (PID)

PID refers to a spectrum of inflammatory disorders of the female upper genital tract and may include any combination of endometritis, salpingitis, tubo-ovarian abscess and pelvic peritonitis.

Common causative organisms: *N. gonorrhoeae*
C. trachomatis
anaerobes
coliform organisms
streptococci

Empirical therapy should be broad spectrum to cover the likely pathogens. Sexual partners should also be followed up and treated as necessary.

Recommended agents	Route	Dose / Duration	Comment
ceftriaxone	im	250 mg single dose	
plus			
doxycycline	po	100 mg bd	doxycycline and metronidazole should be continued for 14 days.
plus			
metronidazole	po	400 mg bd	
or:			
ofloxacin	po	400 mg bd	both drugs for 14 days
plus			
metronidazole	po	400 mg bd	

25.3 Hydrosalpinx Found at Hysterosalpingography

If sexually transmitted infections have not been excluded, treat as per PID. If sexually transmitted infections have already been excluded:

Recommended agents	Route	Dose / Duration	Comment
gentamicin plus co-amoxiclav	iv po	5 mg/kg single dose 625 mg tds 5 days	
Penicillin allergic :		Discuss with microbiology	

25.4 Prostatitis

Acute bacterial prostatitis

This is caused by urinary tract pathogens, most commonly coliforms or enterococci. It may occasionally be caused by *Staphylococcus aureus* secondary to prolonged catheterisation. It is an uncommon complication of UTI. Acute prostatitis is an acute severe systemic illness that may be complicated by prostatic abscess, bacteraemia, epididymitis and pyelonephritis. *Neisseria gonorrhoea* is now an unusual cause. Acute bacterial prostatitis frequently responds very well to antibacterial therapy.

Chronic bacterial prostatitis

This is chronic bacterial infection of the prostate with or without symptoms of prostatitis, and with a history of recurrent urinary tract infections caused by the same bacterial strain with or without any structural abnormalities. The usual causative bacteria are those causing urinary tract infections, most commonly *E.coli*. Chronic bacterial prostatitis is very difficult to cure, with some urologists recommending surgery.

Despite the differences between acute and chronic bacterial prostatitis the initial approach to management with antibiotics is the same:

Recommended agents	Route	Dose / Duration	Comment
First line :			
ciprofloxacin	po	500 mg bd 28 days	
Or			
ofloxacin	po	200 mg bd 28 days or 400 mg od 28 days	
Second line :			
trimethoprim	po	200 mg bd 28 days	

Antibiotics should be continued or changed according to the sensitivity results of any positive urine or blood cultures.

25.5 Epididymo-orchitis

The likely causative organism will depend on the age and sexual activity of the patient. In men under the age of 40 epididymo-orchitis it is most often caused by sexually transmitted pathogens such as *Neisseria gonorrhoea* or *Chlamydia trachomatis*. In men over the age of 40 epididymo-orchitis is most often caused by non-sexually transmitted enteric organisms such as coliforms or enterococci. There will obviously be cross-over between the groups and a complete sexual history is imperative. Patients should be investigated for the presence of sexually transmitted pathogens if appropriate. Sexual partners should be followed-up and treated if investigations reveal a sexually transmitted infection. Testicular torsion is the most important differential diagnosis, it is a surgical emergency and must be considered and excluded in all patients.

Recommended agents	**Route**	**Dose / Duration**	**Comment**
Patient <u>under 40</u> or sexually transmitted infection most likely :			
First line :			
Ceftriaxone **plus**	im	250 mg single dose	If allergic to ceftriaxone a single dose of ciprofloxacin 500mg may be substituted
doxycycline	po	100 mg bd 10 -14 days	Longer courses may be required
Second line :			
ofloxacin	po	200 mg bd 14 days	If patient allergic to cephalosporins and/or tetracyclines.
<u>Recommended agent</u>	**<u>Route</u>**	**<u>Dose/Duration</u>**	**<u>Comment</u>**
Patient <u>over 40</u> or enteric pathogens most likely:			
First line:			
ciprofloxacin or ofloxacin	po po	500 mg bd 14 days or 200 mg bd 14 days	
Second line:		Discuss with microbiology	

25.6 <u>Sexually Transmitted Diseases</u>

It is essential that detection of a sexually transmitted disease, e.g. gonorrhoea or chlamydial infection is followed up by referral to the Department of Genito-Urinary Medicine (GUM), so that screening for other infections and contact tracing of sexual partners is performed.

26.0 MRSA

For detailed information on the diagnosis and treatment of MRSA please see Policy IP 03 'Prevention and Control of MRSA, VRE and other Antibiotic Resistant Organisms' on the Trust Intranet.

26.1 Decolonisation of MRSA Carriage

Decolonisation should be attempted according to the above policy, using the regime described in the table. Further information is available form the Infection Prevention Nurses and the microbiologists.

	Drug Route	**Frequency**	**Length of treatment course**
mupirocin ointment 2% (Bactroban) **or** Polyfax for mupirocin resistant strains	per nasal (to interior nares)	tds	5 days
4% chlorhexidine (Hibiscrub)	topically (as skin wash)	od	5 days
mupirocin ointment 2% (Bactroban)	topically to small wounds if present	bd	5 days

26.2 Treatment of MRSA Infection

MRSA does not require treatment with systemic antibiotics unless it is causing an infection – colonisation does not require oral or intravenous antibiotics. The choice of antimicrobial, if treatment is necessary, will depend on the sensitivity pattern of the isolate.

If oral antibiotics are prescribed, a combination is always preferred (unless linezolid is used), to make further resistance less likely.

For non-severe skin and soft tissue, urinary tract and respiratory tract infections, trimethoprim or doxycycline (or clarithromycin if isolate is reported as sensitive to erythromycin) can be used in combination with either rifampicin or sodium fusidate, according to the sensitivities of the isolate.

Severe respiratory tract infection may require treatment with linezolid, and should be discussed with a microbiologist. Other severe MRSA infections should be treated with intravenous vancomycin plus oral rifampicin or sodium fusidate (according to sensitivities of the isolate). The treatment of severe MRSA infections, or MRSA infections involving bone, joints, the central nervous system, endocarditis or peritonitis should be discussed with the microbiologist.

Recommended agents	**Route**	**Dose / Duration**	**Comments**
trimethoprim **or** doxycycline **plus** rifampicin **or** sodium fusidate	po po po	200 mg bd 5-10 days 100 mg od or bd for 5-10 days 300-600 mg bd 5-10 days 500 mg tds 5-10 days	look at sensitivity of isolate to determine which combination to use monitor liver function in patients on rifampicin or sodium fusidate (do not use these two drugs together unless on Microbiologist advice)

vancomycin **plus**	iv	1 g bd 5-14 days	severe MRSA infection - monitor levels (see Section 6.0)
rifampicin **or** sodium fusidate	po	300-600 mg bd / 500 mg tds	depending on sensitivity data
linezolid	iv/po	600 mg bd 10-14 days	only to be used on Microbiologist advice

28.0 Further Information and Contact Numbers

For further information please contact:

Dr M Cooper	Ext: 8250
Dr H Jones	Ext: 8252
Dr D Dobie	Ext: 8253
Dr M Ashcroft	Ext: 8259

Medicines Information Service Ext. 5136

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28.0 ANTIBIOTICS IN PAEDIATRICS

Summary of recommendations for **initiating** antibiotics for paediatric patients.

This policy does **NOT** apply to children with *cystic fibrosis* or those who are *immuno-compromised*. Please refer to specific protocols for these patients. All antibiotic treatments should be revised according to clinical response or as soon as culture results are available. Remember to *change* antibiotics in those patients on prophylaxis who need infections treating. For specific guidance on the dosage of antibiotics in children consult the 'BNF for Children' or the Summary of Product Characteristics (SPC) for the drug concerned.

Tonsillitis

Amoxicillin po / iv according to clinical condition. NB use penicillin V if glandular fever suspected. 10 days treatment required if throat swab positive Group A Strep.

Clarithromycin po / iv if penicillin allergy.

Otitis Media

High dose amoxicillin po / iv

Co-amoxiclav should be second line choice for treatment failures or if evidence of local sinusitis.

Clarithromycin po / iv if penicillin allergy.

Infected Cervical Lymph Nodes

Co-amoxiclav po / iv

Consider atypical organisms, may need clarithromycin adding.

Chest Infection / Pneumonia

Child not unwell
Oral amoxicillin (consider co-amoxiclav if under 6 months)

Child unwell

Age 0 – 6 months	iv cefuroxime followed by oral co-amoxiclav
Over 6 months:	
Lobar pneumonia	iv benzyl penicillin then oral amoxicillin
Bilateral/diffuse changes	iv cefuroxime then oral amoxicillin
If penicillin allergy	iv cefuroxime or clarithromycin

If mycoplasma suspected from history or 'mycoplasma year' or not responding at 48 hours ADD po clarithromycin for 3 weeks or po azithromycin for 2 weeks. Ideally serology should be sent to confirm diagnosis.

If compliance is a problem po azithromycin for 3 – 5 days could replace amoxicillin / co-amoxiclav.

Cystic Fibrosis: paediatric CF patients require high doses and prolonged course of antibiotics for respiratory exacerbations.
If high dose oral antibiotics have failed, IV antibiotics are usually given.

For further information on the management of infections in children with Cystic Fibrosis please refer to the Trust policy:
http://intranet/pdf/departments/Neonatal&Childrens/PaediatricGuidelines-Cystic_Fibrosis.pdf

If pseudomonas is isolated for the first time: oral ciprofloxacin 30 mg/kg/day for 3 weeks plus nebulised colomycin 1 megaunit bd mixed with normal saline for at least 3 months

Prophylaxis for infection: babies- flucloxacillin 50 mg/kg bd po
Toddlers – co-trimoxazole 240-480 mg bd po
Older children – azilthromycin 250-500 mg od po for 3 days per week

Urinary Tract Infection

Child not unwell
trimethoprim po if no previous antibiotics
cefalexin po if had previous antibiotics

Child unwell or less than 3 months
iv amoxicillin and gentamicin OR
iv cefuroxime if penicillin allergy

If severe penicillin allergy use iv gentamicin alone or po ciprofloxacin.

Follow-on oral antibiotic according to sensitivities or po cefalexin if not known.

Prophylaxis with trimethoprim unless enterococci isolated, then use nitrofurantoin.

Meningitis

iv cefotaxime. **Add** iv amoxicillin if < 3 months or immunosuppressed.

Very Unwell Child – ?cause

Discuss with consultant.

IF blind treatment required consider:
iv cefotaxime (use maximum dose)
Consider adding gentamicin after a few hours if no improvement.

If focus likely to be UTI or chest iv cefuroxime is preferable.

Septic Arthritis / Osteomyelitis

iv benzyl penicillin and flucloxacillin 1 week minimum followed by:
po flucloxacillin and sodium fusidate if staphylococcus aureus.
OR po amoxicillin if group A streptococcus.

If severe penicillin allergy, use iv clindamycin.

Impetigo

Flucloxacillin iv / po

Clarithromycin if penicillin allergy.

Cellulitis

iv benzyl penicillin and flucloxacillin. If mild can use po co-amoxiclav.

Peri-orbital / Orbital Cellulitis

iv cefuroxime ± metronidazole.

NEONATAL UNIT

See Drug Guidelines Folder on the Unit or the monograph on the Trust Intranet for dosages for neonates.

First line antibiotics (where pathogen unknown):
Within 72 hours of birth - iv benzyl penicillin and iv gentamicin
More than 72 hours after birth – iv cefotaxime and iv vancomycin

Second line antibiotics (where pathogen unknown):
iv cefotaxime and iv vancomycin

Necrotising enterocolitis
iv cefotaxime + iv vancomycin + iv metronidazole

Meningitis
iv cefotaxime + iv amoxicillin (high dose)

Group B Streptococcal infection
iv benzyl penicillin and iv gentamicin – see separate guidelines on NNU.

Pseudomonal infection
iv ceftazidime +/- iv gentamicin or iv meropenem (as per sensitivities of isolate).

References

- RCPCH 2003 Medicines for Children
- BNF for Children 2007
- Paediatric Department Guidelines for specific diseases (on Intranet)
- Sanford Guide to Antimicrobial Therapy
- BTS guidelines Community Acquired Pneumonia in Childhood: www.brit-thoracic.org.uk