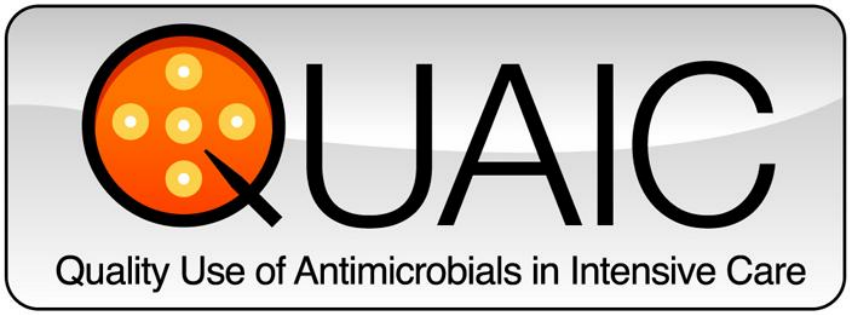

Intensive Care Unit Empirical Antimicrobial Treatment Guidelines

November 2010

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Disclaimer

This guideline is aimed at providing the clinicians of NSW intensive care units (ICU) with recommendations to frame the development of policies and procedures related to empirical antimicrobial therapy.

The guideline is not intended to replace the critical evaluation processes that underpin the development of local policy and procedure nor a clinician's judgment in an individual case. This document is also not intended to replace Therapeutic Guidelines: Antibiotic version 14, 2010.

Users of this guideline should critically evaluate the content as it relates to local circumstances and any changes in the literature that may have occurred since October 2010. In addition NSW Health clinicians should review NSW state government policy documents to identify any directives that may relate to this clinical practice.

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Contents

Disclaimer 3

Rationale 6

General Considerations 6

Prescribing Principles 7

Identification of a potential source for sepsis 9

- Detection of bloodstream events 9
- Detecting central line-associated infection 10
- Other diagnostic methods for bloodstream events 11
- Suspected endocarditis: additional tests to consider 11

Community presentations 11

- Management of sepsis, uncertain focus 12
- Management of sick 'immunocompromised' patient 12
- Management of suspected fungal sepsis 13
- Management of respiratory tract: Community acquired pneumonia 14
- Management of respiratory tract: Aspiration pneumonia 16
- Management of suspected community-acquired meningitis 17
- Management of trauma orthopaedics and multi-trauma 17
- Management of urosepsis 18

Healthcare-associated presentations 20

- Hospital Acquired Pneumonia 20
- Management of early Ventilator Associated Pneumonia 20
- Management of late Ventilator Associated Pneumonia 20
- Management of intra–abdominal sepsis 22
- Management of cholecystitis or biliary sepsis 22
- Management of acute pancreatitis 23

Document History 24

References 25

Rationale

Prompt, appropriate, targeted antimicrobial therapy is life-saving. Patients in ICU often receive antimicrobial therapy that is poorly chosen or is given for too many days. This excess exposure is a potent driver of colonisation and infection by multi-resistant bacteria and *Clostridium difficile*. Prescribed treatment is often empirical and early decisions to shift to directed therapy or cessation of therapy can reduce antibiotic exposure significantly. Reduction in antimicrobial exposure leads to reductions in resistance and less cost. Controlling resistance selection within the ICU has potential spill-over effects for the general hospital.

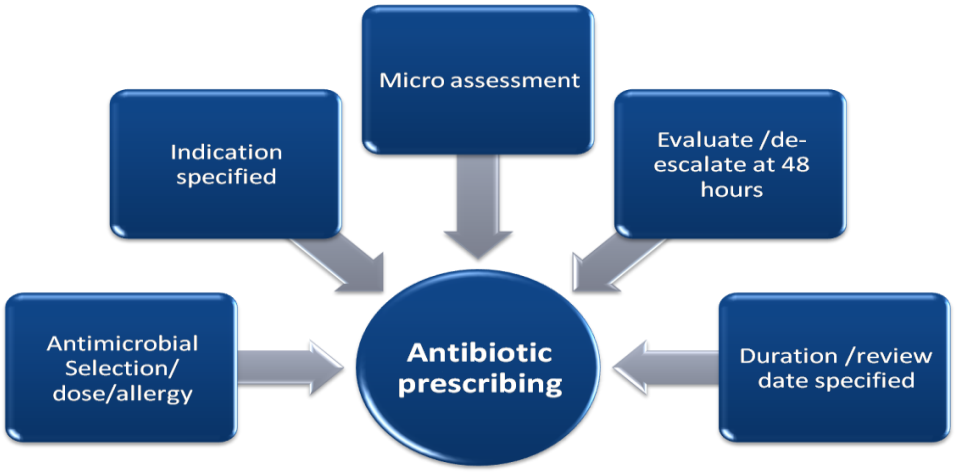
General Considerations

- Empirical antimicrobial choice should be guided by Therapeutic Guidelines: Antibiotic version 14, 2010 (Antibiotic Guidelines 14)[1]. The drug recommendations in this document are based on those in Antibiotic Guidelines 14 with variations to reflect local practice. Only adult doses are provided in this document. Consult Antibiotic Guidelines 14 for paediatric doses.
- In ICU fluid resuscitation and source control are as important as appropriate antimicrobial prescribing[2].
- Time to antibiotic administration should be minimised in severe sepsis. It is suggested that within 1 hour from triage is a reasonable target (in one recent large retrospective study, every additional hour to effective antimicrobial initiation in the first 6 hours after the onset of hypotension was associated with >7% decrease in survival[3]).
- Ensure there are processes in place for clear communication of urgent information between the laboratory and treating medical officers.
- Limit the duration of antibiotic therapy when clinically appropriate to minimise the opportunity for the emergence or selection of multi-drug resistant organisms (MDRO's) and *Clostridium difficile* infection. This is particularly relevant to elective surgical antibiotic prophylaxis where clinicians should be vigilant to ensure appropriate and timely cessation of antibiotics – a single dose is indicated for nearly all types of surgery (see Antibiotic Guidelines 14). Trauma patients may require more prolonged treatment.
- Where an aminoglycoside is given for empirical treatment, a maximum of 48 hours is recommend (equating to 3 daily doses in patients with eGFR > 60mL/min and 1-2 doses in patients with degrees of renal failure) (see Table 24 and 25 from Antibiotic Guidelines 14, reproduced in table 1 and 2 below). If ongoing aerobic Gram negative cover is required, then treat with a non-aminoglycoside agent based on organism ID and susceptibilities if known.

Prescribing Principles

To ensure that appropriate prescribing is supported in the intensive care setting adherence to the following principles based on the AIMED model[4] are encouraged.

Figure 1: AIMED ANTIMICROBIAL PRESCRIBING MODEL



- Select empiric agents in accordance with Antibiotic Guidelines 14 and local antibiogram data.
- Seek Infectious diseases physician /Microbiologist input as required (eg: life threatening penicillin allergy[5] and de-escalation of therapy).
- Investigate patients appropriately prior to antimicrobial treatment if possible. See identification of a potential source and detection of bloodstream events below.
- De-escalate or streamline antimicrobial treatment at 48 hrs based on the clinical picture and relevant microbiological results- where necessary obtain specialist advice.
- Limit duration of therapy according to clinical response, ultimate diagnosis and available evidence by specifying the indication, evaluating at 48 hrs and documenting a specific duration or review date for every antimicrobial course.
- Consider IV to oral switch as soon as clinically feasible.
- Ensure patients discharged from ICU with antimicrobials still prescribed have a review date provided in the discharge summary.
- When prescribing certain agents the need for ongoing therapeutic drug monitoring should be considered (see Antibiotic Guidelines 14).

Aminoglycosides if used beyond 72 hours to detect accumulation.

Vancomycin to ensure adequacy of dosing. Adjust dose according to renal function to achieve recommended concentration. For intermittent dosing the target trough concentration is 12–18 mg/L. For continuous infusion the target concentration is 17–23 mg/L.

- If impending renal failure an issue avoid more than 1 dose of gentamicin and consider an antipseudomonal beta-lactam such as ticarcillin/ clavulanate or piperacillin/tazobactam as an alternative[5].
- If sepsis develops when patient has been on antibiotics for more than 48hrs, discuss with an infectious disease physician or microbiologist before changing drugs[5].

Tables 1 and 2 have been adapted with permission from Antibiotic Expert Group, Therapeutic guidelines: antibiotic, Version 14, Melbourne: Therapeutic Guidelines Limited; 2010, p 360

Table 1: INITIAL AMINOGLYCOSIDE DOSE FOR EMPIRICAL AND DIRECTED THERAPY[1]

Age	Initial gentamicin/ tobramycin dose [NB1]
10–29 years	6 mg/kg up to 560 mg
30 to 60 years	5 mg/kg up to 480 mg
More than 60 years	4 mg/kg up to 400 mg
10 years or more with severe sepsis (sepsis syndrome) [NB2]	7 mg/kg up to 640 mg
Any age with streptococcal and enterococcal endocarditis	3 mg/kg/day [NB3] (use gentamicin only, in divided doses)
NB1: For subsequent empirical dosing, see Table 2. For subsequent directed dosing, see Antibiotic Guidelines 14, p 361.	
NB2: Patients with severe sepsis have higher volumes of distribution and therefore require a higher mg/kg dose.	
NB3: Lower doses are used for synergistic treatment in endocarditis (see Streptococcal endocarditis p 57 and Enterococcal endocarditis p 59 in Antibiotic Guidelines 14).	

Table 2: AMINOGLYCOSIDE DOSING INTERVAL FOR SUBSEQUENT EMPIRICAL DOSES[1]

Creatinine clearance [NB4]	Dosing interval doses as above	Maximum empiric doses
Greater than 60 mL/min	24 hours	3 (at 0, 24 and 48 hours)
40–60 mL/min	36 hours	2 (0 and 36 hours)
30–40 mL/min	48 hours	2 (0 and 48 hours)
Less than 30 mL/min	Give initial dose then seek expert advice	
NB4: Creatinine clearance estimate should be based on a creatinine measurement obtained as recently as possible (eg within the last 12 to 24 hours); however, this might still overestimate renal function in acute renal failure.		

Identification of a potential source for sepsis

- Comprehensive physical assessment including examination of: skin, ulcers, inserted vascular lines and drains, wounds, sinuses, ears, teeth, throat, chest, cardiovascular system, back, abdomen, perianal, genital/ reproductive, urinary, bones and joints including spine and for signs of meningism.
- Collect blood cultures, sputum, urine specimens.
- Culture cutaneous wounds, lesions, invasive devices ulcers, pressure areas
- Consider bronchoalveolar lavage, sampling cerebral spinal fluid, pleural fluid, abdominal collections, stool culture, skin biopsy as clinically appropriate
- Obtain x-rays, CT Scans, surgical consultation as clinically appropriate
- Mark sterile samples appropriately to ensure prompt laboratory assessment
- Where appropriate, also consider non-infective causes of fever or systemic inflammatory responses such as:
    - central cause (eg. Head injured or ICH patient)
    - drugs/medications
    - pulmonary embolism
    - autoimmune disease; e.g. temporal arteritis
    - neuroleptic malignant syndrome
    - malignancy
    - ischaemic gut or other ischaemic tissue
    - pyrogens (e.g. from sterile haematoma in pleural, retroperitoneal or pelvic spaces)
    - factitious disease

Detection of bloodstream events[5]

Detection of bacteraemia or fungaemia in adults is highly dependent on volume of blood added to blood culture bottles[6]. To ensure optimal blood culture collection from septic patients the following practice is recommended: [5, 7– 9]

- Collect 2 blood culture sets (a total of 40mL – at least 10mL per bottle –) from separate venepunctures within 48 hrs to evaluate each sepsis episode[9]. In some circumstances an additional anaerobic bottle may be collected (e.g. neutropaenia, abdo/pelvic surgery, long term invasive devices in situ)
- A blood culture set comprises 2 bottles (aerobic and anaerobic) in an adult or 1 paediatric bottle in infant/ small child although an anaerobic bottle should be added if anaerobic sepsis is considered a diagnostic possibility (eg neutropenia, abdominal/pelvic surgery).
- Adult: for nearly all systems, 8-10mLs of blood is required for each bottle (avoid over-filling as it renders the culture less sensitive)
- Paediatric: generally 0.5–4mLs required (consult local laboratory)

- Routine collection via old or new central or arterial lines is not recommended due to the potential for contamination from hub and/or contamination of line. Lines may have internal colonisation without the patient having systemic sepsis. Studies evaluating the isolation of coagulase negative staphylococci from blood cultures collected via lines indicate false positivity in a significant proportion .[10–11] Discuss the diagnostic methods available for catheter-associated infection with the Microbiologist.
- Use aseptic collection technique in order to avoid contamination and maximise specificity[5]:
    - Collectors should perform hand hygiene and use personal protective equipment.
    - Disinfect skin and top of blood culture bottles with alcohol with chlorhexidine 2% and wait for it to dry
    - Use no-touch needle insertion (many places specify use of sterile gloves)
    - Use vacutainer sleeve with leash for blood culture bottle (safety issue)
    - Do not change needle after collection before bottle inoculation (minimal effect on contamination rates and creates a safety issue)

Persistently febrile patients (eg. neurosurgical) should have regular blood cultures (e.g. every 48 hrs) to detect line-associated sepsis.

Detecting central line-associated infection (for clinical purposes)[5]

- Ensure appropriate blood culture collection when indicated and ensure appropriate audit of results to detect central line-associated events.
- Examine line exit sites daily for exudate and/or inflammation.
- Line-drawn cultures (see cautions above) may be considered in addition to those collected by venipuncture, provided that they are clearly labelled and interpreted as such. The diagnostic significance of a line positive / venipuncture negative result, particularly for common contaminants, will rarely be clear. If line drawn cultures are used to diagnose line sepsis, request differential quantitative cultures where available (see other diagnostic methods below)
- If line sepsis suspected, collect 2 sets of blood cultures by peripheral venipuncture. If alternate venous access is feasible remove the line and submit the aseptically collected tip for semi-quantitative culture. According to a 2005 metanalysis[12]; isolation of 15 or more colonies has 75-84% sensitivity for detection of a true line-associated infection. Line tip cultures may be falsely negative if microbial contamination is predominantly intraluminal. Conversely, the estimated specificity of a positive line tip result is between 71-85%. Isolation of less than 15 colonies from the tip usually represents contamination of the line by skin flora during removal and should be generally disregarded. NB. Culture of line tips in asymptomatic patients, where the line is removed for reasons other than suspected sepsis, is not recommended[13].
- If pathogens are isolated from a line tip culture and coincident blood cultures are negative, then clinical evaluation should occur to determine whether antimicrobial treatment is required. In general coagulase negative staph. isolated from line tip will not require further treatment.

Other diagnostic methods for bloodstream events

Other diagnostic methods are detailed in the referenced metanalysis[12]. Differential quantitative cultures or differential time to positivity (peripheral blood versus blood collected via central line) has the disadvantage of requiring blood withdrawal via the central line with the potential for line contamination. It is a feasible approach for dialysis lines, although one then has to ensure that all line lumens are sampled; another complication for the process. There are other potential practical barriers to the success of this method, in particular ensuring equivalent blood volumes from each sampling site, and "parallel" handling of samples. Consultation with local laboratories regarding the feasibility of this technique may be required.

Suspected endocarditis (culture negative): additional tests to consider[4]

- Additional blood cultures (optimum 3 sets if no recent antibiotic exposure; 6 sets if given antibiotics within the last 30 days)
- Serology for *Bartonella* species and *Coxiella burnetii* (Q-fever) unless explanted valve tissue or skin biopsy is available in which case nucleic acid amplification test (polymerase chain reaction-PCR) should also be performed for these pathogens[14]

C. burnetti, *B. quintana* and *B. henselae* are by far the commonest causes of culture negative endocarditis in patients who have not been exposed to antibiotics[14].

Community presentations

Community presentations encompass patients that are symptomatic on admission or within 48 hours of admission. In general, consult Antibiotic Guidelines 14 for treatment recommendations in accord with likely source of sepsis and local epidemiology of antimicrobial resistance. Selected syndromes are highlighted below.

Risk factors for MDRO include[15]:

- indwelling percutaneous medical devices or catheters
- visits to high-prevalence country within the past 3-6 months (e.g. India has 70-90% ESBL rates in *E. coli*)

Additional risk factors reported in the literature of mostly US publications are[16]:

- recent hospitalization or surgery (previous 12-24 months)
- residence in a long-term care facility
- dialysis
- prolonged or previous antimicrobial use

Management of sepsis, uncertain focus

Empiric treatment[1]

Regimen	Drug	Dose
1	flucloxacillin	2g IV 6 hourly
	gentamicin	7mg/kg for 1 dose, then determine dosing interval for a maximum of either 1 or 2 further doses based on renal function (see Tables 1 and 2)
	Special circumstances	
In cases presenting with shock to provide MRSA cover, **add**	vancomycin	1.5g IV 12 hourly (adjust initial dosage for renal function, and subsequent doses to achieve therapeutic range (Antibiotic Guidelines 14 Table 26 p365). For information on continuous infusion, see Antibiotic Guidelines 14 p365.
For patients with suspected meningococcal sepsis, **add**	benzylpenicillin	1.8g IV 4 hourly

In patients with hypersensitivities see Antibiotic Guidelines 14

Management of sick 'immunocompromised' patient (febrile neutropaenia)

- Neutropaenic patients may present without fever, however, a patient receiving chemotherapy, whether known to be neutropaenic or not, who presents with fever, chills, rigors or unwell should receive empiric antibiotic therapy without waiting for the results of investigations to become available.
- Consider previous antimicrobial exposure and prior microbiology to guide empiric selection.
- Consultation with the patient's haematologist or oncologist is recommended

Diagnostic Work-up

Aggressive diagnostic workup that includes tests for typical and atypical bacteria, viruses, parasites and fungi as appropriate.

Empiric treatment[1]

Regimen	Drug	Dose
1	piperacillin /tazobactam	4+0.5g IV 8 hourly
	or	
In patients with minor penicillin hypersensitivity, **use**	ceftazidime	2g IV 8 hourly
	Special circumstances	
In patients in shock or known to be colonised with methicillin-resistant *Staphylococcus aureus* (MRSA) or has clinical evidence of a catheter-related infection in a unit with a high incidence of MRSA infection **add**	vancomycin	1.5g IV 12 hourly (adjust initial dosage for renal function, and subsequent doses to achieve therapeutic range (Antibiotic Guidelines 14 Table 26 p365). For information on continuous infusion, see Antibiotic Guidelines 14 p365.

Management of suspected fungal sepsis

Refer to Antibiotic Guidelines 14

Empiric treatment[1]

Regimen	Drug	Dose
1 Azole naïve, No prior isolates of *Candida glabrata* or *C. kruzei*:	fluconazole	800mg IV first dose and then 400mg IV daily
	or	
2	amphotericin B	0.5 to 1.0mg/kg IV daily
	or	
3	caspofungin	70mg IV first dose, then 50mg IV daily

Management of respiratory tract: Community acquired pneumonia (CAP)

Assessment

- Explicitly score the severity of pneumonia. There are a number of tools available that are useful in stratifying patients likely to require ICU management.– CORB or SMART-COP pneumonia severity assessment tools are, recommended in Antibiotic Guidelines 14)
- Ensure that severe pneumonia is investigated comprehensively- see example Checklist for severe/ICU community acquired pneumonia investigation (protocols such as this should be discussed with your Clinical Microbiology Service before finalisation).

Diagnostic Work-up

- Sputum for Gram stain and culture and blood cultures[17]
- In severe pneumonia, send at least 2 blood cultures, consider urinary antigens testing for *Legionella pneumophila* type 1 and *Streptococcus pneumoniae* and a nasopharyngeal or BAL for respiratory virus and *Legionella* detection.
- In significant pleural effusions or suspected empyema, aspiration for diagnostic +/- therapeutic purposes should be considered. Pneumococcal antigen testing on empyema fluid and urine, if available, may be a useful adjunct to conventional culture in patients already receiving antibiotics.

Empirical treatment[1]

Initial broad spectrum antimicrobials that provide coverage against *S. pneumoniae*, *Legionella* species and aerobic Gram negatives are used.

- Note for *Streptococcus pneumoniae* there is no evidence that betalactam resistance alters the outcome in the absence of CNS involvement: Intravenous benzylpenicillin remains the drug of choice unless the MIC to penicillin is >= 8mg/L (isolates with MIC> 2 are rarely found in Australia)[18].
- In bacteraemic pneumococcal disease with shock a possible benefit from additional macrolide therapy is probably due to immunomodulatory effects rather than anti-bacterial effects[19-20].

Regimen	Drug	Dose
1	benzylpenicillin	1.2g IV 4 hourly
	azithromycin	500mg IV daily
	gentamicin	4-6mg/kg (severe sepsis : 7mg/kg) for 1 dose, then determine dosing interval for a maximum of either 1 or 2 further doses based on renal function (see Tables 1 and 2)
	or	
2	ceftriaxone	1g IV daily
	azithromycin	500mg IV daily
	or	
In patients with immediate penicillin hypersensitivity	moxifloxacin NB1 and NB2	400mg IV daily
	azithromycin	500mg IV daily
NB1: Extra caution should be exercised when agents that prolong QT interval such as amiodarone are being administered		
NB2: Excessive fluoroquinolone use may be associated with selection of MRSA and quinolone-resistant *C. difficile*.		
	Special circumstances	
In any patient with suspected staphylococcal pneumonia from Gram stain of sputum, clinical picture, radiographic appearance and/or initial blood culture result) **add**	vancomycin	1.5g IV 12 hourly (adjust initial dosage for renal function, and subsequent doses to achieve therapeutic range (Antibiotic Guidelines 14 Table 26 p365). For information on continuous infusion, see Antibiotic Guidelines 14 p365.
In any patient with severe pneumonia with a clinical presentation consistent with severe influenza, during a period where Influenza A is known to be circulating	consider neuramindase inhibitor (oseltamivir, zanamivir)	150mg via nasogastric tube twice daily

Management of respiratory tract: Aspiration pneumonia (eg. post cardiac arrest)

Empirical treatment[1]

Regimen	Drug	Dose
1	benzylpenicillin	1.2g IV 4 hourly
	metronidazole	500mg IV 12 hourly
	or	
In patients with immediate penicillin hypersensitivity as single agent use **either**	lincomycin or	600mg IV 8 hourly
	clindamycin	450mg IV 8 hourly
	Special circumstances	
In patients where aerobic Gram negatives are suspected (eg. in alcoholic patient) **add** (Recommendation by QUAIC Expert Advisory Group not Antibiotic Guidelines 14)	gentamicin	4-6mg/kg (severe sepsis : 7mg/kg) for 1 dose, then determine dosing interval for a maximum of either 1 or 2 further doses based on renal function (see Tables 1 and 2)
In patients with known or suspected pseudomonal pneumonia (eg. bronchiectasis with past pseudomonal colonisation) NB1	piperacillin /tazobactam	4+0.5g IV 6 hourly
	gentamicin	4-6mg/kg (severe sepsis : 7mg/kg) for 1 dose, then determine dosing interval for a maximum of either 1 or 2 further doses based on renal function (see Tables 1 and 2)
	or	
In patients with minor penicillin hypersensitivity **substitute** piperacillin+tazobactam with	ceftazidime	2g IV 8 hourly

NB1: Use two active drugs initially, especially if bacteraemia is present. For severely ill patients, infusing each dose of the piperacillin+tazobactam over 4 hrs may achieve better outcomes.

Management of suspected community-acquired meningitis

Give steroids (dexamethasone10mg, IV) with first dose of antibiotics then 6 hourly for four days.

Empiric treatment[1]

Regimen	Drug	Dose
1	ceftriaxone	4g IV daily
2	cefotaxime	2g IV 6 hourly
where there is a risk of Listeria i.e. very young, pregnant, or immunosuppressed **add**	benzylpenicillin	2.4g IV 4 hourly
if herpes simplex encephalitic picture	acyclovir	10mg/kg IV 8 hourly for at least 14 days

Management of trauma orthopaedics and multi-trauma

If a fracture is debrided, fixed and closed within 6 hours or an external fixature is present, a prophylactic dose of the antibiotic (as per the regimen below) is given with no further doses required. Most cases are considered to be already infected with no symptoms present. In these cases presumptive empiric therapy as per the Gustillo classification in table 3 is recommended. Type I fractures within this classification system has a low risk of infection whereas fractures classified as type IIIC have a 50% chance of infection.

Empiric treatment

Regimen	Drug	Dose
Orthopaedics Non-elective Trauma	cefazolin	2g IV 8 hourly
	or	
Orthopaedics Non-elective Trauma	vancomycin	1.5g IV 12 hourly (adjust initial dosage for renal function, and subsequent doses to achieve therapeutic range (Antibiotic Guidelines 14 Table 26 p365). For information on continuous infusion, see Antibiotic Guidelines 14 p365.

Table 3: GUSTILLO CLASSIFICATION OF OPEN FRACTURES[21]

Gustillo Type	Fracture size	Duration of therapy
I	Less than 1cm	24 hours after wound closure or **2** days for open wounds
II	1–3 cm	24 hours after wound closure or **3** days for open wounds
III	Greater than 3 cm	24 hours after wound closure or **5** days for open wounds
III A	Greater than 3 cm, bone coverable	24 hours after wound closure or **5** days for open wounds
III B	Greater than 3 cm, bone not coverable	24 hours after wound closure or **5** days for open wounds
III C	Greater than 3 cm, arterial injury, bone not coverable	24 hours after wound closure or **5** days for open wounds
Other multi–trauma including brain injury, base of skull fracture and CSF monitoring in place		24 hours (3 doses)

Management of urosepsis

Escherichia coli is responsible for most cases of complicated and uncomplicated urosepsis. Other organisms including *Staphylococcus saprophyticus*, *Proteus*, *Klebsiella*, enterococci and *Streptococcus agalactiae* (group B streptococcus) may also be cultured.

Urinary catheters are common in critical care and asymptomatic bacteriuria and /or pyuria or abnormal urinalysis should not be treated routinely with antimicrobials. Treatment is required where signs of systemic infection exist or significant risk factors such as neutropenia, transplantation or pregnancy are present.

If possible, the indwelling catheter should be removed as a form of source control. Where a catheter is required for ongoing management the catheter should be changed and a sample collected from the new catheter prior to antimicrobial therapy.

Diagnostic Work-up

- urine and blood cultures

Cultures taken from indwelling catheters are unreliable due to the presence of biofilms/colonisation in the catheter lumen and should be collected from a newly inserted catheter.

Empiric treatment[1]

Regimen	Drug	Dose
1	ampicillin	2g IV 6 hourly
	gentamicin	4-6mg/kg (severe sepsis : 7mg/kg) for 1 dose, then determine dosing interval for a maximum of either 1 or 2 further doses based on renal function (see Tables 1 and 2)

Uncomplicated IDC-related infections (without bacteraemia) can be managed with short course treatment (5 days) targeted against demonstrated organism. UTI complicated by bacteraemia, treat for longer 7-10 days, dependent on presence of pyelonephritis and/or urinary tract obstruction. Early conversion to oral therapy is possible if bacteraemia is absent[1].

Healthcare-associated presentations (high risk of MDRO or known MDRO colonisation)

Hospital Acquired Pneumonia

Recommended assessment

- Diagnostic criteria are relatively non specific and there is no gold standard for achieving a reliable diagnosis.
- For practical purposes HAP is divided into early (onset within 5 days of admission) and late (5 days or more) due to differences in the microbiology of pneumonia.
- Diagnostic tests to identify the causative organism should be performed prior to antibiotics, especially in VAP.

Diagnostic Work-up

- Sputum (consider collection by bronchial lavage), blood, urine and
- Perform CXR+/- CT[22]

Management of early Ventilator Associated Pneumonia (VAP) (provided no known colonisation with MRO):

Empiric treatment[1]

Regimen	Drug	Dose
1	benzylpenicillin	1.2g IV 6 hourly
	gentamicin	4-6mg/kg (severe sepsis : 7mg/kg) for 1 dose, then determine dosing interval for a maximum of either 1 or 2 further doses based on renal function (see Tables 1 and 2)
	or	
2	ceftriaxone	1g IV daily

Management of late VAP

Consider previous antibiotic exposure and previous culture results before selection of regimen.

Empiric treatment[1]

Regimen	Drug	Dose
1	piperacillin /tazobactam	4+0.5g IV 6 hourly NB1
	Special circumstances	
If the patient is ventilated, for a maximum of 48 hrs, **add**	gentamicin	4-6mg/kg (severe sepsis : 7mg/kg) for 1 dose, then determine dosing interval for a maximum of either 1 or 2 further doses based on renal function (see Tables 1 and 2)
In patients with minor penicillin hypersensitivity **use as single agent**	cefepime	2g IV 8 hourly
If MRSA colonised, **add**	vancomycin	1.5g IV 12 hourly (adjust initial dosage for renal function, and subsequent doses to achieve therapeutic range (Antibiotic Guidelines 14 Table 26 p365). For information on continuous infusion, see Antibiotic Guidelines 14 p365.
NB1: For severely ill patients, infusing each dose of the piperacillin+tazobactam over 4 hrs may achieve better outcomes.		
NB2: Review all cases at 3 days to assess response to treatment, likely microbial cause (if any) and alternative diagnoses. If rapid response to treatment or an alternative non-infective diagnosis likely, then cease antibiotics at 3 days. Otherwise continue treatment directed against the demonstrated pathogen(s) for 7-8 days. Pseudomonal infection is usually treated for longer.		
NB3: Candida are not considered to have an important role in causing VAP. Non bacterial causes of fever and pulmonary infiltrate need to be considered in the appropriate contexts: HSV, CMV, *Aspergillus*. Nosocomial *Legionella* may also require consideration in some circumstances.		

Management of intra–abdominal sepsis

Empiric treatment[1]

Regimen	Drug	Dose
1 NB1	ampicillin	1g IV 6hourly
	gentamicin	4-6mg/kg (severe sepsis : 7mg/kg) for 1 dose, then determine dosing interval for a maximum of either 1 or 2 further doses based on renal function (see Tables 1 and 2)
	metronidazole	500mg IV 12 hourly
	Special circumstances	
If still septic, evaluate source control and, dependent on intraoperative or other microbiology results, change to mono-therapy with **either**:	piperacillin /tazobactam	4+0.5g IV 6 hourly
	ticarcillin /clavulanate	3+0.1g IV 6 hourly
NB1: Re-evaluate patient at 48-72 hrs. If source dealt with by surgery (eg. closure of perforation and peritoneal lavage) and post-operative course uncomplicated by ongoing sepsis, then cease gentamicin and continue other drugs up a total duration of 5 days.		
NB2: If *Candida* species isolated from intraoperative specimen(s) consider addition of antifungal therapy as well (usually for 2 weeks).		

Management of cholecystitis or biliary sepsis

Causative organisms of acute cholecystitis are usually aerobic bowel flora (eg *Escherichia coli, Klebsiella* species and, less commonly, *Enterococcus faecalis*). Anaerobes are found infrequently, unless biliary obstruction is present. A laparoscopic cholecystectomy should be considered during the presenting admission.

Empiric treatment[1]

Regimen	Drug	Dose
1	ampicillin	1g IV 6 hourly
	gentamicin	4-6mg/kg (severe sepsis : 7mg/kg) for 1 dose, then determine dosing interval for a maximum of either 1 or 2 further doses based on renal function (see Tables 1 and 2)
	Special circumstances	
If biliary obstruction is present, to treat anaerobes **add**	metronidazole	500mg IV 12 hourly

Management of acute pancreatitis

Prophylaxis to prevent pancreatic infection is not recommended. Treatment of choice for infected necrosis is surgical debridement. Patients with severe pancreatitis may appear septic clinically at various times during a prolonged hospitalisation. Before giving antibiotics, it is best practice to perform image-guided percutaneous aspiration.

Empiric treatment[1]

Regimen	Drug	Dose
1	piperacillin /tazobactam	4+0.5g IV 8 hourly

Document History

Document	Version	Document development	Date
Draft ICU Guidelines for Empirical Antimicrobial Treatment	0.1-0.3	Modified by the QUAIC Expert Advisory Group from Draft July 6 2004 Recommendations for First Line Antibiotic Therapy in the ICU, Nepean Hospital	Sep 2009–Aug 2010
Draft	0.4-0.6	Modified based on feedback from the QUAIC Expert Advisory Group	Aug–Sep 2010
Draft	0.7-0.7a	Modified based on feedback from the QUAIC Expert Advisory Group and Therapeutic Guidelines: Antibiotic 14 2010	Oct 2010
Final	1.0	Additional material added and minor errors corrected	Nov 2010

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