SA Health

Hospital-acquired Pneumonia & Ventilator-associated Pneumonia (Adults) Clinical Guideline

Version 2.0

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Government of South Australia

SA Health

Disclaimer

This state-wide guideline has been prepared to promote and facilitate standardisation and consistency of practice, using a multidisciplinary approach. The guideline is based on a review of published evidence and expert opinion, with consideration to antibiotic resistance epidemiology in South Australia. In facilities where the prevalence of multi-resistant organisms may differ, local hospital guidelines may take precedence. Health practitioners in the South Australian public health sector are expected to review specific details of each patient and professionally assess the applicability of the relevant guideline to that clinical situation. If for good clinical reasons, a decision is made to depart from the guideline, the responsible clinician must document in the patient's medical record, the decision made, by whom and detailed reasons for the departure from the guideline.

This state-wide guideline does not address all the elements of clinical practice and assumes that the individual clinicians are responsible for:

- Discussing care with consumers in an environment that is culturally appropriate and which enables respectful confidential discussion. This includes the use of interpreter services where necessary,
- Advising consumers of their choice and ensure informed consent is obtained.
- Providing care within scope of practice, meeting all legislative requirements and maintaining standards of professional conduct and
- Documenting all care in accordance with mandatory and local requirements.

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Hospital-acquired Pneumonia & Ventilator-associated Pneumonia (Adults) Clinical Guideline

1. Name of guideline

Hospital-acquired Pneumonia & Ventilator-associated Pneumonia (Adults) Clinical Guideline

2. Introduction

This guideline has been developed by the South Australian expert Advisory Group on Antimicrobial Resistance (SAAGAR) to guide the management of hospital-acquired pneumonia (HAP) and ventilator-associated pneumonia (VAP) in immunocompetent patients. This guideline should not be used for the management of patients with pneumonia acquired in healthcare facilities such as aged-care facilities, haemodialysis centres, outpatient clinics, or for those hospitalised for more than 48 hours within the past three months (previously referred to as healthcare-associated pneumonia (HCAP)). Based on current available evidence, patients who would have previously been diagnosed with HCAP, are considered at low risk of harbouring multidrug-resistant (MDR) organisms [1, 2], and the majority of these patients can be managed as per the state-wide guideline for Community Acquired Pneumonia in adults.

Key stewardship points

- HAP is defined as a pneumonia occurring ≥ 48 hours after hospital admission that was **NOT** incubating at the time of admission
- For pneumonia occurring < 48 hours after hospital admission, refer to the state-wide guideline for Community Acquired Pneumonia in adults
- Review clinical radiologic and microbiological factors, and consider alternate diagnosis (e.g., atelectasis, heart failure, aspiration pneumonitis) prior to commencing the broad-spectrum antibiotics included in this guideline
- Assess severity of disease before commencing the recommended treatment for HAP
- Review therapy after 24-48 hours; cease antibiotics if an alternate diagnosis is made **OR** consider narrowing the spectrum of antibiotics if appropriate, based on microscopy, culture, and sensitivity
- Most cases of HAP and VAP can be treated effectively with 5-7 days of antimicrobial therapy

3. Background and aetiology

Bacterial HAP is an infection of the pulmonary parenchyma predominantly resulting from micro-aspiration of the bacteria colonising the oropharynx and upper gastrointestinal tract. HAP, by definition, develops in patients who have been admitted to hospital for more than 48 hours, and did not appear to be incubating at the time of admission [1, 3].

The aetiology of HAP is dependent upon the patient microbiome and is altered by duration of hospitalisation, exposure to antibiotics, local epidemiology, and patient characteristics [1, 2]. MDR organisms are associated with duration of inpatient stay and admission to an intensive care unit (ICU) [1, 3]. Critically ill patients become rapidly colonised with nosocomial pathogens and are at higher risk of infection with MDR organisms.

In patients at low risk of MDR pathogens (i.e., patients hospitalised in a low-risk ward for any duration or in a high-risk area (ICU / HDU, or areas with an identified resistance problem) for less than 5 days), the likely causative organisms are *Streptococcus pneumoniae* which is part of the usual respiratory flora, and less commonly, non-MDR Gram-negative bacilli such as *Klebsiella* species and *Escherichia coli* [4].

Patients with severe HAP/VAP or at high risk of MDR pathogens (i.e., prior intravenous antibiotic use within 90 days, patients who are hospitalised for greater than 5 days in a high-risk area (ICU / HDU, or those units with an identified resistance problem), acute renal replacement therapy prior to onset of VAP, acute respiratory distress syndrome (ARDS) preceding VAP [1, 3, 4]), may be associated with methicillin-resistant *Staphylococcus aureus* (MRSA) or MDR Gram-negative bacteria such as Enterobacteriaceae, *Pseudomonas aeruginosa,* and *Acinetobacter* species [4].

VAP is a form of HAP that develops in ICU patients who have been mechanically ventilated for at least 48 hours [3]. Intubation increases the risk of pneumonia because it interferes with the normal physiological defence mechanisms which help prevent bacterial contamination of the airways [4]. Importantly, by the time of VAP onset, patients may have already been extubated [5]. VAP is caused by similar pathogens to those in HAP, however, the aetiology of VAP can vary with location, so awareness of local epidemiology is useful [3].

Aspiration pneumonia that develops in patients who have been hospitalised for less than 48 hours can initially be treated as per CAP. If the patient has been hospitalised for more than 48 hours, treat as per HAP [4].

HAP caused by viruses or fungi are significantly less common, except in the immunocompromised patient [6].

4. Definitions and acronyms

ABW	Actual body weight
AGEP	Acute generalised exanthematous pustulosis
ARDS	Acute respiratory distress syndrome
BMI	Body mass index
BP	Blood pressure
CAP	Community acquired pneumonia
CBE	Complete blood exam
CrCl	Creatinine clearance
DRESS	Drug rash with eosinophilia and systemic symptoms
HAP	Hospital-acquired pneumonia – pneumonia that occurs ≥ 48 hours after admission and did not appear to be incubating at the time of admission
HCAP	Healthcare-associated pneumonia
HDU	High dependency unit
HR	Heart rate
IBW	Ideal body weight
ICU	Intensive care unit
ID	Infectious disease
IV	Intravenous
LDH	Lactate dehydrogenase
LFT	Liver function test

MDR	Multidrug-resistant
MER	Medical emergency response
PaO_2	Partial pressure of oxygen, measured by arterial blood gas
PCR	Polymerase chain reaction – viral diagnostic test
RR	Respiratory rate
SAAGAR	South Australian expert Advisory Group on Antimicrobial Resistance
SBP	Systolic blood pressure
SJS	Stevens-Johnson syndrome
SpO_2	Saturation of peripheral oxygen – an estimation of the oxygen saturation level in the blood measured with a pulse oximeter
TEN	Toxic epidermal necrolysis
VAP	Ventilator-associated pneumonia – pneumonia that develops ≥ 48 hours after endotracheal intubation

5. Diagnostic tests

Microbiological diagnosis in the setting of HAP is important for directing antimicrobial therapy. Lower respiratory tract secretions should be obtained from all patients and sent for Gram stain and culture; always correlate the results of culture with the Gram stain [1, 3]. Cultures of pulmonary secretions are prone to false positives and false negatives and may often represent colonisation, therefore, isolation of an organism from a pulmonary tract sample is not sufficient for a diagnosis of HAP [4, 6]. Collect two sets of blood cultures ideally before starting antibiotic therapy.

Some guidelines advocate the use of invasive sampling methods and quantitative culture methods but this has not been shown to improve clinical outcomes and should be reserved for immunocompromised patients [7] where early investigation for unusual pathogens (e.g., viruses or fungi) should be considered. Medical officers should refer to recommendations listed in the Therapeutic Guidelines (TG): *'Approach to pneumonia in immunocompromised patients'*.

Nosocomial transmission of influenza and respiratory viruses is well documented [8]. Identification of viral pathogens is critical to facilitate early treatment and prevent nosocomial transmission. PCR for respiratory viruses should be performed on sputum or deep nasopharyngeal swab [2].

6. Severity assessment of HAP/VAP

This guideline emphasises the importance of stratifying disease severity, and assessing risk of acquiring MDR organisms, to guide empiric therapy [1, 3, 4]. There are currently no validated severity assessment tools available, however, the *Therapeutic Guidelines: Antibiotic* defines **severe HAP** in patients presenting with any of the following features:

- Septic shock (see Appendix 1 'Assess HAP Severity')
- Respiratory failure, particularly if requiring mechanical ventilation
- Rapid progression of infiltrates on chest x-ray [4].

Whilst the *Therapeutic Guidelines: Antibiotic* no longer considers risk of MDR organisms when assessing the severity of HAP/VAP, SAAGAR recommend considering the risk of infection caused by MDR organisms,

in addition to the features listed above, when assessing the severity of disease. Patients who may be at risk of HAP/VAP caused by MDR organisms include:

- Prior intravenous antibiotic use within 90 days
- Patients who are hospitalised for greater than 5 days in a high-risk area (ICU / HDU, or those units with an identified resistance problem)
- Acute renal replacement therapy prior to onset of VAP
- Acute respiratory distress syndrome (ARDS) preceding VAP [1].

7. Antibiotic choice

This guideline was developed to guide empiric choice of antimicrobial therapy for HAP/VAP. Definitive therapy should be guided by microbiology results.

7.1 Mild to moderate HAP

Oral therapy is recommended for patients with mild to moderate HAP who are at low risk of MDR organisms [4]. If oral therapy is not tolerated, enteral administration can be considered – see MIMS Online "Don't Rush to Crush" for further information. Oral amoxicillin-clavulanic acid provides cover for community-based organisms, Gram-negative pathogens, and anaerobes [4]. For patients unable to tolerate either oral or enteral therapy, IV ceftriaxone may be used. Consider modifying therapy to narrow spectrum directed therapy based on microbiology results, and switch from IV to oral treatment as soon as the patient can tolerate oral therapy.
In the presence of moderate risk penicillin allergy, where it is safe to administer cephalosporins, cefuroxime is the preferred oral option compared to cefalexin or cefaclor because of it's superior antipneumococcal activity [4]. If IV therapy is required, IV ceftriaxone may be given.
In the presence of high risk penicillin or cephalosporin allergy, oral moxifloxacin (or IV if patient is unable to tolerate either oral or enteral therapy) may be given, however, it is recommended that ID / Microbiology consult is sought.

7.2 Severe HAP/VAP

In patients with severe illness or who are at high risk of MDR organisms, IV piperacillin-tazobactam may be used to ensure empiric activity against *Pseudomonas aeruginosa* and methicillin-sensitive *Staphylococcus aureus* (MSSA) [4].

IV cefepime may be used in patients with moderate penicillin allergy, and ciprofloxacin PLUS vancomycin in patients with high risk penicillin or cephalosporin allergy. ID / Microbiology advice is recommended when prescribing ciprofloxacin PLUS vancomycin.

7.3 Additional therapy in HAP/VAP

In all patients with HAP/VAP where there is suspected aspiration or recent thoraco-abdominal surgery, consider adding metronidazole to the cefepime, ceftriaxone, cefuroxime, and ciprofloxacin/vancomycin empirical regimens. Metronidazole is not necessary if the patient is receiving amoxicillin/clavulanic acid, moxifloxacin, or piperacillin/tazobactam, as these antibiotics provide adequate anaerobic cover.

7.4 Additional therapy in severe HAP/VAP

Septic shock
In patients with septic shock, the addition of vancomycin for MRSA cover and gentamicin for MDR Gram-negative bacteria to the empirical regimen should be considered [4].

Suspected staphylococcal pneumonia

If there is microbiological evidence suggestive of staphylococcal pneumonia (e.g., Gram-positive cocci resembling staphylococci identified on sputum Gram stain) or in patients colonised with MRSA, consider adding vancomycin.

Staphylococcus aureus is a major pathogen in the setting of HAP and MRSA will not be covered by piperacillin-tazobactam [1, 4].

Suspected Gram-negative pneumonia

If Gram-negative pneumonia is suspected (e.g., if Gram-negative bacilli are identified on blood culture or culture of lower respiratory tract samples obtained by more invasive methods, or in patients who have chronic suppurative lung disease and known respiratory colonisation with Gram-negative pathogens, such as *Pseudomonas aeruginosa*), consider adding gentamicin [4].

Therapy with gentamicin and vancomycin should be reviewed within 24-48 hours, and ceased if appropriate, based on the results of investigations [4].

Empiric treatment for patients with multiple antibiotic allergies or patients who are colonised with highly resistant bacteria, including MRSA, should be decided in collaboration with Infectious Diseases or Clinical Microbiology.

8. Duration of therapy

Many post-operative patients with shadowing on chest x-ray will represent post-operative atelectasis rather than pneumonia. This does not require antimicrobials and can be effectively treated with chest physiotherapy [4]. Antibiotics can be stopped in patients where an alternative aetiology of pulmonary infiltrate is likely (e.g., rapid improvement in clinical or radiology findings following diuresis).

Review clinical and microbiological status at 24-48 hours and change to directed therapy if a pathogen is identified with susceptibilities in the sputum culture. Switch to oral therapy once there is clinical improvement (refer to the IV to Oral Switch guideline for further information on switching to oral therapy).

In most cases, HAP and VAP can be treated effectively with 5 to 7 days of antimicrobial therapy. If a diagnosis of HAP/VAP is made, a total duration of antibiotics (IV and oral) of 5 days is the minimum recommended and antibiotic treatment should be reviewed at 5 days. Stopping antibiotic treatment should be considered on an individual basis if the patient is judged to be clinically stable at that time.

9. General considerations

9.1 Considerations in pregnancy and lactation

The aetiology of HAP in pregnancy includes the same causes as in the non-pregnant patient, however, aspiration during labour and delivery should be considered. Gram-negative rods including *Pseudomonas* species may also be more common causes of HAP in pregnancy [9].

In general, breastfeeding should not be discouraged because of maternal respiratory infection. The antibiotics included in the treatment recommendations in this guideline are considered safe in breastfeeding.

For more information, contact the Medicines Information Service at the Women's and Children's Hospital (WCH) on 8161 755 Monday to Friday 9.00 am to 5.00 pm.

9.2 Penicillin / cephalosporin hypersensitivity

Penicillin allergy is often misdiagnosed and there is increasing evidence that patients with an inaccurate allergy 'label' receive higher rates of broad-spectrum antibiotics [10]. Alternative antibiotic recommendations are included in this guideline for patients with moderate risk penicillin allergy (e.g., delayed rash which is not urticarial or DRESS / SJS / TEN / AGEP). The guideline also includes recommendations for patients with high risk penicillin or cephalosporin allergy (e.g., anaphylaxis, urticaria, angioedema, bronchospasm, DRESS / SJS / TEN / AGEP), however, it is recommended that expert advice should still be sought from an Infectious Diseases / Clinical Microbiology specialist.

For more information on the classification of penicillin and cephalosporin allergies, see *Appendix 2: Assessment of patients who report hypersensitivity to penicillins*, and refer to Penicillin and Cephalosporin Allergies.

10. Safety, quality and risk management

National Safety and Quality Health Service Standards

Clinical Governance	Partnering with Consumers	Preventing and Controlling Infections	Medication Safety	Comprehensive Care	Communicating for Safety	Blood Management	Recognising and Responding to Acute Deterioration
☐	☐	☒	☒	☐	☐	☐	☐

The following actions of the relevant standards are applicable:

Standard 3 – Preventing and Controlling Infections

- Actions 3.18, 3.19: Antimicrobial stewardship – The health service organisation has systems for the safe and appropriate prescribing and use of antimicrobials as part of an antimicrobial stewardship program.

Standard 4 – Medication Safety

- Action 4.01: Integrating clinical governance – Clinicians use the safety and quality systems from the Clinical Governance Standard when implementing policies and procedures for medication management, managing risks associated with medication management, and identifying training requirements for medication management.

11. Priniciples of the standard

National standard 3, *Preventing and Controlling Infections,* aims to reduce the risk to patients, consumers and members of the workforce of acquiring preventable infections; effectively manage infections, if they occur; prevent and contain antimicrobial resistance; promote appropriate prescribing and use of antimicrobials as part of antimicrobial stewardship; and promote appropriate and sustainable use of infection prevention and control resources.

National standard 4, *Medication Safety,* aims to ensure clinicians are competent to safely prescribe, dispense and administer appropriate medicines and to monitor medicine use. To ensure consumers are informed about medicines and understand their individual medicine needs and risk.

12. Associated policies / guidelines / clinical guidelines / resources

- For the management and treatment of pneumonia in individuals who are not in hospital, or who have been in hospital for less than 48 hours, refer to Community Acquired Pneumonia (Adults) Clinical Guideline.
- IV to Oral Switch Clinical Guideline for Adult Patients: Can Antibiotics S.T.O.P.

13. References

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14. Document Ownership

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15. Document History

Version	Date approved	Approved by	Amendment notes
V2	27/02/2023	Domain Custodian, Clinical Governance, Safety and Quality	Revised as per requirements - guideline has been developed by SAAGAR and approved by SAMAC.
V1	10/05/2018	10/05/2018	Original approved

16. Appendices

16.3 Appendix 1: Assessment & Treatment of HAP / VAP

MEETS DEFINITION OF HAP / VAP

Pneumonia: New pulmonary infiltrate with clinical evidence that the infiltrate is of an infectious origin (new onset fever > 38°C, purulent sputum, leucocytosis, decline in oxygenation).
HAP: Pneumonia occurring ≥ 48 hours after hospital admission that was NOT incubating at the time of hospital admission.
VAP: Pneumonia occurring ≥ 48 hours after endotracheal intubation.

URGENT INVESTIGATIONS

- Chest X-ray
- Electrolytes, urea, creatinine, glucose, LFTs
- CBE and differential
- SpO_2 and arterial blood gases if SpO_2 < 94% on room air
- Consider venous lactate

PRIOR TO ANTIBIOTICS, specimens should be sent for identification of causative organisms:

- Blood cultures (2 sets)
- Sputum Gram stain and culture (or lower respiratory tract secretion in intubated patients)
- Respiratory viral panel
- Consider urinary Legionella antigen and culture in ICU patients

Consult ID / Respiratory for:

- All patients with complicated pneumonia (empyema, lung abscess, parapneumonic effusion, haemoptysis, concurrent bacteraemia, necrotising pneumonia)
- Immunocompromised patients with severe HAP or those with significant immunosuppression (e.g., recent solid organ or haematopoietic transplant)
- Prior to commencing empiric antibiotic treatment for all patients who are colonised with MDR bacteria including MRSA and/or those at high risk of developing HAP/VAP caused by MDR pathogens (see *Severity assessment of HAP/VAP* section above for description)

Completion of investigations should not delay initiation of antibiotic therapy for a critically unwell patient

ASSESS HAP SEVERITY

Treat as severe HAP if any of the following are present (consult ID, consider MER call +/- ICU consultation if it matches the patient's goals of care):

- Hypotension (systolic BP ≤ 90 mmHg)
- Tachycardia (HR ≥ 100 beats/min)
- Tachypnoea (RR ≥ 22 breaths/min)
- Multi-lobar involvement &/or rapid progression of infiltrates on chest X-ray
- Oxygen saturation ≤ 92% on room air (or lower than baseline in patients with comorbid lung disease)
- Respiratory failure, particularly if requiring mechanical ventilation
- Poor peripheral perfusion or mottled skin
- Acute onset confusion
- HAP that develops while on pre-existing broad-spectrum antibiotic therapy (e.g., ceftriaxone)
- Hospitalised in ICU > 5 days
- Acute oliguria or elevated serum creatinine (above baseline)
- Elevated serum bilirubin (> 34 micromol/L)
- Low platelet count (< 100 x 10^9/L)
- Blood lactate concentration ≥ 2 mmol/L

TREATMENT – COMMENCE ANTIBIOTIC THERAPY ASAP

Note: Doses provided are for patients with normal renal function. See Appendix 4 for dose adjustments in renal impairment.
For further information on penicillin / cephalosporin allergies, see Appendix 2.

PENICILLIN / CEPHALOSPORIN HYPERSENSITIVITY LEGEND

No penicillin or cephalosporin allergy	Moderate risk penicillin allergy (e.g., delayed rash which is NOT urticarial or DRESS/SJS/TEN/AGEP)	High risk penicillin or cephalosporin allergy (e.g., anaphylaxis, angioedema, bronchospasm, urticaria, DRESS/SJS/TEN/AGEP)

Mild to moderate HAP (oral / enteral regimen)

Amoxicillin / clavulanic acid 875/125mg orally 12-hourly	**Cefuroxime** 500mg orally 12-hourly	**Moxifloxacin** 400mg orally daily (ID/Microbiology consult recommended)

Mild to moderate HAP (IV regimen)

Ceftriaxone 1g IV daily	**Ceftriaxone** 1g IV daily	**Moxifloxacin** 400mg IV daily (ID/Microbiology consult recommended)

If suspected aspiration or recent thoraco-abdominal surgery:
ADD metronidazole 400mg orally 12-hourly **OR** 500mg IV 12-hourly (only add to cefuroxime or ceftriaxone regimen^)

Switch to oral regimen once patient can take medicines via the oral or enteral route.

Severe HAP or VAP

Piperacillin / tazobactam 4.5g IV 6-hourly	**Cefepime** 2g IV 8-hourly	**Ciprofloxacin** 400mg IV 8-hourly PLUS **Vancomycin#** IV (ID/Microbiology consult recommended)

If in septic shock, ADD: **Gentamicin*** PLUS **Vancomycin#**

If Gram-positive cocci on sputum Gram stain **OR** MRSA colonised, ADD: **Vancomycin#**

If suspected Gram-negative pneumonia, ADD: **Gentamicin***

If suspected aspiration or recent thoraco-abdominal surgery:
ADD metronidazole 500mg IV 12-hourly (only add to cefepime or ciprofloxacin/vancomycin regimen^)

Switch to mild to moderate HAP (oral regimen) once there is clinical improvement.

Total duration of therapy (IV + oral) is 5 – 7 days

Review clinical and microbiology status within 24 to 48 hours:

- Cease therapy if an alternate diagnosis is made
- Narrow the spectrum of antibiotics to cover identified pathogens
- Switch to oral therapy as soon as clinically appropriate (refer to IV to Oral Switch guideline)

Gentamicin** 7mg/kg (ideal body weight¥) IV for the first dose if estimated CrCl > 60mL/min if in septic shock **OR** 4-5mg/kg (ideal body weight¥) IV for the first dose if estimated CrCl > 60mL/min if not in septic shock, then refer to the Aminoglycosides: Recommendations for Use, Dosing and Monitoring Clinical Guideline for subsequent doses. ***Review clinical and microbiology status after 24-48 hours and cease gentamicin if appropriate.

#**Vancomycin** 25mg/kg (actual body weight) IV loading dose (max. 3g), then refer to the Vancomycin Dosing and Monitoring in Adults Clinical Guideline for subsequent doses. ***Review clinical and microbiology status after 24-48 hours and cease vancomycin if appropriate.***

^Metronidazole is not necessary if the patient is receiving amoxicillin/clavulanic acid, moxifloxacin, or piperacillin/tazobactam, as these antibiotics provide adequate anaerobic cover.
¥Use ABW if less than patient's IBW. For obese patients (BMI 30-34kg/m²) use adjusted body weight, for BMI ≥ 35kg/m², seek expert advice.

16.4 Appendix 2: Assessment of patients who report hypersensitivity to penicillins

Therapeutic Guidelines

Suggested management of patients reporting hypersensitivity to penicillins in whom a beta-lactam antibiotic is the preferred drug

Penicillin hypersensitivity reported by a patient in whom a beta-lactam antibiotic is the preferred drug

History of immediate (IgE-mediated) penicillin hypersensitivity (typically occurs within 1 to 2 hours of drug exposure)

Immediate severe penicillin hypersensitivity (eg extensive urticaria, compromised airway, angioedema, hypotension, collapse or anaphylaxis)

Avoid penicillins and cephalosporins [NB1].

Safe to administer a non–beta-lactam antibiotic or aztreonam.

Can consider a carbapenem [NB2].

If a penicillin is essential, perform desensitisation.

In a non-urgent situation, consider specific allergy testing and drug provocation under specialist supervision (where such testing is available).

Immediate nonsevere penicillin hypersensitivity (eg mild urticaria or immediate rash)

Avoid penicillins.

Safe to administer most cephalosporins. Avoid cefalexin and cefaclor in patients with amoxicillin or ampicillin allergy.

Safe to administer a carbapenem [NB2] or aztreonam.

If a penicillin is essential, perform desensitisation.

In a non-urgent situation, consider specific allergy testing and drug provocation under specialist supervision (where such testing is available).

History of delayed (T-cell mediated) penicillin hypersensitivity (typically occurs days after starting treatment, but can occur more rapidly on rechallenge)

Delayed severe penicillin hypersensitivity (eg severe cutaneous adverse reaction [NB3] or significant organ involvement such as acute interstitial nephritis)

Avoid penicillins and cephalosporins [NB4].

Safe to administer a non–beta-lactam antibiotic or aztreonam.

Can consider a carbapenem [NB2].

Avoid desensitisation in patients with a history of delayed severe hypersensitivity because further drug exposure can be fatal.

Delayed nonsevere penicillin hypersensitivity (usually a maculopapular rash or benign childhood rash; **not** a severe cutaneous adverse reaction [NB3] and no significant organ involvement)

Avoid penicillins. However, in a non-urgent situation and under specialist guidance, consider a single dose of a penicillin followed by a prolonged (5 to 7 day) provocation test.

Safe to administer a cephalosporin in patients with a history of a mild reaction or a reaction that occurred in the distant past [NB5].

Safe to administer a carbapenem or aztreonam.

History of penicillin AND cephalosporin immune-mediated hypersensitivity

Avoid all beta lactams, except for aztreonam [NB6].

Refer to specialised antibiotic allergy testing centre.

History of non-immune-mediated adverse effect (eg gastrointestinal intolerance)

Safe to administer any beta lactam.

Remove penicillin allergy from the patient's medical record or annotate the true nature of the reaction.

Penicillins include: phenoxymethylpenicillin, benzylpenicillin, amoxicillin, ampicillin, dicloxacillin, flucloxacillin, piperacillin

Cephalosporins include: cefalexin, cefuroxime, cefaclor, cefazolin, cefalotin, cefoxitin, ceftriaxone, cefotaxime, ceftazidime, cefepime

Carbapenems include: imipenem, meropenem, ertapenem

NB1: In a critical situation, a cephalosporin can be considered in this group after undertaking a risk–benefit analysis and assessment of potential side-chain cross-reactivity. Seek expert advice.

NB2: In patients with penicillin hypersensitivity, the rate of immune-mediated cross-reactivity with carbapenems is approximately 1%; therefore, carbapenems can be considered in supervised settings. However, in patients with a history of a severe cutaneous adverse reaction (eg drug rash with eosinophilia and systemic symptoms [DRESS], Stevens–Johnson syndrome / toxic epidermal necrolysis [SJS/TEN], acute generalised exanthematous pustulosis [AGEP]), consider a carbapenem only in a critical situation when there are limited treatment options.

NB3: For example DRESS, SJS/TEN, AGEP.

NB4: There is limited evidence on the safety of cephalosporins in patients with a history of penicillin-associated acute interstitial nephritis (AIN). In a critical situation, directed therapy with a cephalosporin can be considered.

NB5: In patients who have had a **recent** reaction, consider avoiding cephalosporins with the same or similar R1 side-chain as the implicated penicillin.

NB6: However, avoid aztreonam in patients hypersensitive to ceftazidime; these drugs have the same R1 side-chain, so there is a risk of cross-reactivity.

16.5 Appendix 3: Calculating creatinine clearance

Ideal body weight estimation chart [4]

Height		Ideal body weight (kg)	
Cm	Feet & inches	IBW (female)	IBW (male)
155	5’1	48	53
160	5'3	53	57
165	5'5	57	62
170	5'7	62	66
175	5'9	66	71
180	5'11	71	75
185	6'1	75	80
190	6'3	80	84
195	6'4	84	89
200	6'6	89	93

IBW (female) = 45.5kg + 0.9kg per cm over 152cm

IBW (male) = 50kg + 0.9kg per cm over 152cm

Cockcroft-Gault equation for estimating creatinine clearance

$$\text{CrCl (mL/min)} = \frac{(140 - \text{age}) \times \text{IBW (kg)}^{\wedge} \times 0.85 \text{ (for females)}}{0.815 \times \text{SeCr (micromol/L)}}$$

^ Use actual body weight (ABW) if this is less than ideal body weight (IBW)

^ **If obese** (BMI ≥ 30 kg/m^2) consider using adjusted body weight (AdjBW) to calculate creatinine clearance [11]:

AdjBW = IBW + 0.4 x (ABW - IBW)

Note: Cautions when using Cockcroft-Gault equation:

- Muscle wasting – CrCl will be overestimated
- Acute renal failure – CrCl may represent non-steady state serum creatinine levels and may underestimate the level of renal impairment
- Elderly – CrCl can overestimate renal function in the elderly

16.6 Appendix 4: Medication dose adjustment recommendations in renal impairment [4, 12]

Drug	Adjustment
Amoxicillin / clavulanic acid oral	*CrCl <30ml/min:* 500mg/125mg oral 12-hourly
Cefepime IV	*CrCl 30-60ml/min:* 2g IV 12-hourly *CrCl 11-29ml/min:* 2g IV 24-hourly *CrCl <11ml/min:* 1g IV 24-hourly
Cefuroxime oral	*CrCl <10ml/min:* 500mg oral 24-hourly
Ciprofloxacin IV	*CrCl 31-50ml/min:* 400mg IV 12-hourly *CrCl 10-30ml/min:* 200mg IV 12-hourly **OR** 400mg IV 24-hourly *CrCl <10ml/min*: 400mg IV 24-hourly
Gentamicin IV – single dose Use IBW or ABW, whichever is less. For obese patients (BMI 30-34kg/m^2) use AdjBW – see Appendix 3. For BMI ≥35 kg/m^2, seek expert advice. Refer to the Aminoglycosides: Recommendations for Use, Dosing and Monitoring Clinical Guideline if further dosing is required.	*CrCl 40-60ml/min and severe sepsis:* 5mg/kg IV *CrCl 40-60ml/min no severe sepsis:* 4-5mg/kg IV *CrCl <40ml/min:* 4mg/kg IV
Piperacillin / tazobactam IV	*CrCl 20-40ml/min:* 4.5g IV 8-hourly *CrCl <20ml/min:* 4.5g IV 12-hourly
For dosing in dialysis patients, refer to the *Therapeutic Guidelines: Antimicrobial dosages for adults with impaired renal function.*	