

Policy Classification: I1-A2
Policy No.: CG296

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

Version No.: 1.0
Approval date: 10 May 2018



**Government
of South Australia**

SA Health

Disclaimer

This statewide 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 statewide 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.

Information in this statewide guideline is current at the time of publication. SA Health does not accept responsibility for the quality or accuracy of material on websites linked from this site and does not sponsor, approve or endorse materials on such links.

Contents

1.	Introduction.....	4
2.	Background and aetiology.....	4
3.	Definitions and acronyms.....	5
4.	Diagnostic tests.....	5
5.	Antibiotic choice.....	6
6.	Duration of therapy.....	6
7.	Pathway / Protocol.....	7
8.	General considerations.....	8
	> Considerations in pregnancy and lactation.....	8
	> Penicillin / cephalosporin hypersensitivity.....	8
9.	Safety, quality and risk management.....	9
10.	Principles of the standards.....	9
11.	Appendix – Calculating creatinine clearance.....	10
12.	References.....	11
13.	Document Ownership & History.....	11

INFORMAL COPY WHEN PRINTED

HAP & VAP (Adults) Clinical Guideline

1. Introduction

This guideline has been developed to guide the management of hospital-acquired pneumonia (HAP) and ventilator-associated pneumonia (VAP). This guideline should not be used for the management of patients with healthcare-associated pneumonia (HCAP) – see definition below. Based on current available evidence, patients with HCAP are considered at low risk of multidrug-resistant (MDR) organisms [1, 2]. The majority of patients with HCAP can be managed as per the statewide guideline for [Community Acquired Pneumonia](#) in adults, despite aspiration pneumonia being common in these patients due to stroke, neuromuscular disorders or impaired consciousness [3].

2. 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 admitted to hospital for > 48hours, and did not appear to be incubating at the time of admission [1, 4]. Aspiration pneumonia that develops in patients who have been hospitalised for less than 48 hours can generally be treated as per CAP, according to disease severity [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]. Extended duration of inpatient stay and admission to an Intensive Care Unit (ICU) is associated with an increased risk of infection with MDR organisms [1, 4]. Critically ill patients become rapidly colonised with nosocomial pathogens and are at higher risk of infection with MDR organisms.

VAP is a form of HAP that develops in ICU patients who have been mechanically ventilated for at least 48 hours [4]. Intubation increases the risk of pneumonia because it interferes with the normal physiological defence mechanisms which help prevent bacterial contamination of the airways [3].

In order to rationalise empiric antibiotic therapy and ensure patients at high risk of MDR pathogens receive appropriate therapy, patients can be stratified into risk groups [1]. Those at low risk of MDR organisms include patients hospitalised in a low-risk ward for any duration or in a high-risk area (ICU, high dependency, or areas with an identified resistance problem) for less than 5 days [3]. Patients at high risk of MDR pathogens include patients who are hospitalised for greater than 5 days in a high-risk area (ICU, high dependency, or those units with an identified resistance problem) [1, 3, 4].

In patients at low risk of MDR pathogens, the likely causative organisms are *Streptococcus pneumoniae* and non-multidrug resistant Gram-negative bacilli such as *Klebsiella* species and *Escherichia coli* [3]. *Staphylococcus aureus* and *Pseudomonas aeruginosa* are common causes of VAP or severe HAP [1, 3, 4].

Nosocomial pneumonia due to viruses or fungi is significantly less common, except in the immunocompromised patient [5].

3. Definitions and acronyms

BMI	Body Mass Index
BP	Blood Pressure
CBE	Complete Blood Exam
CrCl	Creatinine Clearance
DRESS	Drug rash with eosinophilia and systemic systems
GPC	Gram positive cocci
HAP	Hospital-acquired pneumonia - pneumonia that occurs \geq 48 hours after admission and did not appear to be incubating at the time of admission
HCAP	Healthcare-associated pneumonia – pneumonia acquired in healthcare facilities such as aged care facilities, haemodialysis centres, outpatient clinics or during a hospitalisation within the past three months
HDU	High dependency unit
ICU	Intensive care unit
ID	Infectious Disease
IV	Intravenously
LDH	Lactate dehydrogenase
LFT	Liver Function Test
MDR	Multidrug-Resistant
MER	Medical Emergency Response
MIC	Minimum Inhibitory Concentration
PaO ₂	Partial pressure of oxygen, measured by arterial blood gas
PCR	Polymerase chain reaction – viral diagnostic test
PO	Per oral
SJS/TEN	Stevens-Johnson Syndrome / Toxic Epidermal Necrolysis
SpO ₂	Saturation of peripheral oxygen – an estimation of the oxygen saturation level in the blood measured with a pulse oximeter
TDS	Three times daily
VAP	Ventilator-associated pneumonia – HAP that develops \geq 48 hours after endotracheal intubation

4. Diagnostic tests

Microbiological diagnosis in the setting of HAP is important for directing antimicrobial therapy and lower respiratory tract secretions should be obtained from all patients and sent for Gram stain and culture [1, 4]. Some guidelines advocate the use of invasive sampling methods and quantitative culture methods but this has not been shown to improve clinical outcomes. Blood cultures in the setting of HAP may only yield a result in 25% of cases but should be collected in febrile patients as positive results may change management [1].

Nosocomial transmission of influenza and respiratory viruses is well documented [6]. 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].

5. Antibiotic choice

This guideline was developed to guide empiric choice of antimicrobial therapy. Definitive therapy should be guided by microbiology results. The guideline acknowledges the importance of risk stratification tools to predict MDR organisms and guide empiric therapy [1, 3, 4].

Oral therapy is recommended for patients with mild to moderate HAP who are at low risk of MDR organisms [3]. Oral amoxicillin-clavulanic acid provides cover for community-based organisms, Gram-negative pathogens and anaerobes [3]. For patients unable to tolerate oral therapy, IV amoxicillin-clavulanic acid may be used. Alternatively, if IV amoxicillin-clavulanic acid is not available, or if the patient has a history of moderate-risk penicillin allergy (delayed rash which is not urticarial or DRESS / SJS / TEN), IV ceftriaxone will provide a similar spectrum of cover to amoxicillin-clavulanic acid. As ceftriaxone does not have anaerobic activity, the addition of metronidazole is required for patients with suspected aspiration pneumonia [3]. 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.

Patients with severe illness or who are at high risk of MDR organisms should receive intravenous piperacillin-tazobactam in combination with gentamicin to ensure empiric activity against *Pseudomonas aeruginosa* and methicillin-sensitive *Staphylococcus aureus* [3]. The addition of gentamicin provides empiric cover against AmpC beta-lactamase producing organisms, such as *Enterobacter species* that may not be effectively treated with piperacillin-tazobactam [1].

Vancomycin should be considered for patients colonised with methicillin-resistant *Staphylococcus aureus* (MRSA) and is recommended for MRSA colonised patients with Gram-positive cocci resembling staphylococci seen on Gram stain and those with severe sepsis. *Staphylococcus aureus* is a major pathogen in the setting of HAP and MRSA will not be covered by piperacillin-tazobactam [1, 3].

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.

6. Duration of therapy

Many post-operative patients will have radiological changes which represent post-operative atelectasis rather than pneumonia. This does not require antimicrobials and can be effectively treated with chest physiotherapy [3]. Review clinical and microbiological status at 48 hours. 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).

HAP and VAP can be effectively treated with 5-7 days of antimicrobial therapy. Longer treatment courses have not been associated with superior outcomes [1, 4]. A Cochrane review which included 6 randomised trials and enrolled 508 patients with HAP/VAP compared durations of therapy, and concluded there was no significant difference in mortality, treatment failure, length of stay or duration of mechanical ventilation, in patients who received shorter courses (7-8 days) compared to longer courses (10-15 days) [7]. Patients treated with short course therapy had more antibiotic free days in the 28 days from onset of illness (mean difference 4.0 days; 95% CI: 2.3 – 5.8 days)[7].

The Cochrane review reported that in the subgroup of patients with infection caused by non-glucose-fermenting Gram negatives, including *Pseudomonas species*, recurrence was higher when treated with short course therapy [7]. A subsequent meta-analysis however demonstrated no significant difference in recurrence rates in patients with *Pseudomonas aeruginosa* VAP treated with short-course therapy [1]. Five to seven days of antimicrobial therapy is therefore recommended for all patients with HAP/VAP regardless of aetiology.

7. Pathway / Protocol

Suspected Hospital Acquired Pneumonia / Ventilator-associated pneumonia

Definition of HAP or VAP:

- > Pneumonia → New pulmonary infiltrate WITH evidence that the infiltrate is of an infectious origin (new onset fever, purulent sputum, leucocytosis, increased oxygen requirement)
- > HAP → Pneumonia occurring ≥ 48 hours after hospital admission that was NOT incubating at the time of the hospital admission
- > VAP → Pneumonia occurring ≥ 48 hours after endotracheal intubation

Urgent Investigations

- > Chest X-ray
- > CBE & differential
- > Electrolytes, urea, creatinine, glucose, LFTs
- > SpO₂ & arterial blood gases if SpO₂ < 94% on air
- > Consider venous lactate

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

- > Blood cultures (2 sets)
- > Sputum (or lower respiratory tract secretion in intubated patients) Gram stain and culture
- > Nasopharyngeal swab in viral transport medium or sputum for respiratory viral PCR
- > Consider urinary Legionella antigen & culture in ICU patients

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

Assess risk of multidrug-resistant (MDR) pathogens & severity of infection

- > **LOW RISK MDR pathogens**
 - Hospitalised in a low risk (general ward) for any duration, OR
 - Hospitalised in ICU / HDU ≤ 5 days
- > **HIGH RISK MDR pathogens**
 - Hospitalised in ICU / HDU > 5 days
 - Prior intravenous antibiotic use within 90 days
 - Acute renal replacement therapy prior to onset of VAP
 - Acute Respiratory Distress Syndrome preceding VAP
- > **CRITERIA FOR SEVERE HAP**
 - Systolic BP ≤ 90 mmHg
 - Multi-lobar chest X-ray involvement
 - Respiratory rate:
 - Age ≤ 50 yrs: ≥ 25 breaths / min
 - Age > 50 yrs: ≥ 20 breaths / min
 - Tachycardia (Heart rate ≥ 125 bpm)
 - Confusion (new onset)
 - Acute hypoxia:
 - Age ≤ 50 yrs: PaO₂ < 70mmHg or SpO₂ ≤ 93%
 - Age > 50 yrs: PaO₂ < 60mmHg or SpO₂ ≤ 90%
 - pH (arterial) < 7.35
 - Lactate ≥ 2mmol/L

Consult ID / Micro & consider ICU review if above criteria met

Treatment – Commence antibiotic therapy ASAP

Note: Doses provided are for patients with normal renal function

Refer to Therapeutic Guidelines: Antibiotic or AMH for dosing adjustment in renal impairment

Low risk of MDR pathogens / Mild to Moderate HAP

(Total suggested antibiotic duration: **5 days**)

Amoxicillin / clavulanic acid 875mg/125mg orally 12-hourly

OR if unable to tolerate oral therapy:

Amoxicillin / clavulanic acid 1.2g IV 8-hourly (ID/micro approval required after 48 hours)

If IV amoxicillin / clavulanic acid unavailable:

Use **Ceftriaxone** 1g IV daily

PLUS if suspected aspiration or recent thoraco-abdominal surgery:

ADD **Metronidazole** 400mg orally 12-hourly
OR 500mg IV 12-hourly

High risk of MDR pathogens / Severe HAP/VAP

(Total suggested antibiotic duration: **5-7 days**)

Piperacillin / tazobactam 4.5g IV 6-hourly PLUS

Gentamicin 5mg/kg (ideal body weight) **single dose**

PLUS if severe sepsis or MRSA colonised or Gram positive cocci on sputum Gram stain

ADD **Vancomycin** 25mg/kg IV (actual body weight) **loading dose** (max 3g).

Continue vancomycin for 24 hours until microbiology results available (Refer to Vancomycin Dosing and Monitoring guidelines for subsequent dosing). If vancomycin contraindicated, contact ID/Micro

Moderate risk penicillin allergy (delayed rash which is not urticarial or DRESS / SJS / TEN)

Replace amoxicillin / clavulanic acid with:

Cefuroxime 500mg orally twice daily

OR if unable to tolerate oral therapy:

Ceftriaxone +/- Metronidazole (as above)

Replace piperacillin / tazobactam with:

Cefepime 2g IV 8-hourly

PLUS if suspected aspiration or recent thoraco-abdominal surgery

ADD **Metronidazole** 500mg IV 12-hourly

High risk penicillin / cephalosporin allergy: History suggestive of high risk (e.g. anaphylaxis, urticaria, angioedema, bronchospasm, DRESS / SJS / TEN)

Consult ID or Microbiology

Review clinical & microbiology status at 48 hours:

- > Cease therapy if an alternate diagnosis is made
- > Narrow the spectrum of antibiotics to cover identified pathogens
- > Switch to oral therapy once there is clinical improvement (Refer to [IV to Oral Switch guideline](#))

8. General considerations

> 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[8].

In general, breastfeeding should not be discouraged because of maternal respiratory infection. The antibiotics included in the HAP Pathway/Protocol are considered safe in breastfeeding.

For more information contact Medicines Information at WCH on 81617222 Monday to Friday 09:00-17:00.











> 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 [9]. Alternative antibiotic recommendations are included in this guideline for patients with moderate risk penicillin allergy (delayed rash which is not urticarial or DRESS / SJS / TEN). For patients with a history suggestive of high risk (e.g. anaphylaxis, urticarial, angioedema, bronchospasm, DRESS / SJS / TEN), expert advice on antibiotic treatment should be sought from an Infectious Diseases / Clinical Microbiology specialist.

For more information on the classification of penicillin / cephalosporin allergies, refer to: <https://www.allergy.org.au/health-professionals/papers/ascia-penicillin-allergy-guide-for-health-professionals>

9. Safety, quality and risk management

National Safety and Quality Health Service Standards

									
National Standard 1	National Standard 2	National Standard 3	National Standard 4	National Standard 5	National Standard 6	National Standard 7	National Standard 8	National Standard 9	National Standard 10
Governance for Safety and Quality in Health Care	Partnering with Consumers	Preventing & Controlling Healthcare associated infections	Medication Safety	Patient Identification & Procedure Matching	Clinical Handover	Blood and Blood Products	Preventing & Managing Pressure Injuries	Recognising & Responding to Clinical Deterioration	Preventing Falls & Harm from Falls
<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

The following criteria of the relevant standards are applicable:

- > Criteria 3.15 – Antimicrobial stewardship: Providing access to, and promotion of, current evidence-based Australian therapeutic guidelines and resources on antimicrobial prescribing.
- > Criteria 4.1 – 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.

10. Principles of the standards

National standard 3, *Preventing and controlling healthcare associated infections*, aims to reduce the risk of patients acquiring preventable healthcare-associated infections, effectively manage infections if they occur, and limit the development of antimicrobial resistance through prudent use of antimicrobials as part of antimicrobial stewardship

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

11. Appendix – Calculating creatinine clearance

Ideal body weight estimation chart

Height		Ideal body weight (kg)	
Feet & inches	Cm	IBW (female)	IBW (male)
5'1	155	48	53
5'2	157	50	55
5'3	160	53	57
5'4	163	55	60
5'5	165	57	62
5'6	168	60	64
5'7	170	62	66
5'8	173	64	69
5'9	175	66	71
5'10	178	69	73
5'11	180	71	76
6'0	183	73	78
6'1	185	76	80
6'2	188	78	82
6'3	191	80	85
6'4	193	82	87
6'5	196	85	89
6'6	198	87	92

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

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

Adapted from Therapeutic Guidelines: Antibiotic (v15, 2014)

Cockcroft-Gault equation for estimating creatinine clearance

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

[^] Use Actual Body Weight (ABW) if this is LESS than IBW

[^] If obese (ABW is $\geq 30\%$ above IBW or **BMI** $> 30 \text{ kg/m}^2$) consider using adjusted body weight (AdjBW) to calculate creatinine clearance [10]:

$$\text{Adjusted Body Weight (AdjBW)} = \text{IBW} + 0.4 \times (\text{Actual Body Weight} - \text{IBW})$$

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

12. References

1. Kalil, A.C., et al., *Management of Adults With Hospital-acquired and Ventilator-associated Pneumonia: 2016 Clinical Practice Guidelines by the Infectious Diseases Society of America and the American Thoracic Society*. Clinical Infectious Diseases, 2016. **63**(5): p. e61-e111.
2. Kollef, M., *UpToDate: Clinical presentation and diagnosis of ventilator-associated pneumonia*. 2017: [www.uptodate.com]. Accessed 02 Oct 2017
3. Antibiotic Expert Group, *Therapeutic Guidelines: Antibiotic (version 15)*. 2014: Melbourne.
4. Torres, A., et al., *International ERS/ESICM/ESCMID/ALAT guidelines for the management of hospital-acquired pneumonia and ventilator-associated pneumonia* Eur Respir J, 2017. **50**: p. 1700582 [<https://doi.org/10.1183/13993003.00582-2017>]
5. File, T.M., Jr., *UpToDate: Epidemiology, pathogenesis, microbiology and diagnosis of hospital-acquired and ventilator-associated pneumonia in adults* 2017: [www.uptodate.com]. Accessed 08 Nov 2017
6. Macesic, N., et al., *Hospital-acquired influenza in an Australian sentinel surveillance system* Med J Aust, 2013. **198** (7): p. 370-2.
7. Pugh, R., et al., *Short-course versus prolonged-course antibiotic therapy for hospital-acquired pneumonia in critically ill adults*. Cochrane Database of Systematic Reviews, 2015 (8): p. CD007577.
8. Larson, L., R. Powrie, and T. File, *Treatment of respiratory infections in pregnant women*. In: *Berghella, V, Bartlett, JG (eds). UpToDate*. 2017: [www.uptodate.com].
9. Chen, J. and D. Khan, *Evaluation of penicillin allergy in the hospitalized patient: Opportunities for antimicrobial stewardship* Curr Allergy Asthma Rep 2017. **17**(6): p. 40
10. Winter, M., K. Guhr, and B. Berg, *Impact of various body weights and serum creatinine concentrations on the bias and accuracy of the Cockcroft-Gault equation* Pharmacotherapy, 2012. **32**(7): p. 604 -12.

13. Document Ownership & History

Document developed by: Infection Control Service, CDCB
File / Objective No.: A780270
Next review due: 10/05/2022 (usually 1-5 years' time)
Policy history: Is this a new policy (V1)? **Y**
 Does this policy amend or update an existing policy? **N**
 Does this policy replace another policy with a different title? **N**

ISBN: 978-1-76083-004-5

Approval Date	Version	Who approved New/Revised Version	Reason for Change
10/05/2018	V1	Safety & Quality Strategic Governance Committee	New guideline