Safer Care Victoria

Maternal Sepsis

Clinical guidance

OFFICIAL

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Contents

Key messages

- Sepsis is one of the leading causes of maternal deaths in Australia.[1]
- This guideline provides an evidence-based guide for clinical staff to identify and manage suspected or confirmed sepsis in pregnant women, from 16 weeks gestation to around 2 weeks postpartum.
- It focuses on ensuring prompt diagnosis, appropriate investigations and antibiotic therapy.
- It has been developed to guide initial diagnosis and management, for health services to adapt as required.

Acknowledgement

This guidance uses the terms ‘woman’ and ‘mother,’ which are intended to be inclusive of anyone who may use other self-identifying terms and aims to encompass all for whom this guidance is relevant.

Consumer Engagement Statement

All interactions between health care staff with consumers (women, mothers, patients, carers and families) should be undertaken with respect, dignity, empathy, honesty and compassion.

Health care staff should actively seek and support consumer participation and collaboration to empower them as equal partners in their care.

Definitions/abbreviations

Term	Definition
CPOs (carbapenem resistant organisms)	Bacteria that have developed resistance to several first line antibiotics, including carbapenems
CSU	Catheter specimen of urine
DBP	Diastolic blood pressure
ESBL (extended spectrum beta lactamase)	Gram negative organisms resistant to treatment with many beta lactam antibiotics
FiO_2	Fraction of inspired oxygen
Group A streptococcus (GAS) infection	Also known as *Streptococcus pyogenes*
HVS	High vaginal swab
LVS	Low vaginal swab
MAP	Mean arterial pressure

Term	Definition
MAP	Mean arterial blood pressure Diastolic BP + 1/3 (systolic BP – diastolic BP)
MROs (multi-resistant organisms)	Organisms that are resistant to first line antimicrobials
MRSA (methicillin-resistant *Staphylococcus aureus)*	*Staphylococcus aureus* that is resistant to methicillin/ flucloxacillin
MSU	Midstream urine
PaO_2	Partial pressure of oxygen (assessed with arterial blood gas)
Puerperal sepsis	Peripartum sepsis resulting from the genitourinary tract
SBP	Systolic blood pressure
Sepsis	Sepsis is a life-threatening condition that arises when the body's response to an infection damages its own tissues and organs
Septic shock	Sepsis with associated circulatory, cellular and metabolic abnormalities (including hypotension, requiring volume resuscitation, elevated lactate and renal impairment) that has a greater risk of mortality than sepsis alone

Local health service adaptation

The specific areas that may need local adaptation are:

- Pathways of escalation, including the availability of senior staff, of expertise in infectious diseases and when intra- or inter-hospital transfer is required.
- Choice of antibiotics depending on local conditions – this is particularly relevant for aminoglycosides. Regimens have been provided for gentamicin, tobramycin and amikacin.

Background

Sepsis is a life-changing event. Serious maternal illness may be disruptive to the woman's passage to motherhood, establishment of breastfeeding and her ongoing connection to her baby.

Clinicians should provide open and consistent communication with the woman (when feasible) and her support people.

Common causes of sepsis in this cohort are:

- Septic abortion, chorioamnionitis, pneumonia/influenza, pyelonephritis, wound infection, mastitis, endometritis. (with or without retained products of conception)
- *E. coli* is the most common cause of maternal bacterial infection. The most frequent cause of maternal death from sepsis is infection with *Group A streptococcus (GAS) species*. Invasive GAS infection typically manifests as sepsis, endomyometritis, cellulitis, necrotising fasciitis, or toxic shock syndrome.

Recognising sepsis

Recognition of sepsis is a critical first step in appropriate assessment and management.

In pregnancy, diagnosis may be more difficult because physiological changes associated with pregnancy and/or labour may mimic the signs of sepsis (e.g. elevated heart rate and respiratory rate, lower blood pressure, raised white blood cell count, increased lactate during labour).

This guidance utilises a modification of the California Maternal Quality Care Collaborative (CMQCC) 2020 screening criteria.[2] The CMQCC reports fewer missed cases with fewer false positives, compared with other screening tools.

Support for ongoing breastfeeding or assistance with expressing of breast milk, in keeping with the woman's wishes, should be offered.

Women and their families should be informed that they have/had a diagnosis of sepsis and provided with appropriate opportunities for information provision and debriefing.

Initial sepsis screen

Recognise

Consider sepsis if the woman has any of the following:

Fevers and rigors	-
Neurological	• altered conscious state • headache • neck stiffness • agitation
Poor peripheral perfusion	• cool peripheries • delayed capillary refill time or mottled skin
Chest	• cough • shortness of breath
Abdomen	• pain/tenderness • peritonism • diarrhoea • vomiting
Malodorous vaginal discharge	-
Urine	• dysuria • frequency • flank pain
Skin and soft tissue	• cellulitis • mastitis
Wound erythema or discharge	-

Line insertion sites	• erythema • pain • swelling • discharge
AND - Two or more of	• temperature < 36°C or > 38°C • respiratory rate > 24 per minute sustained for 15 minutes • heart rate > 110 sustained for 15 minutes • WCC 15 × 109 or < 4 × 109 or > 10% immature neutrophils (bands) (Diagnosis of sepsis should not be delayed while waiting for results. A white blood cell count that has been obtained within 24 hours can be used for the initial screen
OR	• MAP < 65 mmHG

If the initial sepsis screen is positive and there is clinical suspicion or evidence of infection, start treatment.

Respond

Oxygen	• Continuous oximetry • Administer supplementary oxygen to maintain SpO2 > 95%
IV access	• Insert 2 × large bore peripheral cannula
Investigations	• FBE, U&Es, LFTs, INR, APTT • Venous blood gas for lactate • Two sets of anaerobic and aerobic blood cultures
Observations	• Heart rate and blood pressure every 15 minutes for the first hour, then according to local guidance depending on degree of physiological disturbance • Document on Maternal Observations and Response Chart (MORC)
Antibiotics	• Complete intravenous antibiotic administration within 60 minutes of presentation • Refer to Table 1 for empiric antibiotic recommendations where source is chorioamnionitis or unknown • Refer to Therapeutic Guidelines – Antibiotic where the source of infection is known • Refer to Table 2 for additional antibiotic considerations • Refer to Table 3 for administration guidance
Source screening ***Do not delay antibiotic treatment for culture collection.***	• Investigations as determined by clinical assessment of likely source of infection: ○ midstream urine (MSU)/catheter specimen of urine (CSU) ○ high vaginal (HVS) / low vaginal (LVS) / endocervical swab for microscopy/culture/sensitivities (MCS) ○ sputum MCS ○ chest x-ray ○ nasal/ throat swabs for extended panel respiratory viruses multiplex PCR, including COVID-19 ○ wound swab for MCS ○ cultures from lumens of central lines ○ stool testing for faecal multiplex PCR including C. difficile ○ breast milk MCS
Fluid management	• Fluid resuscitation if systolic BP < 90 mmHg (or if lactate ≥ 2 mmol/L in the absence of labour) ○ stat fluid bolus of 500 mL of IV crystalloid, i.e. 0.9% sodium chloride; then further 500 mL STAT if required. Be aware of comorbidities, e.g. cardiac or respiratory disease, that may make fluid overload more likely ○ monitor for fluid overload ○ escalate if no improvement in SBP after 1L of IV fluid. ○ insert IDC with hourly measure ○ monitor urine output hourly ○ escalate if urine output < 20 mL/hr.
Fetal considerations	• Consider fetal surveillance if appropriate for the gestation of the pregnancy. • Consider urgent birth if chorioamnionitis is suspected. At pre- or peri-viable gestations, delivery may be required for maternal wellbeing. • If pre-term birth is likely, give corticosteroids according to local protocol. Maternal health is the priority rather than fetal lung maturity. • Consider contacting PIPER for further advice on 1300 137 650.
Escalate	• Involve senior staff – consider anaesthetics, medical teams, ICU, ED or ARV in line with local escalation procedures • Consider transfer to a higher acuity ward or a higher maternity capability level service.

Confirmation of sepsis

Further tests: These tests/observations may be useful for considering care setting including transfer to a higher level of care or downgrading care. They will not be required for all women and should be undertaken in consultation with senior clinicians.

Measure	Criteria (any one is diagnostic)
Respiration PaO/FiO_2	• Acute respiratory failure as evidenced by acute need for invasive or non-invasive mechanical ventilation **or** • PaO_2/FiO_2 < 300
Coagulation (FBE, INR, APTT)	• Platelets < 100 × 10^9/L **or** • INR > 1.5 **or** • PTT > 60 seconds < 100
Liver (LFT)	• Bilirubin > 30 µmol/L
Cardiovascular	• Persistent hypotension after fluid administration: ○ SBP < 85 mmHg **or** MAP < 65 mmHg **or** BP > 40 mmHg decrease in SBP
Renal (U&E, urine output)	• Serum creatinine > 100 µmol/L **or** • Doubling of creatinine **or** • Urine output < 0.5 mL/kg/hour (for 2 hours)
Mental status assessment	• Agitation, confusion, or unresponsiveness
Lactic acid	• > 2 mmol/L in the absence of labour

Ongoing management

Measure	Criteria (any one is diagnostic)
Reassess management	• The woman requires close observation and re-evaluation • Perform targeted history, examination and investigations to elicit cause of sepsis • Review any modifications to reportable observations / MET criteria • Inform senior staff and document discussion and assessment in medical records • Ensure clinical handover includes sepsis history • Review all antibiotics and de-escalate as appropriate.
General measures	• Consider need for anticoagulation • Consider use of antipyretics • Source control

Antibiotic prescribing and administration

1. **Prescribe** antibiotics

- Unknown source or chorioamnionitis This regimen is for **initial** intravenous doses for **sepsis/septic shock** and should be used for all women to minimise delays to administration (Table 1).
- Known source: According to Therapeutic Guidelines[3] or local guidelines.
- Also consider additional risk factors (Table 2).

2. **Administer** complete dose of antibiotics within 60 minutes of consideration of sepsis

- In the setting of a **critically unwell woman**, antibiotics can safely be given at faster rates than in usual practice and multiple antibiotics can be given concurrently, intravenously at different sites[4] (Table 3). Hospital protocols will dictate administration method of choice – e.g. syringe pump, slow push.

3. **Seek pharmacist/infectious diseases advice** for ongoing maintenance dosing, including in the setting of renal impairment or obesity.

4. Aminoglycosides:

- Each hospital should choose a single agent from gentamicin, amikacin or tobramycin, in consultation with local expertise and then use that agent consistently (Table 1).

Additional considerations

- Abnormal temperature and elevated heart rate may be the most common combination, however not all women with sepsis will have a fever at ≥ 38.0°C.
- Maternal corticosteroid administration often increases the white blood cell count, but the suspicion for infection should not be discounted without further evaluation. White blood cell values peak 24 hours after administration and return close to baseline values by 96 hours after administration.

Summary flow chart

Think sepsis if any 2 of the following are present:

- Temperature < 36°C or ≥ 38°C
- Heart rate > 110 for at least 15 minutes
- Respiratory rate > 24 per minute for at least 15 minutes
- White cell count > 15×10^9 or < 4×10^9
- MAP < 65 mmHg
- Clinical suspicion of sepsis

Call for help flowchart

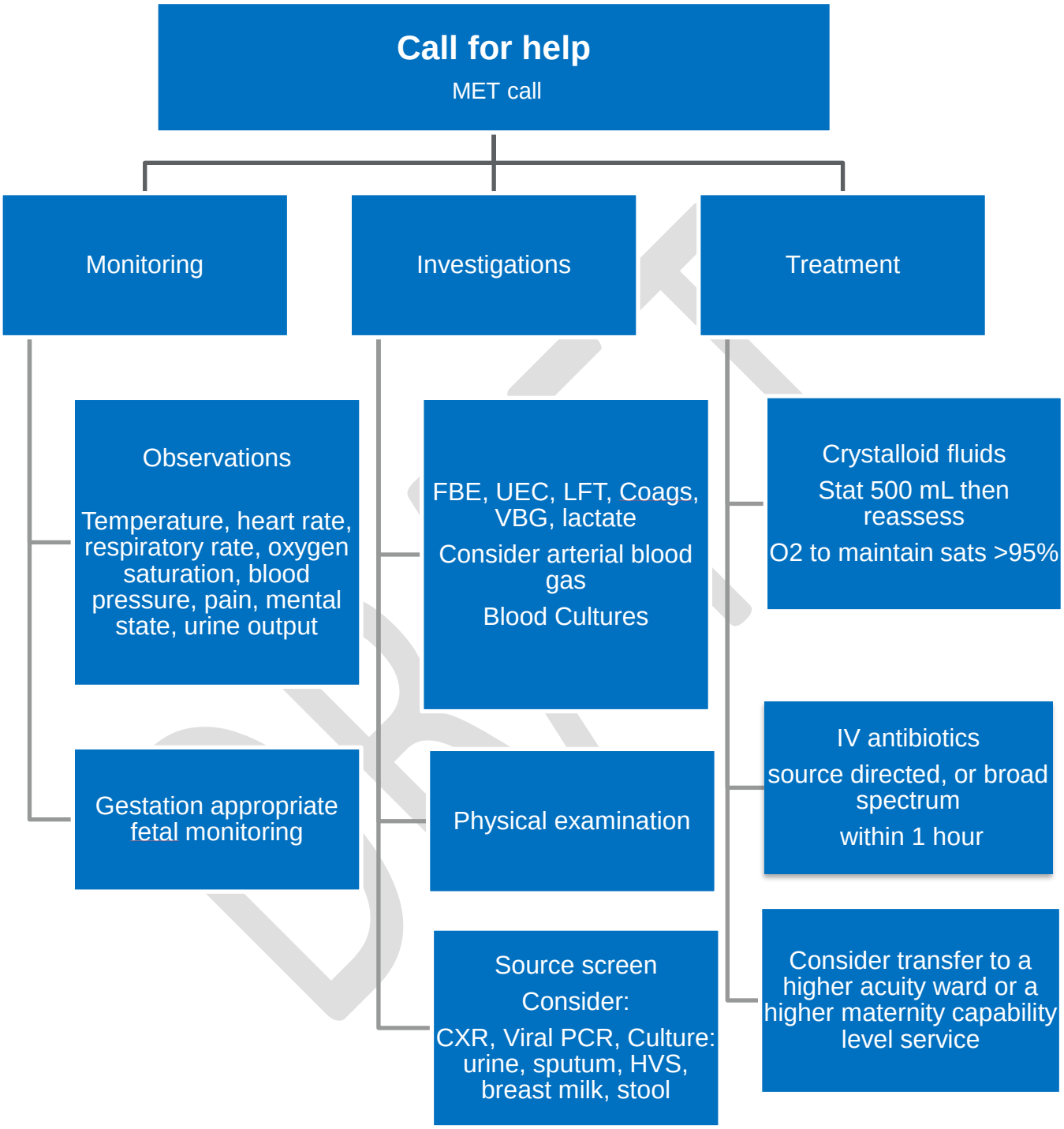

Table 1: Antibiotic recommendations: Unknown source of infection or chorioamnionitis

Indication	No penicillin allergy	Non-severe penicillin hypersensitivity (No features of immediate or delayed severe hypersensitivity e.g., childhood rash, nausea or vomiting)	Severe penicillin hypersensitivity Includes immediate hypersensitivity with urticarial, angioedema, hypotension, collapse, anaphylaxis, or delayed hypersensitivity with severe cutaneous reaction e.g. DRESS or SJS
Community-acquired sepsis **[Infection present before admission]**	Aminoglycoside IV THEN Amoxicillin 2 g IV, 6 hourly PLUS Metronidazole 500 mg IV, 12 hourly	Aminoglycoside IV THEN Cefazolin 2 g, IV, 6 hourly PLUS Metronidazole 500 mg, IV 12 hourly	Aminoglycoside IV THEN Metronidazole 500 mg, IV 12 hourly PLUS vancomycin
Hospital-acquired sepsis **[Infection acquired as a direct or indirect result of healthcare]**	Piperacillin/ tazobactam 4.5 g IV, 6 hourly	Aminoglycoside IV THEN Cefazolin 2 g, IV, 6 hourly PLUS Metronidazole 500 mg IV 12 hourly	Aminoglycoside IV, THEN Vancomycin IV PLUS Metronidazole 500 mg IV 12 hourly

For women with allergies to any of the antibiotics above, escalate for specialist advice.

Aminoglycoside:
Each hospital should choose their primary aminoglycoside in accordance with local susceptibility patterns and in conjunction with regional partners and local expertise. Dosing is based on estimated or measured weight, rather than ideal body weight.

Use the same dose regardless of renal function for initial dose.

- Gentamicin – initial dose 7 mg/kg for septic shock to maximum 600 mg
- Amikacin – 28 mg/kg to maximum 2,800 mg
- Tobramycin 7 mg/kg to maximum 600 mg

Table 2: Additional antibiotic considerations, including Group A Streptococcus

Indications	Antibiotic
Septic shock: persisting hypotension despite resuscitation	ADD vancomycin (if at risk of MRSA colonisation and/or presence of lines)
Group A Streptococcus contact with GAS infection case	ADD clindamycin

Indications	Antibiotic
Toxic shock	CONSIDER IV immunoglobulin 1-2 g/kg IV (with ID consultation)
Suspected Neisseria meningitidis infection, **or** suspected CNS infection	ADD ceftriaxone 2 g IV 12 hourly
Woman with prior history of multi-resistant Gram-negative colonisation – e.g. CPOs, ESBLs, multi-resistant organisms (MRO), **or** Overseas hospitalisation or travel in the previous 6 months	REPLACE all empiric antibiotics with single agent meropenem 2 g IV 8 hourly
MRSA carrier: Based on previous swabs/ cultures or residence in NT, remote communities in FNQ or northern WA or recent incarceration, or recent prolonged hospital stay	ADD vancomycin IV

Table 3: Rapid antibiotic administration advice for sepsis

Antibiotic	Administration instructions
Amoxycillin	1 g with 20 mL water for injection over 3–4 minutes
Clindamycin	Dilute 600 mg in 50 mL sodium chloride 0.9% and infuse over 20 minutes
Ceftriaxone	2 g with 40 mL water for injection and infuse over 5 minutes
Cefazolin	2 g with 19 mL water for injection and infuse over 5 minutes
Flucloxacillin	2 g with 40 mL water for injection and infuse over 6–8 minutes
Gentamicin	Dilute with 20 mL sodium chloride 0.9% and infuse over 3–5 minutes
Metronidazole	Infuse over 20 minutes
Piperacillin/tazobactam	4.5 g with 20 mL water for injection and infuse over 5 minutes
Vancomycin	500 mg with 10 mL water for injection and 1 g with 20 mL water for injection to make a concentration of 50 mg/mL Dilute to 5 mg/mL with sodium chloride 0.9%, i.e. dilute 1g to at least 200 mL* 1 g may be infused over 1 hour, 1.5 g over 1.5 hours and 2 g over 2 hours. * If fluid restriction, max concentration 10 mg/mL, i.e. dilute 1 g in 100 mL

Table 4: White cell count in pregnancy – normal range: a reference table for clinicians

Non pregnant adult[5]	3.5–9.1 × 10^3 mm^3
First trimester	5.7–13.6 × 10^3 mm^3
Second trimester	5.6–14.8 × 10^3 mm^3
Third trimester	5.9–16.9 × 10^3 mm^3

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Additional resource

Australian Commission on Safety and Quality in Health Care. Review of trigger tools to support the early identification of sepsis in healthcare settings. Sydney: ACSQHC; 2021. Available from: https://www.safetyandquality.gov.au/publications-and-resources/resource-library/review-trigger-tools-support-early-identification-sepsis-healthcare-settings.

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