



ORIGINAL ARTICLE

SOMANZ guidelines for the investigation and management sepsis in pregnancy

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SOMANZ (Society of Obstetric Medicine Australia and New Zealand) has written a guideline to provide evidence-based guidance for the investigation and care of women with sepsis in pregnancy or the postpartum period. The guideline is evidence-based and incorporates recent changes in the definition of sepsis. The etiology, investigation and treatment of bacterial, viral and non-infective causes of sepsis are discussed. Obstetric considerations relevant to anaesthetic and intensive care treatment in sepsis are also addressed. A multi-disciplinary group of clinicians with experience in all aspects of the care of pregnant women have contributed to the development of the guidelines. This is an executive summary of the guidelines.

KEYWORDS

practice guideline, pregnancy, prenatal care, sepsis, septic shock

BACKGROUND

Despite an overall decline in maternal mortality in Australia, the maternal mortality rate from sepsis has increased from 0.6 per 100 000 in 2003–2005 to 0.8 per 100 000 in 2008–2012.¹ In the period 2008–2012, sepsis accounted for 11.4% of maternal deaths in Australia.¹ Group A beta haemolytic streptococcal (GAS) infection is the most common pathogen, resulting in 25% of maternal deaths from sepsis in both Australia and the UK.² The ninth Perinatal and Maternal Mortality Review Committee: report on maternal deaths in NZ³ between 2006 and 2013 indicates 50% of deaths from sepsis were related to Group A streptococcus. Sepsis continues to be one of the major causes of maternal mortality among Aboriginal and Torres Strait Islander women.¹

In Australia, the Clinical Excellence Commission developed the 'Sepsis Kills' program to reduce poor outcomes from sepsis by improving recognition and management.⁴ A specific maternal pathway was created.⁵ Sepsis can arise at any time during pregnancy and is often associated with a delay in diagnosis. The normal physiological changes of pregnancy may mask early signs of sepsis.^{6,7} The woman has a unique 'organ perfusion monitor', namely the fetus. Maternal sepsis with or without haemodynamic instability may present with fetal distress as the uteroplacental circulation is not auto-regulated.⁸ Thus any maternal circulatory insufficiency arising from sepsis may result in compromised fetal perfusion. Management plans need to take into consideration the altered immunological response of the woman and altered physiological responses during pregnancy.⁹ Consideration needs to be also given to the impact of the condition as well as the effect of its treatment on the fetus. The additional complexity of sepsis therapy in breast-feeding women also requires appropriate consideration.

These are the recommendations of a multidisciplinary working party convened by the Society of Obstetric Medicine of Australia and New Zealand (SOMANZ).

MATERIALS AND METHODS

The clinical evidence for this guideline has been analysed by the authors according to the GRADE (Grading of Recommendations Assessment, Development and Evaluation) system.^{10,11} The principles followed in the development of these guidelines include: (i) a systematic review of the evidence with at least the following searches deployed: Cochrane library, Medline and EMBASE; (ii) the authors formed a multi-disciplinary team; (iii) financial support for administration was provided by SOMANZ. None of the authors received any direct financial compensation for their time to the development of this guideline. Where there were conflicting views, three authors (HR, LB and AM) reviewed the topic and came to a consensus. All authors reviewed the final guideline.

Definition of sepsis in pregnancy

Despite significant advances, understanding of the pathobiology of sepsis remains incomplete and currently no gold standard diagnostic test exists to confirm the presence of sepsis. Sepsis is broadly defined as life-threatening organ dysfunction caused by a dysregulated host response to infection.¹² It is this dysregulated response and subsequent organ dysfunction that differentiates sepsis from infection. The clinical signs may be insidious until sepsis is far advanced, which may very rapidly occur. Therefore, early detection of sepsis is essential for appropriate multidisciplinary management to ensure the best outcomes for the mother and her baby. Septic patients may progress to develop septic shock, multi-organ failure and death.

Septic shock is defined as a subset of sepsis in which profound circulatory, cellular, and metabolic abnormalities substantially increase mortality.¹² More recently, the Sequential (sepsis-related) Organ Failure Assessment score (SOFA) has been shown to be useful in identifying those patients with a suspected infection who are likely to have a prolonged ICU (Intensive Care Unit) stay or die in hospital.^{12,13} A quick SOFA (qSOFA) score can be used to identify patients promptly at the bedside using only clinical information.¹⁴

SOMANZ definition of sepsis

Recognising the patient with sepsis is paramount and is the first step in appropriate assessment and management. The flowchart in Figure 1 summarises the clinical steps involved in the assessment and management of sepsis in pregnancy.

We recommend using the obstetrically modified qSOFA (omqSOFA) (Table 1). The obstetrically modified SOFA (omSOFA) score should be used for a subsequent, more thorough, assessment.

omqSOFA score

The qSOFA requires only clinical data for assessment and thus can be performed quickly without waiting for the results of biochemical or laboratory tests.¹⁴ In the non-pregnant patient, this score incorporates: systolic blood pressure of 100 mmHg or less, respiratory rate of 22/min or greater and altered mentation; Glasgow coma score (GCS) less than 15. For each variable present, a score of 1 is attributed resulting in a score range of 0–3. A qSOFA score of greater than or equal to 2 has predictive validity for discriminating patients with an increased risk of in-hospital mortality.¹⁴ However, the data from which the score was derived is retrospective and validated in a heterogeneous population, with an average age of 61 years, of whom half were male. Extrapolation to pregnant and postpartum women should be undertaken with caution.

A woman's gravid state will impact some of the variables in the qSOFA. Pregnancy significantly affects systolic blood pressure but not respiratory rate¹⁵ or mentation. During pregnancy,

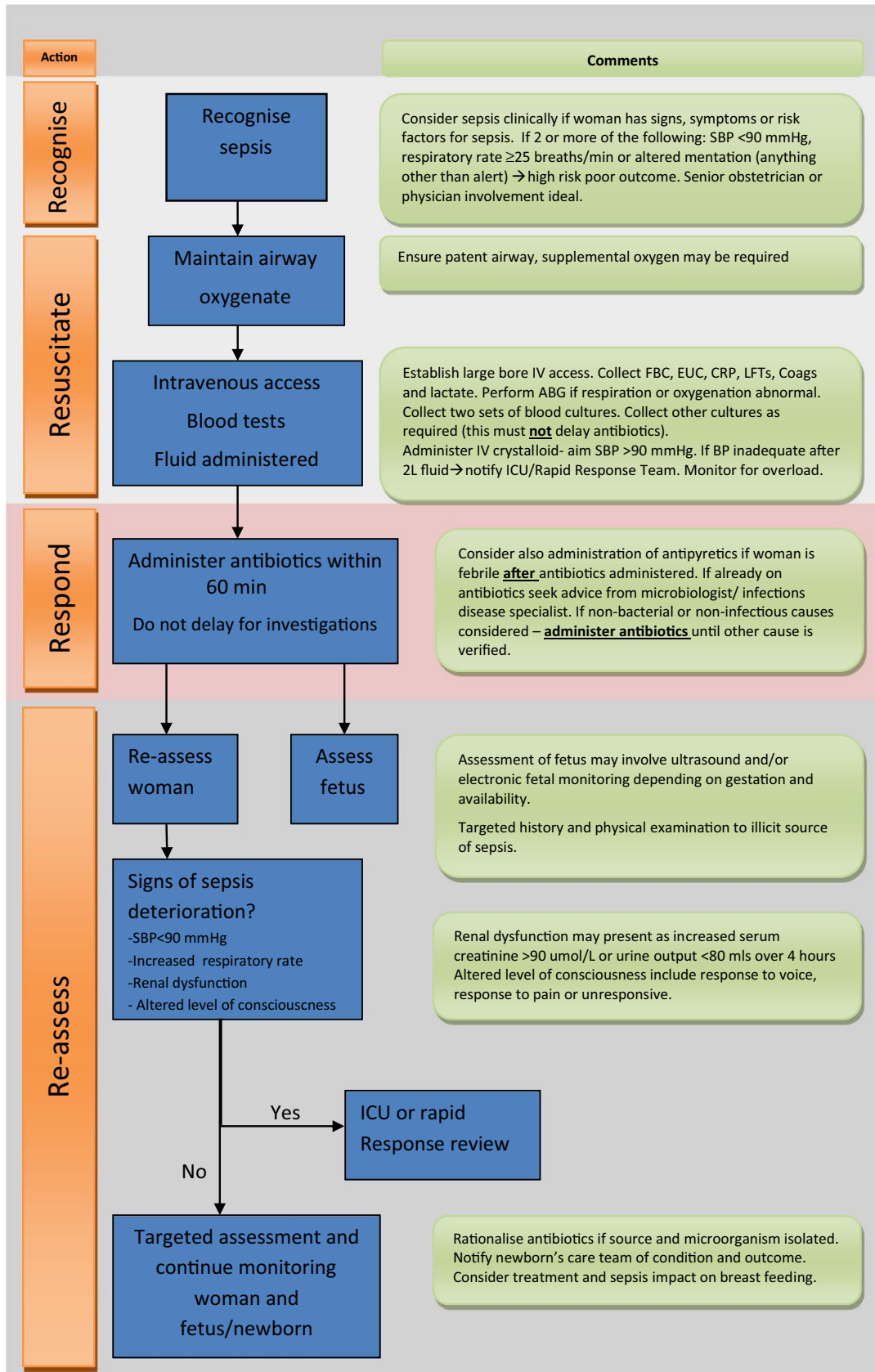


FIGURE 1 Flowchart for the assessment and management of sepsis in pregnancy. The clinically important steps are noted in blue boxes and comments relating to the steps are in neighboring green boxes.

TABLE 1 Obstetrically modified qSOFA score

Parameter	Score	
	0	1
Systolic blood pressure	≥90 mmHg	<90 mmHg
Respiratory rate	Less than 25 breaths/min	25 breath/min or greater
Altered mentation	Alert	Not alert

Min, minute; mmHg, millimetres of mercury; qSOFA, quick Sequential (sepsis-related) Organ Failure Assessment score.

although women normally develop a respiratory alkalosis and compensatory metabolic acidosis, this is not through an increase in respiratory rate.¹⁵ The higher respiratory rate of 25 breaths/min, as compared to 22/min derived from published literature, was agreed upon by the writing committee as it aligned with cut-offs employed on the maternity observation charts. Respiratory rate is poorly assessed in routine clinical practice.¹⁶ Systolic blood pressure usually decreases by 5–10 mmHg in pregnancy.¹⁷ Furthermore a significant number (approximately 15%) of the obstetric population will have a usual systolic blood pressure at any given gestation, of less than 100 mmHg and normal pregnancy outcomes.¹⁸

Given these changes, several modifications are suggested to the qSOFA criteria when applied to pregnancy: omqSOFA. Using the omqSOFA (Table 1), sepsis (as distinct from infection) in pregnant women should be considered where two or more of the following are present:

- systolic blood pressure of 90 mmHg or less
- respiratory rate of 25/min or greater
- altered mentation (any state other than 'Alert' on maternal observation charts). GCS are not typically formally assessed as part of routine observations in obstetric wards.

omSOFA score

If sepsis is suspected based on screening, then assessment for end-organ dysfunction should be undertaken.¹² Sepsis has been defined as an acute change in the total SOFA score of ≥2 points consequent to infection. The baseline SOFA score is generally assumed to be zero where there is no pre-existing organ dysfunction. In the general population a SOFA of ≥2 is associated with an overall mortality of 10%, these data are yet to be validated in the obstetric population. The SOFA score, in observational data, has been found to be significantly higher in pregnant women who have died compared to those who have survived in an intensive care setting.^{19,20} However, the SOFA score has not undergone appropriate prospective validation in pregnant and postpartum populations. The studies that exist to date have been small, retrospective and undertaken in resource-challenged environments which may limit their applicability generally.

TABLE 2 Obstetrically modified SOFA score

System parameter	Score		
	0	1	2
<i>Respiration</i>			
PaO ₂ /FIO ₂	≥400	300 to <400	<300
<i>Coagulation</i>			
Platelets, ×10 ⁶ /L	≥150	100–150	<100
<i>Liver</i>			
Bilirubin (μmol/L)	≤20	20–32	>32
<i>Cardiovascular</i>			
Mean arterial pressure (mmHg)	MAP ≥ 70	MAP < 70	Vasopressors required
<i>Central nervous system</i>			
	Alert	Rousable by voice	Rousable by pain
<i>Renal</i>			
Creatinine (μmol/L)	≤90	90–120	>120

FIO₂, fraction of inspired oxygen (expressed as a decimal); MAP, mean arterial pressure; mmHg, millimetres of mercury; PaO₂, partial pressure of oxygen (in mmHg); SOFA, Sequential (sepsis-related) Organ Failure Assessment score.

This guideline recommends several modifications when applying the SOFA score to pregnancy (omSOFA) as indicated (Table 2).

- In order to demonstrate evidence of end organ dysfunction a score of ≥2 needs to be attained. Therefore, scores of 3 or 4 in each category have been removed for the purposes of simplification.
- During pregnancy, serum creatinine levels are significantly reduced with the normal range being 35–80 μmol/L.²¹ For practical purposes, the serum creatinine cut off for the scores of 0, 1 or 2 have been adjusted to <90, 90–120 or >120 μmol/L, respectively.²²
- As the GCS is not routinely assessed on maternity wards, the central nervous system category has been changed to reflect the maternal observation charts in routine clinical use. Alert will be scored 0, rousable by voice as 1 and rousable only by pain as 2. Any score other than 0 or 'alert' should trigger a GCS to be performed.
- Healthy pregnant women may have a mean arterial pressure less than 70 mmHg. Thus, the SOFA score should be interpreted in the context of the woman's pre-morbid blood pressure.

SOMANZ definition of septic shock

If sepsis progresses, septic shock may ensue and this is associated with a substantial increase in mortality compared to sepsis alone.²³ The clinical criteria validated to identify septic shock in non-pregnant patients include:

- hypotension requiring vasopressor therapy to maintain a mean arterial pressure 65 mmHg or greater (despite adequate fluid resuscitation) and

- serum lactate greater than 2 mmol/L after adequate fluid resuscitation.²⁴

No alterations have been made to these definitions for pregnancy.

C-reactive protein (CRP) has not been included in the current definition. It lacks sensitivity and is highly variable in pregnancy and should not be used to define or diagnose sepsis.²¹ Fever, although helpful in identifying pregnant patients with suspected infections or sepsis, has also not been included, as it lacks sensitivity²⁵ (see section on fever below).

Given that maternal physiology gradually returns to normal postpartum, we recommend the definition of postpartum sepsis be the same as for non-pregnant patients after the first week postpartum.

Key Points 1

- Screen for sepsis using the omqSOFA score
- Assess for evidence of end organ dysfunction using omSOFA score
- Septic shock is a complication of sepsis evidenced by the need for vasopressors and elevated lactate

GRADE: MODERATE QUALITY EVIDENCE

Fever in pregnancy

In a comprehensive systematic review and meta-analysis of fever in human pregnancy and the health impacts on the offspring, Dreier *et al.*²⁶ reported an increase in the rate of pregnancies affected by a neural tube defect in mothers who experienced fever in the first trimester or peri-conceptually (pooled odds ratio (OR) of 2.9, 95% confidence interval (CI) 2.22–3.79). Oral clefts were also more common in mothers with fever early in pregnancy (OR 1.94, 95% CI 1.35–2.79). Congenital heart defects were weakly associated with early maternal fever early in pregnancy (OR 1.54, 95% CI 1.37–1.74). No effect of maternal fever was seen on the risk of miscarriage, stillbirth or preterm labour.

Human studies appear to vary from animal studies in the absence of a dose-response relationship. In animals where a temperature elevation of greater than 2°C was documented there was a greater risk of teratogenic outcome.²⁷ In human studies, reliance on self-reported temperature may lead to inaccurate results.²⁶

Few studies are available to document the long-term developmental outcomes of infants exposed to fever in pregnancy. In the CHARGE (Childhood Autism Risks from Genetics and Environment) study,²⁸ mothers of children diagnosed with autism spectrum disorder (ASD) or developmental delay (DD) were asked retrospectively, 2–5 years after their pregnancy, whether or not they had suffered from flu or a fever in pregnancy. Neither

ASD nor DD were associated with self-reported influenza in pregnancy. However, both ASD and DD were associated with the report of fever during pregnancy (OR 2.12, 95% CI 1.17–3.84 and OR 2.50, 95% CI 1.20–5.20, respectively). The offspring of mothers who took anti-pyretic medications had a lower risk of ASD (OR 1.30, 95% CI 0.59–2.84) compared with those who did not (OR 2.55, 95% CI 1.30–4.99).

High-dose aspirin and non-steroidal anti-inflammatory agents should be used with caution during the third trimester due to the risk of premature closure of the fetal ductus arteriosus.²⁹ Alternative agents should be considered.

Key Points 2

- Fever may be associated with an increased risk of congenital abnormalities
- Antipyretics such as paracetamol, may be beneficial in reducing adverse pregnancy outcomes

GRADE: LOW QUALITY EVIDENCE

Aetiology of sepsis

Although most commonly bacterial in aetiology, sepsis can also result from viral and other causes (Table 3). A number of non-infective conditions can mimic sepsis and should be considered by clinicians (Table 4).

Key Points 3

- Sepsis-related maternal death is most commonly caused by Group A *Streptococcus*
- *Escherichia coli* is the commonest cause of maternal bacterial infection
- Consider non-bacterial and non-infective conditions that may mimic sepsis

GRADE: HIGH QUALITY EVIDENCE

Investigations in sepsis

Obstetric patients with infections may present with nonspecific symptoms and early investigation is necessary to exclude severe infection.³⁰ Maternity units should ensure observations are recorded on maternity-specific charts for all obstetric and postpartum patients.³¹ Utilization of these charts has been shown to promote earlier detection and therefore treatment of pregnant or early postpartum women who are developing a critical illness.³²

Once infection is suspected, treatment should be commenced and the likely source and severity of sepsis elucidated via history, examination and investigations. Investigations are directed at determining the aetiology and risk stratification of sepsis as well as organisation of care for women in the most appropriate clinical

TABLE 3 Infectious causes of sepsis in pregnancy and postpartum

Infection	Pathogens
Bacterial – common	Group A-beta-haemolytic Streptococcus (GAS) pyogenes <i>Escherichia coli</i> Group B Streptococcus <i>Klebsiella pneumoniae</i> <i>Staphylococcus aureus</i> <i>Streptococcus pneumonia</i> <i>Proteus mirabilis</i> Anaerobic organisms
Bacterial – less common	<i>Haemophilus influenza</i> <i>Listeria monocytogenes</i> <i>Clostridium</i> species <i>Mycobacterium tuberculosis</i>
Viral	Influenza Varicella zoster virus Herpes simplex virus Cytomegalovirus

area. Sepsis during pregnancy will require maternal investigations as detailed below and fetal wellbeing assessment with cardiocotograph (CTG) and/or ultrasound. Table 5 lists the first line investigations to be undertaken in sepsis, possible changes in sepsis and normal pregnancy reference ranges if different from the non-pregnant state. Two important considerations are as follows.

- Two sets of peripheral blood cultures should be taken immediately and sequentially if possible before administration of antibiotics. Their collection should not delay antibiotic treatment. Cultures should also be taken from all vascular catheter lines (catheter blood cultures) and any other potential sources of infection. Determining the aetiology of the infection will allow for targeting of antimicrobial therapy.

- Arterial blood gases should be undertaken to determine presence of hypoxia, hypercapnea, metabolic state and lactate level. Elevated lactate levels are an indication of tissue hypoperfusion with values greater than 2 mmol/L being associated with increased mortality in pregnancy.²⁴ The sampling site does not affect the serum lactate results (eg arterial, venous or capillary³³). If unable to obtain an arterial lactate, a venous lactate can be collected.

Additional investigations may be required depending on initial investigation results and the likely source of infection. Appropriate imaging should not be withheld because a woman is pregnant. Concerns about radiation exposure to her developing fetus or proliferating maternal breast tissue need to be balanced against the clinical need for imaging.³⁴

Treatment in the golden hour

Treatment should be commenced as soon as practical — ideally within the first hour ('golden hour') of sepsis being suspected.

Key Points 4

- Maternal observation should be recorded on maternity-specific observation charts
- Blood cultures and other specimens should be obtained before antibiotics given: THIS SHOULD NOT delay therapy.
- Pregnancy-specific reference ranges should be used whenever possible to interpret laboratory investigations
- Imaging, if clinically indicated, should not be withheld because a patient is pregnant or breast feeding

GRADE: HIGH QUALITY EVIDENCE

TABLE 4 Non-infectious conditions that can mimic sepsis in pregnancy

Condition	Common maternal clinical features
Acute pulmonary embolism	Hypotension, tachypnoea, tachycardia, low-grade fever
Amniotic fluid embolism	Hypotension, tachycardia, haemorrhage
Acute pancreatitis	Fever, nausea, vomiting, abdominal pain
Acute fatty liver of pregnancy	Fatigue, nausea, vomiting, abdominal pain, jaundice, impaired level of consciousness
Adverse drug reactions, drug fever	Hypotension, relative bradycardia, fever, rash, angio-oedema
Acute liver failure-drug related, viral	Jaundice, nausea, vomiting, abdominal pain impaired level of consciousness
Acute adrenal insufficiency	Weakness, fatigue, nausea, anorexia, weight loss, hypotension, fever
Acute pituitary insufficiency	Failure to lactate, hypotension, relative bradycardia, polyuria, polydipsia
Autoimmune conditions	Low-grade fever, rash (eg malar rash), arthritis, dry eyes or mouth, mouth ulcers, diagnostic serology
Concealed haemorrhage including ectopic pregnancy	Hypotension, tachycardia, low-grade fever
Disseminated malignancy	Low-grade fever, weight loss
Pelvic thrombosis	Pelvic pain, fever
Transfusion reactions	High fever, rigors, dysrhythmia, tachypnoea, hypotension, rash, bleeding, haematuria

TABLE 5 First line investigations recommended for suspected sepsis

Investigation ⁵¹	Obstetric reference range (if relevant) ²¹
Blood cultures <ul style="list-style-type: none"> • At least two sets, prior to antibiotic commencement as long as there is no delay. • Obtain samples from different sites • Cultures should also be obtained from IV access devices Other cultures <ul style="list-style-type: none"> • Obtain cultures of additional sites as clinically indicated and as soon as possible <ul style="list-style-type: none"> ◦ eg urine MCS, wound swab – episiotomy, caesarean, placental swabs, amniotic fluid, sputum culture, naso-pharyngeal aspirate/swab, cerebrospinal fluid, vaginal swabs, stool culture Arterial blood gases <ul style="list-style-type: none"> • Detect acidosis, hypoxaemia, lactate as below Lactate <ul style="list-style-type: none"> • Elevated levels in sepsis relate to tissue hypoperfusion and are associated with an increased sepsis mortality risk Full blood count Coagulation studies Creatinine urea and electrolytes <ul style="list-style-type: none"> • Measure at baseline and until the patient improves, elevated creatinine is a sign of severe sepsis Liver function tests <ul style="list-style-type: none"> • Baseline test, may be elevated if sepsis source is from hepatic or perihepatic infections • May be elevated due to septic shock affecting hepatic blood flow and metabolism CXR Fetal assessment – CTG and /or fetal ultrasound	PaO ₂ (reference range) : 1st trimester: 93–100 mmHg, 2nd trimester: 90–98 mmHg, 3rd trimester: 92–107 mmHg PaCO ₂ (reference range) : 25–33 mmHg, Arterial pH: 7.4–7.47, HCO ₃ 16–22 mmol/L 0.6–1.8 mmol/L White cell count: 6–17 × 10 ⁹ /L (may increase to 9–15 × 10 ⁹ /L immediately post-delivery). Steroids also increase white cell count No change Creatinine varies with gestation (reference ranges) :1st trimester: 35–62 µmol/L, 2nd trimester: 35–71 µmol/L, 3rd trimester: 35–80 µmol/L AST 3–33 U/L, ALT 2–33 U/L, Alkaline Phosphatase 17–229 U/L GGT 2–26 U/L, Total Bilirubin 1.7–19 µmol/L A non-reassuring CTG suggests inadequate uteroplacental perfusion and may reflect maternal organ hypoperfusion or intrauterine sepsis

ALT, alanine aminotransferase; AST, aspartate aminotransferase; CTG, cardiotocograph; CXR, chest X-ray; GGT, gamma glutamyl transferase; HCO₃, bicarbonate; IV, intravenous; MCS, microscopy, culture and sensitivity; PaCO₂, partial pressure of carbon dioxide (in mmHg); PaO₂, partial pressure of oxygen (in mmHg).

Empiric treatment should include fluid resuscitation, correction of hypoxia and antimicrobials (antibiotics or antivirals as appropriate). Source control, consideration of the appropriate area of care as well as venous thromboembolism prophylaxis also need to be considered.

Fluid resuscitation

In most circumstances, the initial treatment of hypotension in sepsis is fluid administration. Fluid resuscitation is vital in sepsis to optimise circulating volume and improve blood pressure and tissue perfusion. The preferred fluid for resuscitation is an isotonic crystalloid (usually 0.9% normal saline). Blood may also be used as fluid replacement if there is evidence of blood loss or severe anaemia. If, despite fluid resuscitation (1–2 L), the mean arterial pressure and other indices do not improve, care will need to be escalated. Vasopressors may be required;³⁵ see 'Intensive Care Issues' below.

Treatment for bacterial sepsis

When a bacterial source of sepsis in pregnancy or postpartum is suspected, prompt treatment with antibiotics within one hour is critical. Maternal mortality can increase by 8% for each hour's delay in administering antibiotics.³⁶ Following principles of antibiotic stewardship recommended in both Australia and New Zealand, selection of antibiotics needs to be appropriate for the suspected infection, while minimizing the risk of adverse effects and reducing the emergence of antibiotic resistance.^{37,38}

A consultant obstetrician and a physician experienced in the management of sepsis in pregnancy should be involved in the care of a pregnant or postpartum patient from the time of sepsis diagnosis or recognition. However, investigation and treatment should not be delayed while waiting for expert consultation. Once a source of sepsis is identified, source control

is a priority and may involve abscess drainage or delivery of the fetus.

When treating immunosuppressed women, a physician should be involved in decision making as soon as possible after the diagnosis or recognition of sepsis. This should not delay antibiotic treatment. Women may be immunosuppressed with immunomodulators for solid organ transplant, malignancy or autoimmune disease; chronic infection including human immunodeficiency virus or significant medical co-morbidities such as diabetes.

Treatment of sepsis of unknown source

Table 6 summarises the recommendations for empiric antibiotic treatment. Antibiotic resistance patterns and local practices will vary, so it is important to seek local specialist advice as soon as possible. Therapy should be refined as culture and imaging results define the source of sepsis and its culprit organisms. The Australia-wide eTG (electronic antibiotic Therapeutic Guidelines) are available at the following URL: <https://tgldcdp.tg.org.au/guideLine?guidelinePage=Antibiotic&frompage=etgcomplete>.

Treatment of sepsis of viral aetiology – influenza

Neuraminidase inhibitors are recommended for the treatment of influenza.³⁹ Oseltamivir (treatment dose: 75 mg capsule

twice daily for five days) has more obstetric safety data available than zanamivir and is the agent of choice in pregnancy.⁴⁰ There is a low rate of transplacental transfer, estimated at between 1 and 14% of maternal concentrations in ex vivo perfusion studies.⁴¹ In the setting of H1N1 pandemic influenza, early antiviral therapy (initiation < 2 days) in pregnant women was associated with an 84% reduction in admissions to intensive care.⁴²

Thromboembolism prophylaxis

Both pregnancy and sepsis are independent risk factors for venous thromboembolism.⁴³ Thus prevention of venous thromboembolism is critically important. Unfractionated heparin (UH) and low molecular weight heparin (LMWH) have been used extensively in pregnancy and have been shown in large clinical trials to be effective in the prevention of thromboembolism.⁴⁴

Pharmacological considerations for pregnancy and breast feeding

While most antibiotics are found in breast milk of a lactating woman, the relative infant dose is generally small. Breastfed infants should be monitored for side effects such as diarrhoea, vomiting, skin rash or thrush while their mothers are being treated

TABLE 6 Recommendations for antimicrobial treatment of sepsis with unknown source

	Australian and New Zealand antibiotic regimen	Alternative for penicillin hypersensitivity†
Community-acquired sepsis (source not apparent)‡	<p>Aus: amoxicillin/ampicillin 2 g IV Six-hourly PLUS gentamicin 4–7 mg/kg (first dose) IV§ PLUS metronidazole 500 mg IV 12-hourly</p> <p>NZ: cefuroxime 1.5 g IV eight-hourly PLUS gentamicin 4–7 mg/kg (first dose) IV§ PLUS metronidazole 500 mg IV 12-hourly</p> <p>At risk of MRSA sepsis (based on previous swabs/cultures and local epidemiology): ADD vancomycin 25–30 mg/kg (loading dose) IV§</p> <p>At risk of Group A Streptococcal (GAS) sepsis: ADD clindamycin 600 mg IV eight-hourly, PLUS consider normal immunoglobulin 1–2 g/kg IV, for up to two doses during the first 72 h</p>	<p>Clindamycin 600 mg IV eight-hourly PLUS gentamicin 4–7 mg/kg (first dose) IV (severe hypersensitivity)</p> <p>Cefazolin 2 g IV six-hourly PLUS gentamicin 4–7 mg/kg (first dose) IV§ PLUS metronidazole 500 mg IV 12-hourly (mild-moderate hypersensitivity)</p>
Hospital-acquired sepsis (source not apparent)	<p>Aus: piperacillin 4 g + tazobactam 0.5 g IV eight-hourly AND consider gentamicin 4–7 mg/kg (first dose) IV§ (if local epidemiology suggests Gram-negative aminoglycoside susceptibility)</p> <p>NZ: cefuroxime 1.5 g IV 8-hourly PLUS gentamicin 4–7 mg/kg (first dose) IV§ PLUS metronidazole 500 mg IV 12-hourly</p> <p>At risk of MRSA sepsis (based on previous swabs/cultures and local epidemiology or if line sepsis) ADD vancomycin 25–30 mg/kg (loading dose) IV§</p> <p>At risk of multidrug-resistant Gram-negative organisms: use as a SINGLE AGENT meropenem 1 g IV eight-hourly</p> <p>At risk of Group A Streptococcal (GAS) sepsis: ADD clindamycin 600 mg IV eight-hourly PLUS consider normal immunoglobulin 1–2 g/kg IV, for up to two doses during the first 72 h</p>	<p>Severe: ciprofloxacin 400 mg IV eight-hourly PLUS vancomycin 25–30 mg/kg IV§</p>
Consider influenza	<p>Oseltamivir 75 mg BD or Zanamivir two inhalations (each 5 mg) twice daily for five days</p>	

†NZ has increasing Group B strep resistance to clindamycin and macrolides – if penicillin hypersensitivity seek expert advice for best agent.

‡NZ regime does not cover listeria – if suspected use a penicillin as per Australian regime.

§Use local protocols for gentamicin and vancomycin dosing and monitoring. Once daily dosing of gentamicin in pregnancy and postpartum can be used and in pregnancy results in levels below the toxicity threshold for more hours per day than in eight-hourly dosing.

BD, twice daily; IV, intravenous; MRSA, methicillin-resistant *Staphylococcus aureus*.

with antibiotics. Please refer to the eTG for advice on antibiotic use in breast feeding mothers, URL: <https://tgldcdp.tg.org.au.acs.hcn.com.au/quicklinks?type=Pregnancyandbreastfeeding>.

Key Points 5

- Commence fluid resuscitation immediately
- Administer empiric therapy immediately, preferably within one hour
- De-escalate to appropriate antibiotics when the sepsis source is identified
- Thromboembolism prophylaxis should be considered for all women
- Consider the impact of antibiotics on pregnancy and breast feeding

GRADE: MODERATE QUALITY EVIDENCE

Timing and mode of delivery

The timing of delivery will be determined by: (i) the presence of intrauterine sepsis; (ii) the nature of the maternal sepsis and response to initial resuscitation efforts; and (iii) the gestation of the pregnancy and fetal status.

In the setting of intrauterine sepsis, delivery should always be considered regardless of the gestation. Corticosteroids should be considered for fetal lung maturation but this decision needs to be balanced against the urgency of delivery.⁴⁵

Intrauterine sepsis should be suspected in the presence of maternal fever, ruptured membranes or recent intrauterine procedures such as amniocentesis,⁴⁶ maternal tachycardia, fetal tachycardia, uterine tenderness or offensive vaginal discharge. While the onset of chorioamnionitis may be non-specific and insidious, rapid deterioration is possible.

In cases of extra-uterine sepsis, efforts to treat maternal sepsis and prolong gestation should be considered at gestations remote from term, although it is reasonable to consider delivery in term pregnancies as a means of improving maternal resuscitation efforts. Fetal wellbeing should be monitored during maternal sepsis with the most gestation-appropriate method.

Role of the anaesthetist in managing maternal sepsis

The role of the anaesthetist in managing maternal sepsis includes:

- initial resuscitation and stabilisation of the patient
- transfer of the sick patient (to imaging or intensive care unit)
- intra-operative care during delivery
- anaesthesia for surgical management of sepsis

Key Points 6

- Monitor fetal well-being during maternal sepsis with appropriate method
- If a pre-term delivery is required, give corticosteroids for fetus: sepsis is not a contraindication
- Chorioamnionitis may be insidious and require urgent delivery

GRADE: MODERATE QUALITY EVIDENCE

Patient transfer

The transport team must be experienced in securing airways, ventilation, resuscitation and other anticipated emergency procedures. A comprehensive hand-over should take place at the receiving facility. The responsibility of intra- and inter-hospital transfers often rests with the anaesthetist to provide the standard of care as set out in The Australian and New Zealand College of Anaesthetists professional document, PS52 (2015) Guidelines for Transport of Critically Ill Patients. These guidelines state, 'the level of care provided during transport must aim to at least equal that at the point of referral and must prepare the patient for admission to the receiving services'.⁴⁷

Spinal anaesthesia

Underlying sepsis is a risk factor for infectious complications of regional anaesthesia. The greatest concern is infection around the spine and spinal cord, presenting either as meningitis or cord compression secondary to abscess formation with the potential for permanent neurological deficit. It is difficult to accurately quantify the risk of infection following neuraxial analgesia and anaesthesia due to the great variability in the reported incidence in the literature; from an estimated incidence of spinal/epidural abscess after epidural analgesia of one in 1930 to 1.1 infections per 100 000 neuraxial blocks.⁴⁸ However, epidural anaesthesia carries a greater risk of infectious complications than spinal techniques.⁴⁹

Despite the low risk of central nervous system infection, which may potentially occur in any bacteraemic patient, the decision to proceed with neuraxial blockade in a febrile or infected patient must be carefully considered and made on a case by case basis.⁵⁰⁻⁵²

- Except in the most extraordinary circumstances, central neuronal block should not be performed in patients with untreated systemic infection.
- Patients with evidence of systemic infection may safely undergo spinal anaesthesia, provided appropriate antibiotic therapy is initiated before dural puncture and the patient has shown a

TABLE 7 Indications for involvement of ICU

Indications for ICU involvement	Signs or observations
Cardiorespiratory compromise	Hypotension, circulatory instability, worsening tachypnoea, worsening hypoxia, increasing supplemental oxygen requirements
Evidence of organ dysfunction	Altered mental status, oliguria, worsening urea and creatinine, other eg coagulation failure, cytopenias, worsening hepatic dysfunction
Other evidence of hypoperfusion	Metabolic/lactic acidosis, signs of poor tissue perfusion, signs of inadequate placental perfusion
Other serious clinical concern	

response to therapy; placement of an indwelling epidural or intrathecal catheter remains controversial.

- Spinal anaesthesia may be safely performed in patients at risk for low-grade transient bacteraemia after dural puncture.

General anaesthesia

The septic obstetric patient often exhibits haemodynamic instability and has a greater (than just pregnancy-induced) metabolic oxygen demand. In practice, relevant issues for the administration of general anaesthesia include:

- **A – Airway:** delayed gastric emptying with increased risk of reflux and aspiration. It is recommended that women are premedicated with combination antacid antihistamine prophylaxis (eg effervescent ranitidine 150 mg). A rapid sequence induction is also recommended.
- **B – Breathing:** It is recommended women receive adequate pre-oxygenation prior to anaesthesia induction. There is reduced functional residual capacity with increased ventilation/perfusion mismatch. It is recommended ventilation strategies to maintain oxygenation and minimise further lung injury are employed.
- **C – Circulation:** It is recommended to avoid aortocaval compression using a lateral uterine tilt, ensure adequate fluid resuscitation including the appropriate use of blood products and if required, inotropic support. Alpha adrenergic agonists (specifically noradrenaline) are the agents of choice for maintenance of uteroplacental flow.

Intensive care issues

Adequate initial resuscitation and treatment of sepsis may result in stabilisation and prevent progression and deterioration, averting the requirement for intensive care. However, as stated early consideration should be given to establishing the most appropriate venue of care for these women. The indications for ICU admission will vary depending on local resources and expertise. It is preferable that an ICU opinion and /or admission should occur before the development of severe complications such as frank organ failure or catastrophic shock. If any clinical concern exists then escalation of care should be considered early. Table 7 sets

Key Points 7

- Neuraxial blocks in women with untreated sepsis are associated with increased complications
- Septic women experience increased haemodynamic instability during anaesthesia

GRADE: LOW QUALITY EVIDENCE

out in general terms when an ICU opinion should be obtained and an ICU admission considered.

Key Points 8

- Liaise with ICU where there is evidence of organ dysfunction, hypotension or cardiorespiratory compromise
- Early ICU involvement is preferable and encouraged
- Indications for ICU admission vary based on local resources and experience

GRADE: LOW QUALITY EVIDENCE

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