MATERNAL SEPSIS

This guideline is a Te Whatu Ora – Health NZ Waitaha Canterbury **reference guide** for the recognition, diagnosis and early management of maternal sepsis. For more detailed sepsis guidance please refer to the Best Practice Advisory Centre (BPAC) guideline (2018) and the Society of Obstetric Medicine Australia and New Zealand (SOMANZ) guideline (2017).

The Te Whatu Ora Waitaha Canterbury Hospital Antimicrobial Stewardship Committee supports the antimicrobial use in accordance with this guideline.

DEFINITIONS

Sepsis is a life-threatening organ dysfunction caused by abnormal physiological response to Infection[6].

Sepsis with septic shock is characterised by low blood pressure (despite adequate fluid replacement) and organ dysfunction or failure[1].

Maternal sepsis is when sepsis presents for women who are pregnant or have recently been pregnant (ie. given birth or had a miscarriage or termination within the last six weeks).

INCIDENCE

Sepsis is a relatively infrequent but serious condition that requires early recognition and response.[1, 3]

Morbidity: sepsis is the third most common cause for maternal admission to ICU/HDU (15.1%), after postpartum haemorrhage (33.9%) and hypertensive disorders (30.2%).[4]

Mortality: between 2006 and 2018 the ratio per 100,000 maternities was 0.74 for pregnancy-related infection (4.8% of 126 maternal deaths) and 1.11 for infections *not* directly related to the pregnancy (7.1% of 126 maternal deaths).[9]

RISK FACTORS

Women who are pregnant or have recently been pregnant are in a high-risk group for sepsis. Maternal sepsis is more likely to occur in women who:[1,5,7]

- Have **impaired immune systems** because of illness or drugs
- Have gestational **diabetes** or diabetes or other **comorbidities** (eg. obesity)
- Needed **invasive procedures** (eg. caesarean section, forceps delivery, removal of retained products of conception, cervical suture)
- Have indwelling lines or catheters
- Had prolonged rupture of membranes
- Have or have been in close contact with people with **group A streptococcal infection**, for example, scarlet fever
- Have continued vaginal bleeding an offensive vaginal discharge or a wound infection

- Obesity
- Anaemia
- History of pelvic infection
- Māori or Pacific ethnicity
- Non – reassuring CTG / fetal tachycardia antenatally or in labour

CAUSES

Maternal sepsis is most commonly bacterial in aetiology but may also result from viral and other causes. Infectious causes of sepsis in pregnant and recently-pregnant women are listed in table below[7]:

INFECTION	PATHOGENS
Bacterial – common	Group A streptococcus (*Streptococcus pyogenes*) *Escherichia coli* Group B streptococcus *Klebsiella pneumoniae* *Staphylococcus aureus* *Streptococcus pneumoniae* *Proteus mirabilis* Anaerobic organisms
Bacterial – less common	*Haemophilus influenzae* *Listeria monocytogenes* *Clostridium* species *Mycobacterium tuberculosis*
Viral	Influenza Varicella zoster virus Herpes simplex virus Cytomegalovirus SARS-CoV-2

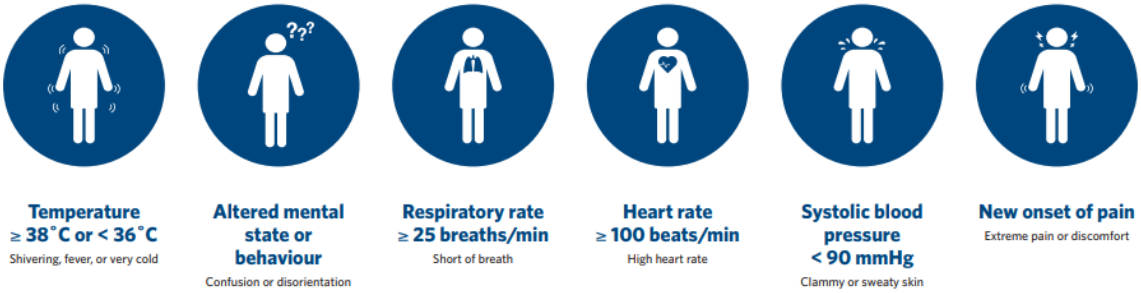
Management and administration of prophylactic antibiotics for maternal Group B Streptococcus is covered in a separate Te Whatu Ora Waitaha Canterbury guideline.

RECOGNITION

Sepsis can be challenging to identify early on as the symptoms may be subtle and mimic other symptoms of pregnancy. In some cases, in particular with streptococcal infection, women may show extremely rapid clinical deterioration. Early recognition of sepsis is vital to improving outcomes. A 2017 UK NHS campaign highlighted the importance of asking ourselves the question, "Could this be sepsis?"[1]

In all cases of suspected sepsis, promptly assess a full set of maternal vital signs, plot on a MEWS chart and escalate appropriately according to the MEWS Score.

The signs and symptoms of sepsis which are represented in the infographic below were highlighted in a report on New Zealand maternal morbidity[3]**:**



Women are more likely to have severe illness or death from sepsis if they have the following high-risk criteria:[1,3]

TEMPERATURE OVER AND **ABOVE 38^{0}C** *OR* **LOWER THAN 36^{0}C**

Ask the woman/family/whānau about any recent fever, shivering, or rigors. Do not use temperature as sole predictor of sepsis. People who are severely ill with sepsis may not develop a raised temperature. Temperature can be caused by a physiological response, for example after surgery or trauma.

ALTERED MENTAL STATE

Interpret mental state in the context of the woman's normal function and treat changes as significant. Changes in cognitive function such as confusion, heightened anxiety and disorientation may be subtle. In some situations, women may report a feeling of 'impending doom'.[5] Assessment should include a history from the woman's family/whānau where possible. In woman with altered mental state, consider the use of AVPU (Alert, Voice, Pain, Unresponsive) scale. If concerned, mark on MEWS chart as abnormal level of consciousness.

RESPIRATORY RATE OVER AND **ABOVE 25 BREATHS/MIN**

and/or shortness of breath

and/or oxygen saturation under 95% or new need for supplemental oxygen.

Oxygen saturation may be difficult to measure in case of septic shock due to poor peripheral circulation.

HEART RATE OVER AND **ABOVE 100 BEATS/MIN** AND CIRCULATORY CHANGES

Baseline heart rate in pregnancy is 10-15 beats/minute more than normal. Interpret heart rate in context considering that a woman may have an increased heart rate in response to exertion and/or medication.

Response to circulatory dysfunction may also include: mottled or ashen appearance; cyanosis of skin, lips or tongue; non-blanching rash of skin; cold hands or feet; leg pain.

BLOOD PRESSURE: **SYSTOLIC BELOW 90 MMHG**

Interpret blood pressure in context considering known hypertension or hypotension.

Hypotension may be accompanied by clammy or sweaty skin.

NEW ONSET OF PAIN

Any newly reported extreme pain or discomfort, particularly abdominal pain.

OTHER SYMPTOMS

Woman with genital tract sepsis may also report: increased and/or offensive vaginal discharge; diarrhoea; nausea and/or vomiting; sore throat; upper respiratory tract infection.

In pregnant women, an abnormal fetal heart rate may be the first indicator that maternal cardiovascular insufficiency has affected fetal perfusion[7].

Non-infectious conditions that can mimic maternal sepsis include amniotic fluid embolism, pulmonary embolism, adverse drug reactions and concealed haemorrhage. For a full list of conditions refer to SOMANZ guideline.[7]

RESPONSE

Essential factors in improving maternal sepsis outcomes include: rapid recognition; a structured interprofessional approach; appropriate investigations and treatment; early microbials and prompt involvement of senior staff.[7,5]

THE SEPSIS 6+2

A set of interventions known as the Sepsis 6+2, may simplify the initial management of women with maternal sepsis.[3] Treatment should be commenced as soon as practical. Completing the following 6 actions (3 diagnostic and 3 therapeutic) **within the first hour** can double a woman's chance of survival:

GIVE 3	TAKE 3	CONSIDER 2
Give high-flow oxygen	Take appropriate cultures	Assess fetal state and consider delivery or evacuation of retained products of conception
Give a fluid challenge	Measure lactate	Consider thromboprophylaxis
Give IV antibiotics	Measure urine output	

Take two blood cultures (more if endocarditis suspected) before initiating empiric antimicrobial therapy. Also culture for other sources of infection, if possible, but do not delay in initiating antimicrobial therapy in a deteriorating woman. Refer to the form in **Appendix 1** for management and documentation of maternal sepsis.

CLINICAL EXAMINATION

In addition to the Sepsis 6+2, a thorough clinical examination will assist in identifying the cause and severity of sepsis. This examination will be a top-to-toe assessment plus, where appropriate:[1,7,5]

- Blood tests in addition to cultures and lactate: full blood count, C-reactive protein (CRP), urea and electrolytes, creatinine, clotting screen
- Swabs from all potential sources of sepsis (eg. throat, wounds: nipple/abdominal/perineum, vagina, placenta)
- Culture/samples from all potential sources of sepsis (eg. sputum, urine, stool)
- Chest x-ray
- Abdominal/pelvic ultrasound scan
- Vaginal examination to exclude retained tampons or swabs

EQUIPMENT

A sepsis equipment box may assist in prompt and thorough emergency management.
(see **Appendix 2**)

MANAGEMENT OUTSIDE HOSPITAL SETTINGS

In a primary setting, if any high-risk criteria present in a woman with suspected sepsis (see above) arrange immediate transfer. Complete as many of the Sepsis 6 actions as possible prior to transfer. Inform ambulance services of suspected sepsis. Paramedics in NZ are equipped to give antibiotics with a provisional diagnosis of sepsis if this has not been possible in the primary unit prior to transfer [9].

ONGOING MANAGEMENT

Early advice should be sought from other specialist teams such as anaesthetics, intensive care, haematology, infectious diseases and microbiology. Critically ill women must be transferred either to the Acute Observation Unit (AOU) on Birthing Suite or to the Intensive Care Unit (ICU).[5]

Where the source of sepsis is identified, de-escalate to appropriate antibiotic.[6] Seek advice from Infectious Diseases/Clinical Microbiology if needed.

Ensure that an appropriate team member is nominated to give information to the woman and her family/whānau members on the diagnosis, the management plan and regular updates on progress. Check regularly that people understand the information and explanations they are given.[1]

Ensure discharge notifications to Lead Maternity Carers (LMCs) and GPs include the diagnosis of sepsis.

ANTIBIOTIC REGIMENS

Empiric antibiotics for sepsis with source not apparent

First choice:

- Cefuroxime IV 1.5 g 8-hourly, AND
- Metronidazole IV 500 mg 12-hourly, AND
- Gentamicin IV 5 mg/kg ideal body weight stat dose (*given in sodium chloride 0.9% 100 mL over 30 min)(CWH only)*

Alternative – severe penicillin allergy

- Clindamycin IV 600 mg 8-hourly, AND
- Gentamicin IV 5 mg/kg ideal body weight stat dose (*given in sodium chloride 0.9% 100 mL over 30 min) (CWH only)*

SPECIAL CONSIDERATIONS

***At risk MRSA, initiate antibiotics and consult Infectious Diseases/Microbiology:**

- Vancomycin IV 25-35 mg/kg loading dose and then as per Pink Book guidelines, AND
- Cefuroxime IV 1.5 g 8-hourly, AND
- Metronidazole IV 500 mg 12-hourly

***Risk factors**

- A history of being MRSA positive
- Close contact with others with known MRSA infection e.g. at home (especially in overcrowded household settings), school, work or in sport
- Admitted to a hospital or care facility overseas within the past 12 months, or any facility with known MRSA
- Skin or soft tissue infection not responding to an appropriate trial of first-line antibiotics (including adequate dose and satisfactory source control)

****At risk multi-drug resistant gram-negatives**

- Meropenem IV 1 g 8 hourly (single agent)

****Risk factors**

- Recent admission to overseas healthcare facility
- Multidrug-resistant Gram-negative bacilli positive
- Travel to developing country in previous six months
- Household contact with MDR-GNB
- Residence or admission to any facility with high prevalence of MDR-GNB
- Broad spectrum antimicrobial treatment

GROUP A STREPTOCOCCUS (GAS)

This requires a specific mention as it is the most common pathogen associated with death from genital sepsis.

Once shock develops, mortality approaches 60%[2].

Pregnant or postnatal women are at a 20-fold increased risk of infection[2].

The key characteristic that distinguishes GAS from other sepsis is the rapid deterioration in clinical condition of the woman, with sudden onset shock and organ dysfunction.

Can cause:

- Endometritis
- Necrotising fasciitis (which can affect uterus, vagina, external genitalia)
- Toxic shock syndrome

Typically presents with fever and abdominal pain.

Streptococcal Toxic Shock Syndrome – hypotension, tachycardia and leucocytosis.

Initial treatment is with aggressive fluid resuscitation and antibiotics (usually with regimen that includes clindamycin[2] IV 600mg 8-hourly, which inhibits exotoxin production).

Source control may be required with wound or vulval debridement, hysterectomy.

The administration of intravenous immunoglobulin in streptococcal toxic shock syndrome is made on a case-by-case basis, after discussion with Infectious Diseases regarding suitability.

Regimen: Intravenous Immunoglobulins (IVIg): 1-2 g/kg IV (up to 2 doses within the first 72 hours).

Requests can be made via Blood Bank.

ADDITIONAL NOTES

Blood cultures

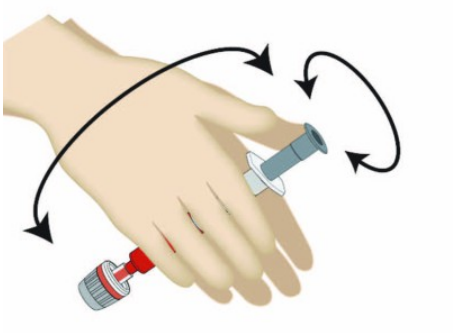
For best results ensure the following:

- 2 sets of blood cultures are required from 2 separate sites.
- **Blood cultures should be taken before administration of antibiotics.**
- Asepsis is critical to the process of blood cultures – ensure skin and bottle tops are cleaned and dry before taking blood sample.
- 1 set = 1 aerobic (blue cap) followed by 1 anaerobic (purple cap) bottles. Fill blue bottle first followed by purple.
- Keep bottles in upright position during collection. Use the bottle graduation lines to accurately gauge sample volume. Collect 10mL into each blood culture bottle.
- Gently mix each bottle.
- Ensure barcode is not covered when labelling bottles.

Arterial and Venous blood gas sample

For best results ensure the following:

- The sample should not be taken unless on site at Christchurch Women's Hospital due to the test being time critical.
- The sample should be capped and delivered within 15 minutes of collection if being processed by the laboratory.
- 500 µL whole blood required in hep blood gas syringe for laboratory process.
- Air bubbles should be immediately expelled from the syringe by gently tapping the sides of the syringe allowing them to go to the top of the syringe for expulsion in order to avoid an air contamination and falsely altering the pO2 results.



- Following air-bubbles expulsion, homogenization of the sample with the anticoagulant should be done to avoid formation of the clots. For optimal anticoagulation, rolling of the syringe between the palms, and then inverting it vertically is recommended (as above).

DELIVERY CONSIDERATIONS

- Early involvement of the obstetric anaesthetist should be routine in cases of sepsis, specifically if anaesthesia is likely to be required for delivery or postpartum transfer to Theatre. There exists concern around epidural/spinal anaesthesia in the setting of sepsis – this needs to be balanced on a case-by-case basis against the option of GA.
- Extrauterine sepsis should be treated with a view to prolonging preterm pregnancies. It may be reasonable to consider delivery at term to simplify maternal resuscitation.
- Intrauterine sepsis should be strongly suspected with fetal tachycardia, uterine tenderness, offensive discharge, ruptured membranes or recent intrauterine procedure.
- Delivery should be considered if intrauterine sepsis is suspected. Consideration should be taken as to the severity of maternal infection and gestational age of the fetus.

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APPENDIX 1 MATERNAL SEPSIS PATHWAY

RECOGNISE SEPSIS

Commence **maternity vital signs chart**. Calculate **MEWS** score and escalate as per MEWS score.

- ☐ Temp ≥ 38 or ≤ 36°C, shivering, fever or very cold
- ☐ Systolic BP < 90 mmHg: clammy or sweaty
- ☐ Altered mental state or behaviour, confusion or disorientation
- ☐ Other signs/symptoms: .....
- ☐ Heart rate ≥ 100 bpm
- ☐ New onset of pain
- ☐ Respiratory rate ≥ 25 breaths/min, short of breath

Call for help and complete all 'sepsis 6' actions **within one hour**.

Time zero: .....

☐ **Insert IV cannula (2 x 18g)**

PRIMARY UNITS – CONSULT WITH OBSTETRIC TEAM AND ARRANGE TRANSFER

TAKE 3 – Cultures, Lactate, Urine Measurement

- ☐ **Take blood cultures** (aerobic + anaerobic)
- ☐ **Take urine measurement** (IDC + hourly bag + MSU)
- ☐ **Take venous lactate** (blood gas syringe)

ONLY IF AT CWH AS BLOOD GAS TEST IS TIME CRITICAL

Consider arterial blood gas if abnormal RR or O2 sats

Consider appropriate swabs and cultures

Additional bloods:

- ☐ Coagulation studies *(blue tube)*
- ☐ U&E ☐ Creatinine ☐ CRP
- ☐ LFT *(green or gold tube)*
- ☐ Full blood count *(purple tube)*
- ☐ Group & Hold *(pink tube)*

GIVE 3 – Antibiotics, Fluids, Oxygen

☐ **Give antibiotics** after taking blood cultures **Check for allergies**	TIME AND DATE	LIST OTHER ANTIBIOTICS USED *(in case of allergies/ special considerations*
First choice: ☐ Cefuroxime IV 1.5 g 8-hourly ☐ Metronidazole IV 500 mg 12-hourly ☐ Gentamicin IV 5 mg/kg ideal body weight stat *given in sodium chloride 0.9% 100 mL over 30 min) (CWH only)*		
Alternative – severe penicillin allergy: ☐ Clindamycin IV 600 mg 8-hourly, AND ☐ Gentamicin IV 5 mg/kg ideal body weight stat dose *(given in sodium chloride 0.9% 100 mL over 30 min) (CWH only)*		
SPECIAL CONSIDERATIONS * **At risk MRSA, initiate antibiotics and consult Infectious Diseases/Microbiology:** ☐ Vancomycin IV 25-35 mg/kg loading dose and then as per Pink Book guidelines, AND ☐ Cefuroxime IV 1.5 g 8-hourly, AND ☐ Metronidazole IV 500 mg 12-hourly ** **At risk multi-drug resistant gram-negatives** ☐ Meropenem IV 1 g 8 hourly (single agent)		

☐ **Give IV fluid** bolus: sodium chloride 0.9% 500mL over less than 15 minutes. ☐ Repeat bolus if no improvement

☐ **Give high flow Oxygen** via rebreather mask (titrate to achieve saturations 95-98%)

CONSIDER 2 – Delivery, Thromboprophylaxis

Assess fetal state ☐ CTG ☐ USS Consider delivery or evacuation of retained products	☐ Birth or OT
Consider VTE risk ☐ Thromboprophylaxis	

ASSESS SEVERITY

Severe sepsis indicated by one or more of the following: consider ICU review

☐ Systolic BP < 90 mmHg or 40 mmHg from baseline	☐ Platelets < 150	☐ Lactate > 2 mmol/L
☐ New confusion or drowsiness	☐ O2 ≥ 2 L/min required to maintain SATS	☐ Bilirubin > 35
☐ Decreased urine output < 80 mL/4 hours	☐ Creatinine > 90	

REFER

INADEQUATE RESPONSE OR SIGNS OF DETERIORATION

If there is an **inadequate response to initial management OR signs of deterioration** are present this should be recognised as having an increased risk of mortality.

BEWARE the woman who initially responds to resuscitation and then deteriorates.

☐ Initiate 777 – request Obstetric & Adult Teams	☐ **Extend coverage for Grp A strep**
☐ **Involve** ICU team	☐ **Clindamycin 600mg IV 8 hourly**
☐ **Liaise** with Infectious Diseases	☐ Discuss with Infectious Diseases suitability of IVIG 1-2 g/kg IV (up to 2 doses within the first 72 hours)

APPENDIX 2 SEPSIS BOX CHECKLIST (MATERNITY AND GYNAECOLOGY)

DOCUMENTATION

Maternity Sepsis Pathway (Ref.2408196)	1
Maternity Vital Signs Chart (Ref.2406285)	1
Fluid Balance Chart	1
Laminated copy of maternal Sepsis guideline	1

IV ACCESS

Tourniquet	1
Alcohol swabs	2
IV cannula 16 g	2
IV cannula 18 g	2
Gauze/cotton balls pack	1
IV extension kit	1
Lignocaine injection 5 mL	1
Syringe with needle 1 mL	1
Luer locks/bungs	2
Sodium chloride 0.9% (Posiflush) 10 mL	1
Roll of tape / Tegaderm	1

BLOOD CULTURES AND BASELINE BLOODS

Blood culture sets (each set = 1 aerobic (blue cap) and 1 anaerobic (purple cap) bottles	2
Blood gas syringe (venous lactate)	1
Purple top blood tube (full blood count)	1
Green / Gold top blood tube (Urea, electrolyte, creatinine, LFT, CRP)	1
Blue top blood tube (coagulation screen)	1
Alcohol swabs	3
Vacutainer blood collection tube and needle	1
Butterfly Blood collection set	1
Blood transfer device (Pink)	1
Blood transfer device (Blue)	1
Permanent marker pen	1
Laboratory form and bag	1
Blood Bank form and bag	1
Pressure pad/spot plaster	1
Medication added sticker	2
Green IV cannula sticker	3
Tegaderm	1

OXYGEN

High concentration mask	1
Oxygen tubing	1

IV ANTIBIOTICS

Intravenous pump giving set	1
20 mL syringe	2
Drawing up needles (red)	2
Sodium chloride 0.9% (Posiflush) 10 mL	3
Cefuroxime 1.5 g add to water for injection 20 mL	1 pk
Metronidazole 500mg IV (prefilled bag)	1
Gentamicin box 80 mg/2 mL add to sodium chloride 0.9% 100 mL bag	1 pk

FLUID CHALLENGE

Sodium chloride 0.9% 500mL	2
IV giving set	1
Intravenous pump giving set	1

MEASURE URINE OUTPUT

Catheterisation pack	1
Foley catheter size 14	1
Lubricating jelly	1
Sodium Chloride for irrigation 30 mL	1
Syringe 10 mL	1
Water for injection 10 mL	1
Urine drainage bag	1
Catheter leg tape	1
Urine meter	1

FURTHER INVESTIGATIONS

Specimen container	2
Sterile transport swab	2