

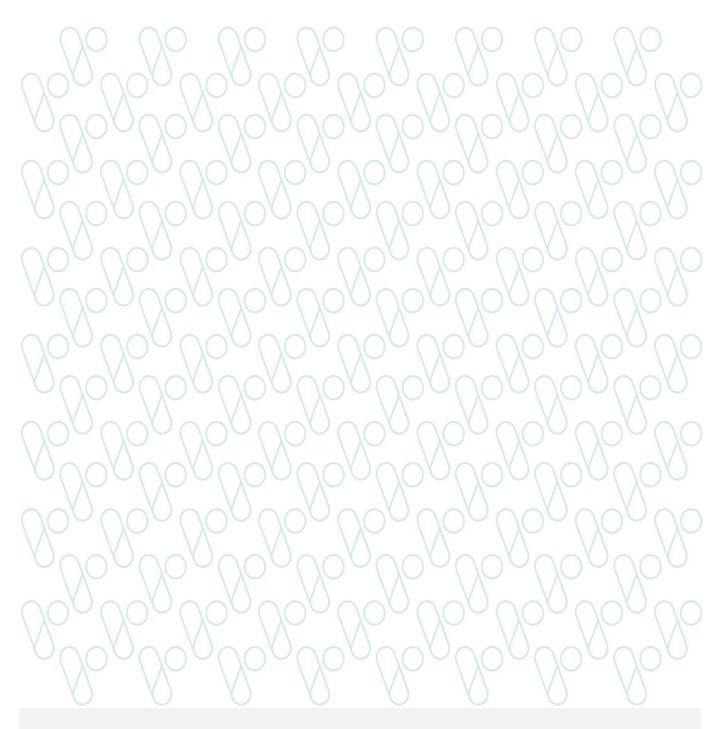
December 2024

# **Maternal Sepsis**

Clinical guidance

**OFFICIAL** 





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## Key messages

- Sepsis is one of the leading causes of maternal deaths in Australia.<sup>1</sup>
- 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 (Carbapenemase Producing Organisms)	Bacteria that have developed resistance to several antibiotics, including carbapenems
CSU	Catheter specimen of urine
DBP	Diastolic blood pressure
ESBL (extended spectrum beta lactamase)	An enzyme found in some strains of bacteria. ESBL-producing bacteria can't be killed by many antibiotics such as penicillins and some cephalosporins.
FiO <sub>2</sub>	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 blood pressure
	Diastolic BP + 1/3 (systolic BP – diastolic BP)
MROs (multi-resistant organisms)	Organisms that are resistant to some antimicrobials

Term	Definition
MRSA (methicillin-resistant Staphylococcus aureus)	Staphylococcus aureus that is resistant to methicillin/ flucloxacillin
MSU	Midstream urine
PaO <sub>2</sub>	Partial pressure of oxygen (assessed with arterial blood gas)
Puerperal sepsis	Peripartum sepsis resulting from the genitourinary tract
SBP	Systolic blood pressure
Sepsis	A life-threatening organ dysfunction caused by a dysregulated host response to infection. A diagnosis of sepsis is considered in any patient with an acute illness or clinical deterioration that may be due to infection <sup>6</sup> Sepsis is a life-threatening condition
Septic shock	Septic shock is defined as 'a subset of sepsis in which the underlying circulatory, cellular and metabolic abnormalities are associated with a greater risk of mortality than sepsis alone <sup>6</sup>

#### 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 can be a life-threatening condition that requires a time critical response. The effects can be life-changing, leading to lasting maternal illness affecting the woman's passage to motherhood, the 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, regardless of the care setting, in community or a hospital. Consider sepsis in all patients with acute illness or physiological deterioration who may have an infection and ask the question 'could it be sepsis?' as part of regular clinical assessments.

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).

Risk factors that may assist with the early recognition of maternal sepsis could include bleeding in pregnancy, miscarriage, prolonged rupture of membranes, prolonged labour, retained products of conception and fetal tachycardia.

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

# **Initial sepsis screen**

### Recognise

Consider sepsis if there is evidence of an infection and the woman has two or more of the following:

Site of concern	Signs or symptoms	
Fevers and rigors	self-reported or observed	
Neurological	altered conscious state	
	• headache	
	• neck stiffness	
	agitation	
Poor peripheral	• cool peripheries	
perfusion	delayed capillary refill time or mottled skin	
Chest	• cough	
	shortness of breath	
Abdomen	• pain/tenderness	
	• peritonism	
	diarrhoea	
	• vomiting	
Malodorous vaginal discharge	self-reported or detected	
Urine	dysuria	
	• frequency	
	flank pain	
Skin and soft tissue	• cellulitis	
	• mastitis	
	wound erythema or discharge	
Line insertion sites	erythema	
	• pain	
	• swelling	
	discharge	
Blood pressure	• MAP < 65mmHg	
Two or more of the	• temperature < 36°C or > 38°C	
following	<ul> <li>respiratory rate &gt; 24 per minute sustained for 15 minutes</li> </ul>	
	<ul> <li>heart rate &gt; 110 sustained for 15 minutes</li> </ul>	
	<ul> <li>WCC 15 x 109 or &lt; 4 x 109 or &gt; 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</li> </ul>	

If the initial sepsis screen is positive and there is clinical suspicion or evidence of infection,  $\underline{\text{start}}$   $\underline{\text{treatment.}}$ 

## Respond

### Rapid response - most tasks will need to be carried out concurrently

Oxygen	Continuous oximetry
	<ul> <li>Administer supplementary oxygen to maintain SpO2 &gt; 95%</li> </ul>
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 antibiotic recommendations where source is chorioamnionitis or unknown
	Refer to Therapeutic Guidelines – Antibiotic where the source of infection is known
	· ·
	• Refer to <u>Table 2</u> for additional antibiotic considerations
Source	Refer to <u>Table 3</u> for administration guidance
screening	Investigations as determined by clinical assessment of likely source of infection:
Do not delay	o midstream urine (MSU)/catheter specimen of urine (CSU)
antibiotic	<ul> <li>high vaginal (HVS) / low vaginal (LVS) / endocervical swab for</li> </ul>
treatment for	microscopy/culture/sensitivities (MCS)
culture collection.	o sputum MCS
conection.	o chest x-ray
	o nasal/ throat swabs for extended panel respiratory viruses multiplex PCR, including COVID-19
	o wound swab for MCS
	o cultures from lumens of central lines
	<ul> <li>stool testing for faecal multiplex PCR including C. difficile</li> <li>breast milk MCS</li> </ul>
Fluid	
management	<ul> <li>Fluid resuscitation if systolic BP &lt; 90 mmHg (or if lactate ≥ 2 mmol/L in the absence of labour)</li> <li>stat fluid bolus of 500 mL of IV crystalloid, i.e. 0.9% sodium chloride; then further 500 mL</li> <li>STAT if required. Be aware of comorbidities, e.g. cardiac or respiratory disease, that may make fluid overload more likely</li> </ul>
	o monitor for fluid overload
	o escalate if no improvement in SBP after 1L of IV fluid.
	o insert IDC with hourly measure
	o monitor urine output hourly
Fetal	o escalate if urine output < 20 mL/hr and/or 0.5mL/kg/hour
considerations	Consider fetal surveillance if appropriate for the gestation of the pregnancy.
	<ul> <li>Consider urgent birth if chorioamnionitis is suspected. At pre- or peri-viable gestations, delivery may be required for maternal wellbeing.</li> </ul>
	<ul> <li>If pre-term birth is likely, give corticosteroids according to local protocol. Maternal health is the priority rather than fetal lung maturity.</li> </ul>
	Consider contacting PIPER for further advice on 1300 137 650
Escalate	<ul> <li>Involve senior staff – consider anaesthetics, medical teams, ICU, ED or ARV in line with local escalation procedures</li> </ul>
	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 <sub>2</sub>	<ul> <li>Acute respiratory failure as evidenced by acute need for invasive or non-invasive mechanical ventilation or</li> <li>PaO<sub>2</sub>/FiO<sub>2</sub> &lt; 300</li> </ul>	
Coagulation (FBE, INR, APTT)	<ul> <li>Platelets &lt; 100 x 10<sup>9</sup>/L or</li> <li>INR &gt; 1.5 or</li> <li>PTT &gt; 60 seconds &lt; 100</li> </ul>	
Liver (LFT)	• Bilirubin > 30 μmol/L	
Cardiovascular	Persistent hypotension (SBP < 85 mmHg) after fluid administration or  MAP < 65 mmHg  Or  BP > 40 mmHg decrease in SBP	
Renal (U&E, urine output)	<ul> <li>Serum creatinine &gt; 100 µmol/L or</li> <li>Doubling of creatinine or</li> <li>Urine output &lt; 20mL/hr and/or 0.5 mL/kg/hour (for 2 hours)</li> </ul>	
Mental status assessment	Agitation, confusion, or unresponsiveness	
Lactate	≥ 2 mmol/L in the absence of labour	

# **Ongoing management**

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

# Antibiotic prescribing and administration

#### 1. Prescribe antibiotics

 Unknown source or chorioamnionitis These regimens are for initial intravenous doses for sepsis/septic shock and should be used for all women to minimise delays to administration (<u>Table</u> 1).

- Known source: According to Therapeutic Guidelines<sup>3</sup> or local, evidence-based guidelines.
- Also consider additional risk factors (<u>Table 2</u>).
- 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<sup>4</sup> (<u>Table 3</u>). 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 (<u>Table 1</u>).

### Additional considerations

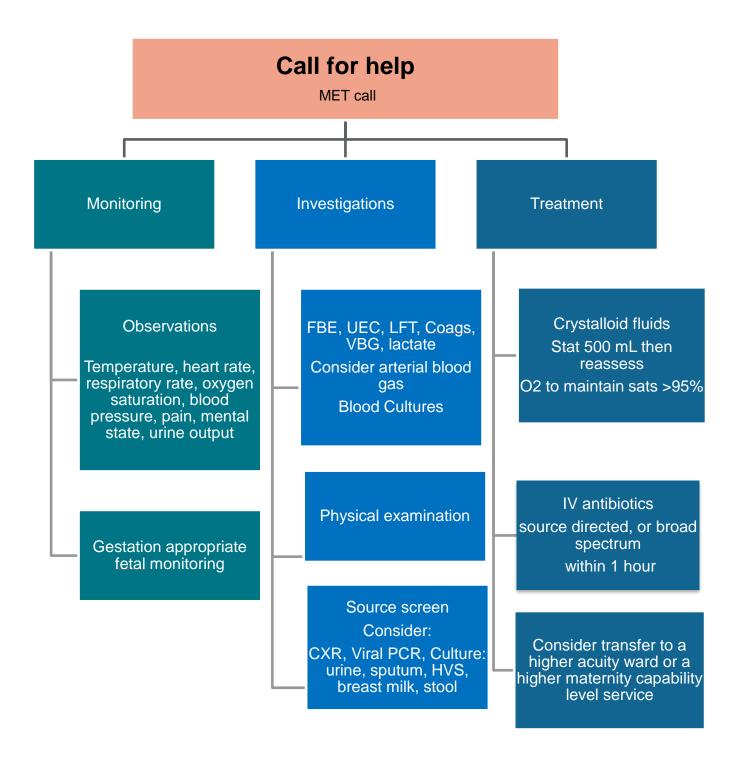
- Abnormal temperature and elevated heart rate may be the most common combination, however not all women with sepsis will have a fever at ≥ 38.0°C.
- Maternal corticosteroid administration often increases the white blood cell count, but the suspicion for infection should not be discounted without further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

## **Summary flow chart**

Think sepsis if any 2 of the following are present, plus a clinical suspicion of sepsis:

- 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 x 10<sup>9</sup> or < 4 x 10<sup>9</sup>
- MAP < 65 mmHg</li>

# **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 flucloxacillin 2g IV, 4-hourly PLUS metronidazole 500mg IV, 12-hourly	*aminoglycoside IV THEN cefazolin 2g IV, 6-hourly PLUS metronidazole 500mg IV, 12-hourly	*aminoglycoside IV  THEN  metronidazole 500 mg, IV, 12 hourly  PLUS  vancomycin 25mg/kg loading dose, then 1.5g IV 12-hourly Check level before the 4th dose
Hospital-acquired sepsis [Infection acquired as a direct or indirect result of healthcare]	piperacillin/ tazobactam 4.5g IV, 6-hourly	*aminoglycoside IV THEN cefazolin 2g IV, 6-hourly PLUS metronidazole 500mg IV, 12-hourly	*aminoglycoside IV  THEN  vancomycin IV 25mg/kg loading dose, then 1.5g IV 12-hourly.  Check level before the 4th dose  PLUS  metronidazole 500mg, IV, 12 hourly
Chorioamnionitis	*aminoglycoside IV THEN amoxicillin 2g IV 6- hourly PLUS metronidazole 500 mg IV 12-hourly	*aminoglycoside IV THEN cefazolin 2g IV, 6-hourly PLUS metronidazole 500mg IV 12-hourly	*aminoglycoside IV PLUS metronidazole 500 mg IV, 12 hourly PLUS vancomycin 25mg/kg loading dose, then 1.5g IV 12-hourly Check level before the 4 <sup>th</sup> dose

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. (adjusted body weight for women with a BMI>30)

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

Gentamicin – initial dose 7 mg/kg for septic shock to maximum 600 mg (Routinely used in pregnancy) 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 25mg/kg loading dose, then 1.5g IV 12-hourly (if at risk of MRSA colonisation and/or presence of lines)
Group A Streptococcus Contact with GAS infection case Toxic shock	ADD clindamycin 600mg IV 8 hourly CONSIDER IV immunoglobulin 1-2 g/kg IV (with ID consultation)
Suspected Neisseria meningitidis infection, <b>or</b> suspected CNS infection	ADD ceftriaxone 2g, IV, 12 hourly
Woman with prior history of multi-resistant Gram-negative colonisation – e.g. CPOs, ESBLs, multi-resistant organisms (MRO), <b>or</b> Overseas hospitalisation or travel in the previous 6 months	REPLACE all empiric antibiotics with single agent meropenem 2g, 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 25mg/kg loading dose, then 1.5g IV, 12-hourly

# Table 3: Rapid antibiotic administration advice

Antibiotic	Administration instructions
Amoxycillin	1g with 20 mL water for injection over 3–4 minutes (2x1g amoxicillin vials are needed)
Clindamycin	Dilute 600 mg in 50 mL sodium chloride 0.9% and infuse over 20 minutes
Ceftriaxone	2g with 40 mL water for injection and infuse over 5 minutes
Cefazolin	2g with 19 mL water for injection and infuse over 5 minutes
Flucloxacillin	2g 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	4.5g with 20 mL water for injection and infuse over 5 minutes
Vancomycin	500 mg with 10 mL water for injection and 1g with 20 mL water for injection to make a concentration of 50mg/mL. Dilute to 5 mg/mL with sodium chloride 0.9%, i.e. dilute 1g to at least 200 mL.* 1g may be infused over 1 hour, 1.5g over 1.5 hours and 2g over 2 hours.  * If fluid restriction, max concentration 10 mg/mL, i.e. dilute 1g in 100 mL

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

Non pregnant adult <sup>5.</sup>	$3.5-9.1 \times 10^3 \mathrm{mm}^3$	
First trimester	$5.7-13.6 \times 10^3 \mathrm{mm}^3$	
Second trimester	$5.6-14.8 \times 10^3 \mathrm{mm}^3$	
Third trimester	5.9–16.9 × 10 <sup>3</sup> mm <sup>3</sup>	

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## **Additional resources**

- 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:
  <a href="https://www.safetyandquality.gov.au/publications-and-resources/resource-library/review-trigger-tools-support-early-identification-sepsis-healthcare-settings">https://www.safetyandquality.gov.au/publications-and-resources/resource-library/review-trigger-tools-support-early-identification-sepsis-healthcare-settings</a>.
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- Australian Commission on Safety and Quality in Health Care. <u>Lactate in the deteriorating patient and sepsis</u> Factsheet
- Australian Commission on Safety and Quality in Health Care. <u>Antimicrobial guidance for sepsis programs</u>
   Factsheet
- Australian Commission on Safety and Quality in Health Care. <u>Information for people with sepsis and their families (for adults)</u> Factsheet.
- Australian Commission on Safety and Quality in Health Care. <u>National Consensus Statement:</u>
   Essential elements for recognising and responding to acute physiological deterioration

## Citation

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#### MATERNAL SEPSIS PATHWAY

UR number ..... Health service Family name..... Given name..... DOB..... **MATERNAL SEPSIS** Address..... **PATHWAY** COMPLETE ALL FIELDS OR AFFIX LABEL HERE For pregnant women and up to six weeks post-partum, including perinatal loss at any gestation, in any setting R Ε Fevers and rigors C Neurological: Altered conscious state, headache, neck stiffness, agitation 0 Peripheral perfusion: Cool peripheries, delayed capillary refill, mottling G Chest: Cough, shortness of breath N Abdomen: Pain/tenderness, peritonism, diarrhoea, vomiting 1 S Malodorous vaginal discharge Ε Urine: Dysuria, frequency, flank pain Skin and soft tissues: Cellulitis, mastitis Wound erythema or discharge Line insertion sites: Erythema, pain, swelling, discharge And two or more of: Temperature  $<36^{\circ}$ C or  $>38^{\circ}$ C, respiratory rate >24 per minute for 15 minutes, HR 110 for >15minutes, WCC 15x109 or <4x109 or>10% immature neutrophils (bands) **OR** MAP < 65mmHg Diagnosis of sepsis should not be delayed while waiting for results A white cell count obtained within 24 hours START TREATMENT PROMPTLY AND COMPLETE 1st DOSE OF ANTIBIOTICS WITHIN 60 MINUTES Oxygen: Continuous oximetry. Maintain SpO2 >95% ■ IV access: Insert 2X large bore peripheral cannulas ☐ Investigations: FBE, U&E's, LFT's, INR, APTT. Venous blood gas for lactate. 2 sets of anaerobic blood cultures R Observations: HR and BP every 15 minutes for first hour then according to clinical picture. Document. Ε Antibiotics: Promptly administer. See guidance - Rapid antibiotic administration advice (Table 3) plus tables 1-2 S Source screening: P Midstream urine (MSU)/catheter specimen of urine (CSU) o high vaginal (HVS) / low vaginal (LVS) / endocervical 0 swab for microscopy/culture/sensitivities (MCS) N Sputum MCS & Chest x-ray D □ 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: if systolic BP < 90 mmHg (or if lactate ≥ 2 mmol/L in the absence of labour)</p> Stat fluid bolus of 500 ml of IV crystalloid, i.e. 0.9% sodium chloride; then further 500 ml STAT if required. Consider Ε comorbidities, and monitor for fluid overload S ☐ Escalate if no improvement in SBP after 1L of IV fluid. C Insert IDC with hourly measure A Monitor urine output hourly □ Escalate if urine output < 20 ml/hr</p> A Fetal considerations: Т ☐ Fetal surveillance if appropriate for gestation Е ☐ Expediate birth if chorioamnionitis is suspected Corticosteroids for preterm birth Escalate to senior staff, transfer to acute ward/ICU or higher maternity capability service. Call PIPER 1300 137 650.

**Designation:** 

Date:

Clinician name:



