

Detection, investigation and management of maternal sepsis

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Key Amendments

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Introduction

In the UK, sepsis remains one of the leading causes of direct maternal death. The most recent triennial report of maternal deaths from Saving Lives, Improving Mothers' Care (MBRRACE 2013-2015) found that deaths from sepsis occurred after women presented with clear signs of sepsis, or potential sepsis. It was highlighted that early recognition and completion of the sepsis care was missing in these cases. With this aim the Sepsis Trust have produced, and National Institute for Health and Care Excellence endorsed improved maternal sepsis screening tools (Sepsis trust and NICE 2016). The Surviving Sepsis campaign has updated the management of sepsis and septic shock (Dellinger et al 2008). The speed and appropriateness of therapy administered in the initial hours after severe sepsis develops are likely to influence outcome with early resuscitation improving survival rates. The focus of good sepsis management centres on early recognition and prompt treatment. The goals of sepsis management should be to restore intravascular volume, and to ensure an adequate blood pressure and cardiac output to perfuse vital organs. Treating early with appropriate antibiotics (with source control when possible) improves outcomes (Kumar et al), and it is therefore important to take microbiological cultures and have local antibiotic policies that reflect local resistance patterns (PHE). It is important that a senior doctor experienced in sepsis management reviews all patients who have sepsis at an early stage

Definitions

These have now been simplified for all cases and include only sepsis and septic shock

SEPSIS - is defined as life-threatening organ dysfunction caused by a dysregulated host response to infection.

SEPTIC SHOCK - is a subset of sepsis with circulatory and cellular/metabolic dysfunction associated with a higher risk of mortality. Septic shock is defined as persisting hypotension and having a serum lactate level of greater than 2 mmol/l despite adequate volume resuscitation in the context of sepsis. (ref ICM 2017)

Features of septic shock include

- Hypotension – systolic blood pressure 90mmHg or below in the absence of other causes e.g. bleeding
- Hypoxaemia
- Poor peripheral perfusion, mottled skin
- Oliguria
- Metabolic acidosis
- Elevated lactate (Serum lactate ≥ 4 mmol/L is indicative of tissue hypoperfusion)
- Positive blood cultures
- Abnormal coagulation and bleeding

- Abnormal renal and liver function tests
- Plasma glucose >7.7 mmol/l in the absence of diabetes is one of the diagnostic criteria for sepsis

Risk Factors For Maternal Sepsis

- Obesity
- Impaired glucose tolerance / diabetes
- Impaired immunity/ immunosuppressant medication
- Anaemia
- GAS infection in close contacts / family members
- History of group B streptococcal infection
- Black or other minority ethnic group origin
- Amniocentesis and other invasive procedures
- Cervical cerclage
- Prolonged spontaneous rupture of membranes
- History of pelvic infection
- Vaginal discharge
- Vaginal trauma, caesarean section, wound haematoma
- Retained products of conception

Possible causes of sepsis in pregnancy and puerperium include:

- Chorioamnionitis
- Postpartum endometritis/ infected retained products
- Genital tract infections
- Wound infections (including perineum)
- Intra-abdominal collections
- Pharyngitis
- Pneumonia
- Mastitis
- UTI
- Skin and soft-tissue infection
- Gastroenteritis
- Acute appendicitis/ pancreatitis/ cholecystitis
- Infection related to regional anaesthesia (meningitis/ spinal abscess)

N.B. Mastitis may lead to breast abscesses, necrotising fasciitis and toxic shock syndrome and must never be overlooked

Common Organisms Responsible For Maternal Sepsis

The most common organisms identified in pregnant women dying from sepsis are Lancefield group A beta-haemolytic Streptococcus (GAS) and E. Coli.

Mixed infections with both Gram-positive and Gram-negative organisms are common, especially in chorioamnionitis. Coliform infection is associated with urinary sepsis, preterm premature rupture of membranes, and cerclage.

The major pathogens causing sepsis in puerperium are GAS, E. Coli, Staphylococcus aureus, Streptococcus pneumoniae, methicillin-resistant S. aureus (MRSA), Clostridium septicum and Morganella morganii.

Influenza remains a cause of maternal death and should be considered as a possible source of infection, particularly during peak seasonal periods (usually January) (MBRRACE 2017)

Signs And Symptoms

All healthcare professionals should be aware of the symptoms and signs of maternal sepsis and of the rapid, potentially lethal course of severe sepsis and septic shock.

Red flags for maternal sepsis – initiate sepsis 6 (see below)

- Responds only to voice or pain/ unresponsive
- Systolic B.P \leq 90 mmHg (or drop >40 from normal)
- Heart rate $>$ 130 per minute
- Respiratory rate \geq 25 per minute
- Needs oxygen to keep SpO₂ \geq 92%
- Non-blanching rash, mottled/ ashen/ cyanotic
- Not passed urine in last 18 hours
- Urine output less than 0.5 ml/kg/hr
- Lactate \geq 2 mmol/l

Amber flags - Send bloods if 2 criteria present, consider if 1, Include lactate, FBC, U&Es, CRP, LFTs, clotting, Immediate call to ST3+ doctor/Shift Leader For review within 1hr

- Relatives concerned about mental status
- Acute deterioration in functional ability
- Respiratory rate 21-24 OR breathing hard
- Heart rate 100-130 OR new arrhythmia
- Systolic B.P 91-100 mmHg
- Not passed urine in last 12-18 hours
- Temperature $<$ 36°C or $>$ 38°C
- Immunosuppressed/ diabetes/ gestational diabetes
- Has had invasive procedure in last 6 weeks
- (e.g. CS, forceps delivery, ERPC, cerclage, CVs, miscarriage, termination)
- Prolonged rupture of membranes
- Close contact with GAS
- Bleeding/ wound infection/ vaginal discharge
- Non-reassuring CTG/ fetal tachycardia $>$ 160

Agonising pain out of proportion to the clinical signs may suggest deep infection, and necrotising fasciitis/myositis must be considered

Management Of Patients With Suspected / Confirmed Sepsis

Management of patients with severe sepsis is aimed at stabilising the patient while diagnosing and treating the underlying cause. The response to treatment in this group of patients is highly unpredictable and mortality is high. Treatment is more likely to be effective, and severe sepsis avoided, if appropriate therapy is started early.

A multidisciplinary team approach is required including obstetricians, midwives, anaesthetists, microbiologists and critical care staff. Inform infection control team if necessary. Critically ill patients should be cared for in level II or intensive care with facilities for invasive techniques and monitoring. Care must be undertaken by experienced nursing/midwifery staff.

The following sepsis bundles have been recommended by the Surviving Sepsis Campaign (Dellinger RP et al 2008).

All women with suspected sepsis should be screened utilising the INPATIENT MATERNAL SEPSIS TOOL (see appendix 1) and the sepsis six pathway initiated immediately if needed.

SEPSIS BUNDLE-TASKS TO BE PERFORMED WITHIN THE FIRST HOUR OF THE IDENTIFICATION OF SEVERE SEPSIS: THE GOLDEN HOUR

1. **SEPSIS 6**

1. Give oxygen to keep saturations > 94%
2. Give IV antibiotics. According to Trust protocol. Consider allergies prior to administration
3. Give IV fluids. If hypotensive/lactate >2mmol/l, 500ml stat (can repeat up to 30ml/kg). Ask doctor regarding fluids, if not hypotensive and lactate normal.
Ask Anaesthetist regarding fluids if patient has pre-eclampsia
4. Take blood cultures. At least a peripheral set. Consider e.g. urine, sputum, vaginal swabs, breast milk culture, throat swabs. Think source control & timing of delivery of baby- start CTG
5. Take serial lactate Corroborate high VBG lactate with arterial sample. If lactate >4mmol/l, call Critical Care and recheck after each 10ml/kg challenge
6. Take urine output May require urinary catheter

N.B. NSAIDS should be avoided for pain relief in cases of sepsis as they impede the ability of polymorphs to fight GAS infection.

MONITORING

Observations should be recorded on a WOW HDU chart

- Pulse, BP, respiratory rate, oxygen saturations every 15 minutes (frequency may be altered depending on maternal condition)
- Temperature hourly (frequency may be altered depending on maternal condition)
- Strict fluid balance – consider urinary catheter/ hourly catheter bag
- In antenatal patients
 - if ≥28 weeks, perform CTG (between 26-28 weeks CTG at the discretion of consultant)
 - if <28 weeks, auscultate fetal heart intermittently
 - Observe PV loss/amniotic fluid

- In postnatal patients, observe lochia/wound or drain sites and perineum
- In case of severe sepsis observations listed above plus
 - Level of consciousness
 - 3 Lead ECG
 - consider CVP

INVESTIGATIONS

- Arterial blood gas measurement (to assess for hypoxia and measurement of serum lactate)
- FBC, Coagulation, Group and Save, U&E's, LFTs and CRP
- Obtain blood cultures prior to antibiotic administration (provided this does not delay antibiotic administration)
- Culture of other sites as guided by clinical suspicion of the focus of infection e.g. MSU, HVS, wound swab, breast milk, stool, respiratory secretions, CSF, placental swabs (send placenta to histology at Birmingham Women's Hospital, if sepsis is suspected) and neonatal swabs
- Throat swab if woman presents with sore throat/ respiratory symptoms
- If MRSA status is unknown, a pre-moistened nose swab may be sent for rapid MRSA screening
- Check previous and recent microbiology results as there may be clues as to the nature of the likely pathogen
- Imaging studies (USS/ CXR, CT scan) to identify/sample any source of infection as appropriate
- Check blood glucose in severe sepsis

Airway And Breathing

Maintain adequate oxygenation i.e. Check patent airway, adequate breathing, use supplemental oxygen High flow Oxygen therapy (15L/min) via non-re-breathe mask to maintain SpO₂ >94%, unless CO₂ retainer, in which case, contact medical staff.

Circulation

Hypovolaemia is present in almost all patients with septic shock. Fluid resuscitation is mainstay of management. In the event of hypotension and/or lactate >2mmol/l, 500ml stat (can repeat up to 30ml/kg). Ask doctor regarding fluids, if not hypotensive and lactate normal. Ask Anaesthetist regarding fluids if patient has pre-eclampsia. Use vasopressors for hypotension not responding to initial fluid resuscitation to maintain mean arterial pressure (MAP) > 65mmHg. Invasive monitoring should be considered if not responding to simple resuscitation, and will be directed by anaesthetic staff.

Antibiotic Therapy

Intravenous broad-spectrum antibiotics should be started as early as possible, always within the first hour of recognising severe sepsis.

INITIAL ANTIBIOTICS (all IV)

Antenatal: Cefotaxime 2g QDS + Metronidazole 500mg TDS

Postnatal: Co-amoxiclav Dose 1.2g TDS

If severe infection ADD clindamycin 900mg QDS to above

SEVERE PENICILLIN ALLERGY (antenatal and postnatal)

Clindamycin 900mg QDS AND Gentamicin Dose 5mg/kg ideal body weight (3mg/kg if renal dysfunction) OD

In severe sepsis or septic shock seek urgent consultant microbiologist advice

If Group A streptococcal infection is suspected

clindamycin (600mg to 1.2mg 6-8hrly) is more effective than penicillin as it inhibits exotoxin production

Liaise with Consultant microbiologist for further advice and therapy especially in any of the following situations:

- a)** Patient known to have been recently (in the past year) colonised or infected with an antibiotic-resistant bacterium (e.g. MRSA).
- b)** Patient has a history of an in-patient hospital stay in the past 1 year (other than for straightforward childbirth).
- c)** Patient has received antibiotic therapy in the past 4 weeks (other than perioperative prophylaxis).
- d)** Patient has a urinary or vascular catheter that has been in situ for 24 hours or more at the time of onset of infection.

The antimicrobial regimen should be reassessed daily to optimise activity, to prevent the development of resistance, to reduce toxicity and to reduce costs. If and when a specific organism is identified, antibiotic therapy can then be modified to the most appropriate regimen. Duration of therapy should be typically 7–10 days; longer courses may be appropriate in women who have a slow clinical response, non-drainable focus of infection, or immunological deficiencies, including neutropenia.

Remove Infected Foci

- The focus of infection should be identified as a priority and dealt with.
- This may be by uterine evacuation or by drainage of breast, wound or pelvic abscess, haematoma drainage or removal of potentially infected devices such as cannulas.

Blood Products

Red blood cells should be given when the haemoglobin is less than 70g/l with the aim of achieving a target haemoglobin of 70-90g/l. This will increase oxygen delivery. A higher Hb may be required in special circumstance e.g. acute haemorrhage or lactic acidosis. It is common for patients with severe sepsis to develop a coagulopathy and thrombocytopenia. If the patient is not actively bleeding and no invasive procedures are planned it may be possible to manage coagulopathy conservatively. Do not use FFP to correct laboratory clotting abnormalities unless there is bleeding or any invasive procedures are planned.

Administer platelets only when platelet count is

<5 x 10⁹ regardless of bleeding

5 – 30 x10⁹ and there is a significant risk of bleeding

> 50 x 10⁹ are required for surgery or invasive procedures

Thromboprophylaxis

- Refer to trust guideline
- Measure for and fit TEDs

Fluid Balance

- Careful monitoring of fluid balance is important and should be documented on the WOW HDU chart
- Hourly documentation of all input and output (indwelling urinary catheter with hourly urometer). This will allow for significant fluid deficit or excessive input to be detected, to evaluate the woman's response and to help avoid the development of pulmonary oedema. A central line may be required to help monitor fluid balance.

Indications For Transfer To ITU

The overriding principle is that sepsis can be a life threatening emergency so continued involvement of the consultant obstetrician and consultant anaesthetist is vital. If the woman fails to respond to initial management (the sepsis six) then early involvement of the ICU team is needed.

SYSTEM	INDICATION
• Cardiovascular:	Hypotension or raised serum lactate persisting despite fluid resuscitation, suggesting the need for inotrope support
• Respiratory :	Pulmonary oedema Mechanical ventilation Airway protection
• Renal :	Renal dialysis
• Neurological :	Significantly decreased conscious level
• Miscellaneous:	Multi-organ failure Uncorrected acidosis Hypothermia

Fetal Monitoring and Delivery

In a critically ill pregnant woman, birth of the baby may be considered if it would be beneficial to the mother or the baby or to both. Decision on the timing, place and mode of birth should be made by a consultant obstetrician following discussion with the woman if her condition allows.

If preterm delivery is anticipated, cautious consideration should be given to the use of antenatal corticosteroids for fetal lung maturity in the woman with sepsis.

During the intrapartum period, continuous cardiotocograph (CTG) is recommended and changes in the CTG, such as changes in baseline rate, variability or new onset decelerations, must prompt reassessment of maternal mean arterial pressure, hypoxia and acidaemia.

Epidural/spinal anaesthesia should be avoided in women with sepsis and a general anaesthetic will usually be required for caesarean section. The presence of sepsis is not an absolute contraindication and the mode of anaesthesia will depend upon patient comorbidities with particular reference for chest infection and obesity. The choice of anaesthesia for individual patients should be discussed with the Consultant Obstetric anaesthetist.

Prophylaxis For The Neonate, Other Family Members And Health Care Workers

When a mother has been found to have invasive group A streptococcal infection in the peripartum period, the neonatologist should be informed and prophylactic antibiotics administered to the baby.

Close household contacts of women with group A streptococcal infection should be warned to seek medical attention should symptoms develop, and the situation may warrant antibiotic prophylaxis.

Healthcare workers who have been exposed to respiratory secretions of women with group A streptococcal infection should be considered for antibiotic prophylaxis.

Infection Control Issues

Group A Streptococcus and MRSA are easily transmitted via the hands of healthcare workers and via close contact in households. Local infection control guidelines should be followed for hospital specific isolation and contact precautions.

Women with previously documented carriage of or infection with multiresistant organisms (e.g. Extended Spectrum Beta-Lactamase (ESBL) producing organisms, MRSA, GAS or Panton-Valentine Leukocidin producing staphylococci (PVL) should prompt notification of the infection control team.

Invasive group A streptococcal infections are notifiable and the infection control team and the consultant for communicable diseases should be informed.

Women suspected of or diagnosed with group A Streptococcus sepsis should be isolated in a single room with en suite facilities to minimise the risk of spread to other women. Local advice from infectious control colleagues should always be sought.

Debrief

Women whose pregnancies have been complicated by severe sepsis should be reviewed and debriefed by consultant prior to discharge and if needed, a formal review should be arranged to discuss the events.

References

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therapy is the critical determinant of survival in human septic shock'. *Crit Care Med* 2006; 34(6):1589-
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Appendix 1 – Inpatient Maternal Sepsis Tool

Please note that the key documents are not designed to be printed, but to be used on-line. This is to ensure that the correct and most up-to-date version is being used. If, in exceptional circumstances, you need to print a copy, please note that the information will only be valid for 24 hours and should be read in conjunction with the key document supporting information and/or Key Document intranet page, which will provide approval and review information.

INPATIENT MATERNAL
SEPSIS TOOL



To be applied to all women who are pregnant or up to six weeks postpartum (or after the end of pregnancy if pregnancy did not end in a birth) who have a suspected infection or have clinical observations outside normal limits

<p>Staff member completing form: Date Name Designation Signature</p>	<p>Low risk of sepsis. Use standard protocols, consider discharge with safety netting. Consider obstetric need.</p> <p style="text-align: center;">NO</p>
<p>1. Has WOWS triggered? <input type="checkbox"/> OR does woman look sick? <input type="checkbox"/> OR is baby tachycardic (≥ 160 bpm)? <input type="checkbox"/></p> <p style="text-align: center;">NO</p>	<p>4. Any Maternal Amber Flag criteria?</p> <p>Relatives concerned about mental status Acute deterioration in functional ability Respiratory rate 21-24 OR breathing hard Heart rate 100-130 OR new arrhythmia Systolic B.P 91-100 mmHg Not passed urine in last 12-18 hours Temperature $< 36^{\circ}\text{C}$ or $> 38^{\circ}\text{C}$ Immunosuppressed/ diabetes/ gestational diabetes Has had invasive procedure in last 6 weeks (e.g. CS, forceps delivery, ERPC, cerclage, CVs, miscarriage, termination)</p>
<p style="text-align: center;">YES</p> <p>2. Could this be an infection?</p> <p>Yes, but source unclear at present <input type="checkbox"/> Chorioamnionitis/ endometritis <input type="checkbox"/> Urinary Tract Infection <input type="checkbox"/> Infected caesarean or perineal wound <input type="checkbox"/> Influenza, severe sore throat, or pneumonia <input type="checkbox"/> Abdominal pain or distension <input type="checkbox"/> Breast abscess/ mastitis <input type="checkbox"/> Other (specify):..... <input type="checkbox"/></p> <p style="text-align: center;">NO</p>	<p>Prolonged rupture of membranes Close contact with GAS Bleeding/ wound infection/ vaginal discharge Non-reassuring CTG/ fetal tachycardia > 160</p> <p style="text-align: center;">YES</p>
<p style="text-align: center;">YES</p> <p>3. Is ONE maternal Red Flag present?</p> <p>Responds only to voice or pain/ unresponsive <input type="checkbox"/> Systolic B.P ≤ 90 mmHg (or drop > 40 from normal) <input type="checkbox"/> Heart rate > 130 per minute <input type="checkbox"/> Respiratory rate ≥ 25 per minute <input type="checkbox"/> Needs oxygen to keep SpO₂ $\geq 92\%$ <input type="checkbox"/> Non-blanching rash, mottled/ ashen/ cyanotic <input type="checkbox"/> Not passed urine in last 18 hours <input type="checkbox"/> Urine output less than 0.5 ml/kg/hr <input type="checkbox"/> Lactate ≥ 2 mmol/l <input type="checkbox"/> <small>(note- lactate may be raised in & immediately after normal labour & delivery)</small></p> <p style="text-align: center;">NO</p>	<p>Send bloods if 2 criteria present, consider if 1 Include lactate, FBC, U&Es, CRP, LFTs, clotting Time Complete <input type="text"/></p> <p>Immediate call to ST3+ doctor/ Shift Leader For review within 1hr <input type="text"/></p> <p>Time clinician/ Midwife attended <input type="text"/></p> <p style="text-align: center;">YES</p> <p>Is AKI present? (tick) YES <input type="checkbox"/> NO <input type="checkbox"/></p> <p style="text-align: center;">YES</p> <p>Clinician to make antimicrobial prescribing decision within 3h Time Complete <input type="text"/></p>
<p style="text-align: center;">YES</p>	<p style="text-align: center;">YES</p>
<p>Red Flag Sepsis - Start Sepsis 6 pathway NOW (see overleaf) This is time critical, immediate action is required.</p>	



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**SEPSIS SIX
PATHWAY**

To be applied to all women who are pregnant or up to six weeks postpartum (or after the end of pregnancy if pregnancy did not end in a birth) who have a suspected infection or have clinical observations outside normal limits

	TIME ZERO	CONSULTANT INFORMED?	INITIALS
Inform Consultant Obstetrician & Obstetric Anaesthetist; OR consider transfer to Obstetric Unit. State patient has Red Flag Sepsis			

Action (complete ALL within 1 hour)			
	TIME COMPLETE	INITIALS	REASON NOT DONE / VARIANCE
1. Administer oxygen Aim to keep saturations > 94%			
2. Take blood cultures At least a peripheral set. Consider e.g. urine, sputum, vaginal swabs, breast milk culture, throat swabs Think source control & timing of delivery of baby-start CTG			
3. Give IV antibiotics According to Trust protocol Consider allergies prior to administration			
4. Give IV fluids If hypotensive/lactate >2mmol/l, 500ml stat (can repeat up to 30ml/kg). Ask doctor regarding fluids if not hypotensive and lactate normal. Ask Anaesthetist regarding fluids if patient has pre-eclampsia			
5. Check serial lactates Corroborate high VBG lactate with arterial sample If lactate >4mmol/l, call Critical Care and recheck after each 10ml/kg challenge			Not applicable- initial lactate <input type="checkbox"/>
6. Measure urine output May require urinary catheter Ensure fluid balance chart commenced & completed hourly			

<p>If after delivering the Sepsis Six, patient still has:</p> <ul style="list-style-type: none"> • systolic B.P <90 mmHg • reduced level of consciousness despite resuscitation • respiratory rate over 25 breaths per minute • lactate not reducing <p>Or if patient is clearly critically ill at any time then call Critical Care Outreach immediately and Contact Obs Consultant Immediately</p>	<p>INITIAL ANTIBIOTICS (all IV)</p> <p>Antenatal:Cefotaxime 2g QDS+Metronidazole 500mg TDS</p> <p>Postnatal: Co-amoxiclav Dose 1.2g TDS</p> <p>If severe infection ADD clindamycin 900mg QDS to above</p> <p>SEVERE PENICILLIN ALLERGY (antenatal and postnatal)</p> <p>Clindamycin 900mg QDS AND Gentamicin Dose 5mg/kg ideal body weight (3mg/kg if renal dysfunction) OD</p> <p>IF FAILURE TO RESPOND CONTACT MICROBIOLOGIST</p>
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Appendix 2- Maternal Telephone Triage Sepsis Tool

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