Sepsis

Chapter contents

There is an increasing awareness of the importance of sepsis, associated with its apparently increasing incidence and because it was the most common cause of direct maternal death in the 2006-08 triennium. This reduced significantly in the 2009-12 triennium [300] a position that has been maintained [301]. While the UK mortality rate is low at 0.6 per 100,000 maternities, the rate of severe maternal morbidity is fifty times higher [302].

Sepsis can be difficult to diagnose in pregnancy. This is because the criteria overlap with the signs and investigation results of healthy pregnant women during the second trimester, third trimester, and in labour for every criterion (respiratory rate, $PaCO_2$, heart rate, and white cell count) except temperature [303].

'Think Sepsis' at an early stage when presented with an unwell pregnant or recently pregnant woman: take all appropriate observations and act on them [304].

Sepsis

The key actions for diagnosis and management of sepsis are:

- Timely recognition – the patient is not always febrile.
- Fast administration of intravenous antibiotics.
- Quick involvement of experts – senior review is essential.

Maternal sepsis is defined as life-threatening organ dysfunction caused by a dysregulated host response to **infection** resulting from infection during pregnancy, childbirth, post-abortion, or the postpartum period [305,306].

Septic shock is a subset of sepsis in which underlying circulatory and cellular/metabolic abnormalities are profound enough to substantially increase mortality. Patients have persisting hypotension requiring vasopressors to maintain a mean arterial pressure of 65 mmHg or more and have a serum lactate level of greater than 2 mmol L^{-1} despite adequate volume resuscitation.

Sepsis with acute organ dysfunction has a mortality rate of 20% to 40%, increasing to 60% if septic shock develops. Survival rates following sepsis are related to early recognition and initiation of treatment. Disease progress may be rapid, and the course may be lethal.

This chapter is written with reference to the hospital clinical guideline on maternal sepsis [307].

In maternity, it is usually caused by bacterial infection and the diagnosis is complicated by the normal physiological response to pregnancy [308,309]. Women may be able to withstand the physiological insult of widespread inflammation for prolonged periods before sudden collapse. Progression can be extremely rapid: Group A streptococcus can typically move from the first sign of systemic inflammatory response syndrome (SIRS) to septic shock in less than two hours for 50% of women and in less than nine hours for 75% of women [310].

Diagnosis of sepsis

Diagnosis of sepsis should be followed by activation of the current sepsis guideline. The following is a set of general principles drawn from national and international guidelines, and the UK Sepsis Trust tool.

The systemic signs and symptoms of sepsis are common in pregnancy and in the puerperium, the main differences being in causative organisms and sites of infection.

Haemorrhage is the most common cause of shock in pregnancy but if it has been excluded, or treatment fails to produce the expected improvement, then consider sepsis as a potential cause.

Genital tract sepsis will often be due to chorioamnionitis before delivery or surgical infection after delivery. Remember that genital tract infection will predispose to uterine atony and postpartum haemorrhage.

Risk factors

Parturients at higher risk have been identified by NICE [311] as women who:

- Have impaired immune systems because of illness or drugs.
- Have gestational diabetes or diabetes or other comorbidities.
- Needed invasive procedures (for example, caesarean section, forceps delivery, removal of retained products of conception).
- 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 or an offensive vaginal discharge.

Clinical presentation

The onset of sepsis is characterised by a hyperdynamic circulation, reduced systemic vascular resistance secondary to arteriolar vasodilatation, and increased respiratory rate in association with the development of anaerobic metabolism and lactic acidosis [312].

Sepsis

Clinical signs suggestive of sepsis include one or more of the following: pyrexia, hypothermia, tachycardia, tachypnoea, hypoxia, hypotension, oliguria, impaired consciousness and failure to respond to treatment.

These signs, including pyrexia, may not always be present and are not necessarily related to the severity of sepsis. A widespread rash may be an early sign of toxic shock syndrome.

The primary responsibility for diagnosing and managing sepsis rests with the obstetricians. As a doctor you may be involved in helping with this and in particular anaesthetists have a specific role in determining whether the patient needs critical care.

Assessment scoring – qSOFA

The quick sepsis-related organ failure assessment score (qSOFA) ranges from 0-3 points; the presence of 2 of 3 qSOFA points in adult patients (including maternity) with suspected infection indicates a greater risk of death or prolonged ICU stay [313; this reference is a good recent review].

Assessment	**qSOFA score**
Tachypnoea (rate ≥ 22 breaths min^{-1})	1
Hypotension (SBP ≤ 100 mmHg)	1
Altered mentation (GCS < 15)	1

Criteria

UHCW has adopted the Inpatient Maternal Sepsis Tool from the UK Sepsis Trust [314]. Review the criteria below if there is a clinical suspicion of infection.

White cell count

WCC is raised in pregnancy and a count > 15 x 10^9 L^{-1} in the antenatal period should be investigated. In the peripartum period:

Day 0 (day of delivery) Accepted upper limit of WCC 25 × 10^9 L^{-1}.

Day 1	Accepted upper limit of WCC 20×10^9 L^{-1}.
Day 2	Accepted upper limit of WCC 15×10^9 L^{-1}.
Day 3-5	Trend towards pre-pregnancy values by day 5

An isolated raised WCC or CRP around delivery should not be treated as sepsis without other features.

Maternal red flags

If one is present along with a clinical suspicion of infection, start the sepsis 6 pathway immediately.

- Responds only to voice or pain; unresponsive.
- Systolic BP ≤ 90 mmHg (or drop > 40 from normal).
- Heart rate > 130 per minute.
- Respiratory rate ≥ 25 per minute.
- Needs oxygen to keep SpO_2 ≥ 92%.
- Non-blanching rash, mottled / ashen / cyanotic.
- Not passed urine in last 18 hours. (Caution PET.)
- Urine output less than 0.5 mL kg^{-1} hr^{-1}. (Caution PET.)
- Lactate ≥ 2 mmol L^{-1}. (Lactate may be raised during and immediately after normal labour and delivery.)

Maternal amber flags

If no red flag, then check for amber. If none present, there is a low risk of sepsis; use standard obstetric care.

If two amber flags are present then make sure that blood samples have been sent including lactate, FBC, U&E, CRP, LFTs and coagulation studies, and consider sending blood samples if only one amber flag is present.

- Any concerns about mental status.
- Acute deterioration in functional ability.
- Respiratory rate 21-24 or breathing hard.

- Heart rate 100-130 or new arrhythmia.
- Systolic BP 91-100 mmHg.
- Not passed urine in last 12-18 hours. (Caution PET.)
- Temperature < 36°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 group A streptococcus (e.g. scarlet fever).
- Bleeding / wound infection / offensive vaginal discharge.
- Non-reassuring CTG / fetal tachycardia > 160 per minute.

If any amber flags are present, check if the woman has acute kidney injury. If so, then treat as for red flag sepsis and start the sepsis 6 pathway immediately.

Multidisciplinary review for women in labour with suspected or actual sepsis

You should take part in ongoing multidisciplinary review takes place, at least once every 12 hours, and seek senior advice and assistance as necessary.

Include a senior intensivist where a woman in labour has sepsis and any of the following signs of organ dysfunction [315]:

- Altered consciousness.
- Hypotension (systolic blood pressure less than 90 mmHg).
- Reduced urine output (less than 0.5 mL kg^{-1} h^{-1}).
- Need for 40% oxygen to maintain oxygen saturation above 92%.
- Tympanic temperature of less than 36°C.

Sepsis 6 pathway – actions in the first hour

1. Give high-flow oxygen to maintain SpO_2 above 94%.
2. Blood cultures before antibiotics.
3. Intravenous antibiotics – broad-spectrum (see below).
4. Intravenous fluid resuscitation (see below).
5. Check serial lactate levels. If venous lactate > 2 mmol L^{-1}, insert an arterial line and check arterial blood gases. If lactate ≥ 4 mmol L^{-1}, call critical care outreach on bleep 2909; if not reducing call registrar on bleep 1684.
6. Hourly urine measurement; may need catheterisation if organ dysfunction is apparent.

A patient with diagnosed sepsis should have observations recorded on the enhanced maternal care chart.

Antibiotic therapy for maternal sepsis

These change from time to time. Refer to the hospital's adult antibiotic guideline and if the source of the infection is known, use antibiotics specific for that source. Broad spectrum antibiotics should be given intravenously for at least 24 hours and then converted to the oral route if the patient improves.

Fluid resuscitation

In the event of hypotension and/or a serum lactate > 2 mmol L^{-1} (indicative of tissue hypoperfusion), deliver an initial 500 mL bolus of Hartmann's solution over 15 minutes, repeated if there is no improvement up to 30 mL kg^{-1} [316].

The place of aggressive fluid therapy remains controversial in maternal sepsis owing to the reduction in serum albumin concentration and the concomitant decrease in capillary oncotic pressure; the administration of large quantities of fluid to pregnant women might result in an increased propensity to fluid overload, pulmonary oedema and myocardial

dysfunction, potentially worsening outcomes [317]. Keep the patient under close review for fluid overload.

Administer vasopressors for hypotension that is not responding to initial fluid resuscitation to maintain mean arterial pressure (MAP) > 65mmHg. Use noradrenaline as first-line treatment; vasopressin and adrenaline as second-line.

Indications for transfer to critical care

In the event of persistent hypotension (SBP < 90 mmHg) despite fluid resuscitation and/or lactate > 4mmol L^{-1}, or reduced level of consciousness, septic shock is likely. The patient needs immediate treatment to restore normal tissue perfusion; refer her to the general adult critical care unit. These patients are not suitable for management on the labour ward.

System	*Indication*
Cardiovascular	Hypotension or raised serum lactate persisting despite fluid resuscitation, suggesting the need for vasopressor support.
Respiratory	Pulmonary oedema.
	Rising oxygen requirement.
	Mechanical ventilation.
	Airway protection.
Renal	Renal replacement therapy.
Neurological	Decreased conscious level.
Miscellaneous	Multi-organ failure.
	Uncorrected acidosis.
	Hypothermia.

Anaesthetic considerations

For women in labour with sepsis and any signs of organ dysfunction (altered consciousness, hypotension, oliguria, hypoxia, hypothermia), only use regional analgesia with caution and advice from a consultant obstetric anaesthetist; only provide regional anaesthesia for such a woman with consultant advice and a senior anaesthetist present [318]. Make sure that any antibiotics for suspected sepsis are administered to the woman before inserting the needle for a regional block.

Neuraxial anaesthesia in sepsis

There is no direct evidence concerning the use of neuraxial anaesthesia in sepsis. Diagnostic lumbar puncture is often undertaken in patients with fever or bacteraemia of unknown origin, and yet no epidemiological studies have shown a relationship to the subsequent development of meningitis or epidural abscess; most cases of meningitis or epidural abscess occur spontaneously [319]. There is a very low incidence of CNS infection after neuraxial anaesthesia, and good evidence from NAP3 that it is lower still in obstetric patients [56].

Central neuraxial blocks may be employed safely in patients with evidence of systemic infection provided that appropriate intravenous antibiotic therapy has started [319]; spinal anaesthesia is preferred [320]. Epidurals are not necessarily contraindicated and, in each case, senior advice should be sought. Rarely, general anaesthesia may be indicated for caesarean section in the collapsed patient undergoing caesarean section: consider using ketamine 0.5-1 mg kg^{-1} as the induction agent.

Cell salvage and infection

Intrauterine infection is a relative contraindication to the salvage of red blood cells. In this circumstance, you should weigh the relative benefits of red cell recycling with the potential risk of contamination: discuss with relevant consultants. Remember that intramyometrial infection is a potent cause of uterine atony and obstetric haemorrhage.

Sepsis

Systemic sepsis is not a contraindication to using intraoperative red cell salvage. The patient is likely to benefit from not being exposed to allogeneic blood if haemoglobin is low.

---

300. MBRRACE-UK *Saving Lives, Improving Mothers' Care: Lessons learned to inform future maternity care from the UK and Ireland Confidential Enquiries into Maternal Deaths and Morbidity 2009-2012*. Oxford: MBRRACE-UK, 2014; page 27.

301. MBRRACE-UK. *Saving Lives, Improving Mothers' Care: Lessons learned to inform maternity care from the UK and Ireland Confidential Enquiries into Maternal Deaths and Morbidity 2014-16*. Oxford: MBRRACE, November 2018.

302. Acosta CD, Harrison DA, Rowan K, Lucas DN, Kurinczuk JJ, Knight M. Maternal morbidity and mortality from severe sepsis: a national cohort study. *BMJ Open* 2016;**6**:e012323.

303. Bauer ME, Bauer ST, Rajala B *et al*. Maternal physiologic parameters in relationship to systemic inflammatory response syndrome criteria: a systematic review and meta-analysis. *Obstet Gynecol* 2014; **124**:535-541.

304. NHS England. Patient Safety Alert NHS/PSA/R/2014/015, 2014.

305. Singer M, Deutschman CS, Seymour CW *et al*. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). *JAMA* 2016; **315**:801-10. doi:10.1001/jama.2016.0287

306. Bonet M, Nogueira Pileggi V, Rijken MJ, *et al*. Towards a consensus definition of maternal sepsis: results of a systematic review and expert consultation. *Reprod Health* 2017; **14**:67.

307. Maitra M, Munthali P, Shoebridge N, Farrall L. *Management of sepsis in pregnancy, labour and postnatal period.* UHCW clinical guideline CG 2105, March 2018.

308. Royal College of Obstetricians and Gynaecologists. *Bacterial Sepsis in Pregnancy.* London: RCOG Clinical green top guideline number 64a, 2012.

309. Royal College of Obstetricians and Gynaecologists. *Bacterial Sepsis following Pregnancy.* London: RCOG Clinical green top guideline number 64b, 2012.

310. Acosta CD, Kurinczuk JJ, Lucas DN, Tuffnell DJ, Sellers S, Knight M. Severe maternal sepsis in the UK, 2011–2012: a national case-control study. *PLoS Med* 2014; **11**: e1001672.

311. National Institute for Health and Care Excellence. *Sepsis: recognition, diagnosis and early management.* NICE guideline NG51, published 13 July 2016; nice.org.uk/guidance/ng51, section 1.2.2.

312. Lucas DN, Robinson PN, Nel MR. Sepsis in obstetrics and the role of the anaesthetist. *Int J Obstet Anesth* 2012; **21**:56-67.

313. Burlinson CEG, Sirounis D, Walley KR, Chau A. Sepsis in pregnancy and the puerperium. *Int J Obstet Anesth*. 2018 Nov; **36**:96-107.

314. Maternal sepsis screening tool. https://sepsistrust.org/wp-content/uploads/2017/08/Inpatient-maternal-NICE-Final-1107-2.pdf, accessed 18 January 2018.

315. National Institute for Health and Clinical Excellence. *Intrapartum care for women with existing medical conditions or obstetric complications and their babies.* London: NICE, 2019; NG121, section 1.13.6.

316. National Institute for Health and Care Excellence. *Sepsis: recognition, diagnosis and early management.* NICE guideline NG51, published 13 July 2016; nice.org.uk/guidance/ng51, section 1.8.1.

317. Frankling CC, Finfer S, Lissauer D, Perner A, Patel JM, Gao F. The dark ages of maternal sepsis: time to be enlightened. *Br J Anaes* 2017; **120**:626-628.

318. National Institute for Health and Clinical Excellence. *Intrapartum care for women with existing medical conditions or obstetric complications and their babies.* London: NICE, 2019; NG121, sections 1.13.11-12 and 14.

319. Segal S. *Neuraxial Anesthesia in the Febrile or Infected Patient*. In: Chestnut DH, Wong CA; Tsen LC; Ngan Kee WD; Beilin Y, Mhyre J. Chestnut's Obstetric Anesthesia: Principles and Practice, 5th edition, 2014. Philadelphia: Elsevier Health Sciences.

320. Wedel DJ, Horlocker TT. Regional anesthesia in the febrile or infected patient. *Reg Anesth Pain Med*. 2006; **31**:324-33.