



Antenatal Guidelines

No. 36 Sepsis, infection and prophylaxis in obstetric patients

Introduction

Sepsis is among the more common causes of direct maternal death with a rising incidence of group A streptococcal disease. The incidence of severe maternal sepsis is 4-5 per 10,000 pregnancies¹⁻³ A woman may rapidly decompensate and develop life-threatening sepsis especially with group A streptococcal sepsis within 12-24 hours.

The treatment of sepsis is challenging due to complex maternal and fetal physiology and may require ITU admission. Early detection, accurate diagnosis and aggressive treatment strategies are essential to improve outcomes and prevent mortality and morbidity.

2. Definitions

Sepsis

Sepsis is the presence (probable or documented), of infection together with systemic manifestations of infection. Severe sepsis is when there is sepsis-induced organ dysfunction or tissue hypoperfusion.

Sepsis is the systemic inflammatory response syndrome (SIRS) due to a confirmed (or suspected) infection. The SIRS covers a broad range of causes and but is generally defined as:

- Temperature $<36^{\circ}\text{C}$ or $>38.3^{\circ}\text{C}$
- Heart rate >90 beats per minute
- Tachypnea >20 breaths per minute or an arterial partial pressure of carbon dioxide less than 4.3 kPa (32 mmHg)
- Leukocytes $<4 \times 10^9$ cells/L or $>12 \times 10^9$ cells/L; or the presence of greater than 10% immature neutrophils (band forms)

SIRs criteria are notoriously nonspecific and have not been adequately validated in pregnant women⁴. No all-encompassing definition of sepsis can be offered here other than to note the various features of infection that are often seen.

Associated '*red flag*' signs and symptoms that should prompt urgent referral for hospital assessment, by emergency ambulance if the lady is unwell:

- abdominal or chest pain
- diarrhoea and/or vomiting
- reduced or absent fetal movements, or absent fetal heart beat
- uterine or renal angle pain and tenderness
- The woman is generally unwell or seems unduly anxious, distressed or panicky

Intrapartum Pyrexia

Maternal pyrexia is defined as a temperature of $\geq 38^{\circ}\text{C}$ on one occasion or $\geq 37.5^{\circ}\text{C}$ on two occasions two hours apart. Intrapartum pyrexia constitutes high risk labour and should be transferred to Consultant led care and the high risk path way.

3. Causes

Common causes include:

- Urinary tract infection, pyelonephritis
- Premature pre-labour rupture of the membranes, prolonged rupture of the membranes at term, chorioamionitis
- Puerperal sepsis (septic miscarriage, endometritis following delivery or termination)
- Wound infection
- Mastitis
- Pneumonia

4. Management

4.a.Sepsis

**GOLDEN HOUR RULE –
Blood cultures taken and 1st dose of antibiotics administered
within 1 hour**

Physiologically young women compensate well therefore signs and symptoms of sepsis occur late in the course of the illness. Early recognition is vital as aggressive resuscitation significantly improves survival. Treatment must firmly prioritise the mother since fetal compromise results mainly from maternal decompensation.

- Prompt initial baseline observations, use MOEWS chart. If patient is tachypnoeic (RR > 20/min), tachycardic (HR > 100/min), hypotensive (systolic BP < 90mmHg), confused, sweating profusely, shivering or if you are worried, commence high flow oxygen (12L O₂ via reservoir bag) and alert medical staff
- Initial baseline bloods and IV cannula: full blood count (FBC), clotting, urea and electrolytes (U&Es), liver function tests (LFTs), C-reactive protein (CRP), glucose and urine dipstick

- Take two sets of blood cultures from separate venepuncture sites regardless of temperature to improve chances of isolating an organism
- Swabs which are relevant according to the presenting symptoms and signs (Throat, vagina, placenta, and baby), midstream urine and any other relevant sample (e.g. sputum, breast milk, and stool) for microbiology.
- Strict fluid balance- record and chart input and output hourly, catheterise early and alert medical staff if urinary output < 0.5ml/kg/hr or 40ml/hr
- Repeat observations at least every 30min initially and chart, use MOEWS and alert medical staff as indicated

Please note pathway on reverse of MOEWS chart for contacting medical staff and outreach team.

Remember, sepsis is a clinical diagnosis, treat the patient in front of you and do not wait for WBC/CRP to commence initial resuscitation.

- Airway: Is the patient maintaining their airway? Are they confused?
- Breathing: look & listen, RR, SpO₂, consider arterial blood gases (assess acid-base status, PaO₂/FiO₂ ratio and lactate), consider chest x-ray (CXR)
- Circulation: HR, BP, CRT, jugular venous pressure (JVP), pulses, peripheral perfusion (skin, urinary output, confusion), fetal tachycardia? Ensure patient has appropriate IV access and baseline bloods were taken. If any concerns liaise early with the Anaesthetic Team and discuss invasive hemodynamic monitoring (central venous/ arterial line)
- Check the patient has a urinary catheter- if not insert one
- Aggressive initial fluid resuscitation: give 20mls/kg (approx 1500ml of crystalloids), aim to restore tissue perfusion within 6hrs of admission, maintain mean BP of 65-70mmHg or a central venous pressure of 8-12mmHg
- Treatment of the infection: make sure you perform septic screen prior to commencing antibiotics (blood cultures, high vaginal swab, mid-stream urine, +/- sputum cultures, consider CXR if clinically indicated).
- If clinically septic broad-spectrum antibiotics should be administered as soon as possible, at least within one hour.
- Liaise with the Microbiology on-call no later than 24hrs after sepsis alert/ problem being identified or sooner if assistance required. Modify antibiotic regimen according to culture results/sensitivities

Any patient who meets the criteria of sepsis and is not responding to initial resuscitation or any patient with severe sepsis should be managed in HDU. Both senior obstetrician (consultant or senior registrar) and senior anaesthetist should be promptly informed of their admission and review the patient.

If at any point in time the patient meets the criteria of septic shock or sepsis with further deterioration of organ dysfunction both senior obstetrician and senior anaesthetist should be contacted immediately and transfer to HDU / ITU considered.

4.b Intrapartum Pyrexia

- Continuous electronic fetal monitoring should be used in presence of suspected chorioamnionitis, sepsis or maternal pyrexia. CTG changes should prompt a maternal assessment as it may be an early warning sign for derangements in maternal end organ systems. There is insufficient evidence regarding FBS sampling in the presence of maternal sepsis to guide clinical practice.
- Take two sets of blood cultures from separate venepuncture sites regardless of temperature to improve chances of isolating an organism. Urine culture and LVS/HVS should also be obtained. Consider the need for other investigations as outlined above
- IV antibiotics should be commenced following collection of blood cultures and paracetamol infusion given every 4-6 hours (max 4g/24 hours). Reduction of intrapartum fever with antipyretics may not only improve the fetal heart trace but also reduce the risk of neonatal encephalopathy⁵.

In the presence of chorioamnionitis antibiotics are administered and control the intrauterine infection but intra amniotic infection can only be considered cured after delivery of the infected products of conception. Intra amniotic infection cannot be cured without delivery. Prompt induction/augmentation of labour, where appropriate, is advised.

Chorioamnionitis leads to a higher risk of caesarean section, endometritis, wound infection, pelvic abscess and post-partum haemorrhage. The new born carries a greater risk of death, asphyxia, early onset sepsis, pneumonia, meningitis, IVH and long term disability. The risk to the fetus is even greater for premature infants.

Regional Anaesthetics

In the presence of intra-partum pyrexia or suspected infection, caution should be exercised when considering siting an epidural due to the potential for increased risk of epidural abscess. If any doubt exists then senior opinion should be sought. It may be reasonable to consider a spinal anaesthetic for delivery in theatre if maternal observations are reassuring. The risks/benefits will need to be considered on a case by case basis.

All discussions with the patient and senior clinicians should be documented, including the potential risks and benefits of each option.

Epidurals can, in some cases, cause maternal pyrexia, however this should be a diagnosis of exclusion and should not delay prompt administration of antibiotics

5. Empirical antibiotics therapy

- Intravenous antibiotic therapy should be started as early as possible and within the first hour of recognition of septic shock and severe sepsis. Each hour of delay is associated with a measureable increase in mortality.
- Cultures should be obtained before starting antibiotics but should not delay antibiotic therapy
- In case of hepatic or renal impairment, advice must be sought from the critical-care team or a consultant physician.

- Duration of therapy should be typically no longer than one week in severe sepsis, longer if slow response or undrainable focus
- Blood cultures may often be negative and in polymicrobial infections only one infecting microbe may escape to the bloodstream. Negative cultures should not be the sole criterion for cessation of treatment or de-escalation to narrower spectrum or oral antibiotics.

Healthcare associated risk factors

Exposure to antibiotics is the single most important risk factor for multi-drug resistant (MDR) pathogens. Where this exposure is associated with in patient care the risk of MDR is further increased. Healthcare associated infection risk factors are surrogates for exposure to antibiotics and MDR pathogens and include:

- Onset of infection during current hospitalisation
- Recent exposure to inpatient hospital care eg last 90 days
- Recent intensive outpatient medical therapies (adapted from American Thoracic Society)

Haemodialysis

Recent intensive exposure to healthcare environment eg

IV line infusions or wound care necessitating outpatient clinic care

Oracle: Pregnancy and neonatal enterocolitis⁶

The Oracle 1 trial suggested an association between preterm pre-labour exposure to co-amoxiclav and subsequent neonatal NEC⁴. Based on this it has been decided locally to avoid co-amoxiclav in pregnant women and use alternative agents.

In a pregnant woman avoid co-amoxiclav if a reasonable alternative exists.

In the postpartum period co-amoxiclav can be used but if an alternative eg cefuroxime has been started prenatally then persist with this unless clinical/microbiological factors dictate otherwise.

If in doubt discuss with a senior colleague or contact the on call Microbiologist

[a]. Community associated (note Healthcare risk factors, note Oracle)

[i]. Antibiotics

- **Preferred**

Co-amoxiclav 1.2g tds IV or cefuroxime 1.5g tds IV plus IV metronidazole 500mg tds IV

Consider once daily gentamicin 5mg/kg in severe sepsis, where poor renal function precludes the use of gentamicin *step up* to piperacillin/tazobactam monotherapy

- **Alternative**

Clindamycin 900mg tds IV plus once daily gentamicin 5mg/kg

Regardless of primary therapy

Consider teicoplanin in those with a past history of MRSA or transferred from a healthcare environment and no recent negative MRSA screen.

Past history of ESBL infection/colonisation

In patients previously infected with an ESBL bacterium consider using empirical meropenem and discuss with on call Microbiologist

[b]. Hospital or healthcare associated (see Healthcare risk factors)

[i]. Antibiotics

- **Preferred**

Piperacillin/tazobactam 4.5 g tds IV plus teicoplanin IV if past history of MRSA

Consider once daily gentamicin 5mg/kg in severe sepsis.

Where poor renal function precludes the use of gentamicin *step up* to meropenem 1g tds IV

- **Alternative**

Clindamycin 900mg tds IV plus once daily gentamicin 5mg/kg

Past history of ESBL infection/colonisation

In patients previously infected with an ESBL bacterium consider using empirical meropenem and discuss with on call Microbiologist

Severe maternal sepsis, suspected or confirmed Group A streptococcal disease

Add clindamycin at a dose of 1.2g qds IV and urgently discuss with a Senior colleague and on call Microbiologist.

Stop clindamycin promptly if Group A streptococcus is excluded as a cause of the sepsis.

[ii]. Microbiological Sampling

Blood cultures

Baseline CRP

Urinalysis and culture if positive

Screen for MRSA carriage, if using an anti-MRSA agent stop this if screens are negative

[iii] Oral switch

Severe sepsis: Duration of therapy should be typically no longer than one week, longer if slow response or undrainable focus

Chorioamnionitis: In the absence of a confirmed or suspected collection antibiotic treatment for chorioamnionitis / intra partum fever can stop 48 hours after the baby has been delivered⁷ providing the patient has been afebrile for at least 24 hours, clinically improving, have normal observations and normalising markers. Antibiotics can be discontinued without

the need for an oral switch.

Endometritis: Antibiotics for endometritis should also be discontinued after 48 hours providing the patient has been afebrile for at least 24 hours, clinically improving, have normal observations and normalising markers. There is no need for an oral switch in the absence of positive blood cultures⁸.

For other aetiologies a co-amoxiclav or cefuroxime /metronidazole regimen can be converted to oral co-amoxiclav 625mg tds

Clindamycin and gentamicin have few suitable oral switches. Cephadrine and metronidazole may be suitable in those with a non-severe allergy to penicillin

See appendix for further details

[iv]. Duration

Depends on ultimate underlying cause. See appendix for guide.

6. Fluid balance in septic shock

- Septic shock is sepsis with hypotension that is refractory (non-responsive) to fluid resuscitation.
- Fluid overload may lead to fatal pulmonary or cerebral oedema.
- Clear, accurate documentation and careful monitoring of fluid balance is essential to avoid fluid overload in women who are unwell, especially when hourly urine output is low or renal function is impaired.
- The advice of an anaesthetist and the critical care team should be sought at an early stage.

7. Operative intervention

- Persistent or swinging pyrexia or failure to respond to the treatment may be the result of a persistent deeply seated focus of infection.
- TVS, Pelvic USS and MRI should be considered early to locate focus of infection. If surgery is needed to remove focus of infection, it should be carried out earlier rather than later or as a last resort as it could be life-saving.
- Laparotomy for suspected intra-abdominal infection should involve a general surgeon.

8. Neonatal Sepsis

Bacterial sepsis is a major cause of morbidity and mortality in the new born. The incidence is higher in pre-term and low birth weight infants. The clinical presentation of sepsis in the new born can be non-specific with acute deterioration. When a neonate presents with sepsis Legionnaires disease should be considered when the birth was in water. Neonatal legionella is a rare diagnosis and the bacterium is inherently resistant to beta lactams (penicillins, cephalosporions and meropenem) and has recently been associated with heated home pools (the hot water is held at temperature for days to weeks pre partum). Septicaemia in the new born can kill within a few hours, even in a term infant.

If in any doubt, seek a senior opinion

See neonatal guidelines for further information

9. Leadership and continuity of care

- When managing complex cases, it must be clear who is in charge of the women's care. This may not be the named consultant so the lead clinician should be agreed and clearly documented in the patient record.
- Anaesthetic and critical-care staff play a vital role in the management of sepsis and should be involved as early as possible particularly when there is circulatory or respiratory failure.

10. Record Keeping

It is expected that every episode of care be recorded clearly, in chronological order and as contemporaneously as possible by all healthcare professionals as per Hospital Trust Policy. This is in keeping with standards set by professional colleges, i.e. NMC and RCOG. All entries must have the **date and time** together with **signature and printed name**.

11. Education

- There is a clear need to raise both the maternal and professional awareness about antenatal, intrapartum and puerperal sepsis, so that it can be prevented where possible, recognised quickly and managed effectively and immediately.
- As most of the cases are acquired in community, importance of good personal hygiene should be emphasised especially hand washing **before** and after using lavatory and changing sanitary towels.
- To seek advice early when the women or her family or close contacts have a sore throat or upper respiratory tract infection.
- AN advice to women re: general hand washing, care of child with a sore throat, etc.
- Staff awareness of sepsis to be incorporated on PROMPT day

Appendix 1

Surgical antimicrobial prophylaxis/treatment in Obstetric Patients

(see individual guidelines for details, use in conjunction with guideline 36)

Procedure	Antimicrobial, not penicillin allergic	Antimicrobial, mild penicillin allergy	Antimicrobial, severe penicillin allergy	Duration of treatment
Caesarean Section	Co-amoxiclav 1.2g iv	Cefuroxime 1.5g and metronidazole 500mg iv	Teicoplanin 400mg, metronidazole 500mg and gentamicin 240mg iv	Pre-incision only
Manual Removal of placenta	Co-amoxiclav 1.2g iv	Cefuroxime 1.5g and metronidazole 500mg iv	Teicoplanin 400mg, metronidazole 500mg and gentamicin 240mg iv	Pre-operative only
Group B Streptococcus	Benzylpenicillin 3g iv followed by 1.8g every 4 hours whilst in labour	Clindamycin 900mg eight hourly whilst in labour	Clindamycin 900mg eight hourly whilst in labour	Labour
Third degree tear	Co-amoxiclav 1.2g iv (oral switch co-amoxiclav 625mg TDS)	Cefuroxime 1.5g and metronidazole 500mg iv (oral switch cefradine 1g QDS and metronidazole 400mg TDS)	Teicoplanin 400mg, metronidazole 500mg and gentamicin 240mg iv (oral switch – liaise microbiology)	Continue oral antibiotics for 1 week
ERPC	Metronidazole	S/A	S/A	7 days

	1g PR stat, doxycycline 100mg BD 7 days			
Cervical cerclage	At the discretion of the operating team			
Intrapartum pyrexia (one temp $\geq 38.0C$ or 2 measurements $\geq 37.5C$ 2 hours apart	Cefuroxime 1.5g TDS , metronidazole 500mg TDS	Cefuroxime 1.5g iv TDS , metronidazole 500mg iv TDS	Clindamycin 900mg TDS, gentamicin 5mg/kg	Review and aim to stop 48h after delivery. In the clinically stable patient with no evidence of bacteraemia antibiotics should stop if afebrile, clinical improvement with improving pain and wcc normalising
Endometritis	Augmentin 1.2g iv or 625 mg PO TDS depending on presentation	Cefuroxime 1.5g iv TDS, metronidazole 500mg TDS or oral cefradine 1g QDS and metronidazole 400mg TDS	Teicoplanin 400mg, metronidazole 500mg and gentamicin 240mg iv or liaise with microbiology	In the clinically stable patient with no evidence of bacteraemia antibiotics should stop at 48h if afebrile, clinical improvement with improving pain and wcc normalising
UTI (*)	Nitrofurantoin MR100mg BD (not after 36 weeks) or cephalexin	Nitrofurantoin MR100mg BD (not after 36 weeks) Or cephalexin	Nitrofurantoin MR 100mg BD (not after 36 weeks)	7 days Followed by a test of cure

	500mg BD 7 days	500mg BD 7 days		
UTI prophylaxis (**)	Nitrofurantoin MR 100mg OD or cephalexin 250mg OD	Nitrofurantoin MR 100mg OD or cephalexin 250mg OD	Nitrofurantoin MR 100mg OD	Stop nitrofurantoin at 36 weeks. Stop cephalexin in the early postpartum period.
Pyelonephritis	Consider trimethoprim or ertapenam with caution. Liaise with microbiology.	Consider trimethoprim or ertapenam with caution. Liaise with microbiology	Consider trimethoprim or ertapenam with caution. Liaise with microbiology	14 days

* Positive nitrites using dipstick may be sufficient to prompt commencement of empirical antimicrobial. Any treatment should be reviewed and changed depending on antimicrobial sensitivity. (9)

**UTI prophylaxis must be used only for patients with at least 2 confirmed symptomatic UTIs within the last 6 months, eradication of last UTI and consideration to latest organisms and sensitivities. It should not be used for persisting bacteriuria after treatment. Patient advice should be given regarding good hydration, emptying bladder before and after intercourse, frequent and complete bladder emptying and hygiene.

Appendix 2 – From trust guidelines on antimicrobial treatment guidelines

Safe	Avoid
<p>Penicillins (see later for co-amoxiclav)</p> <p>Cephalosporins</p> <p>Erythromycin</p> <p>Nitrofurantoin (avoid from 36 weeks)</p>	<p>Tetracyclines</p> <p>Trimethoprim (Discuss with Microbiology if no alternative, do not give if folate deficient, taking folate antagonists or had treatment with trimethoprim in the last year)</p> <p>Quinolones including levofloxacin</p> <p>Metronidazole (probably safe in 2nd and third trimester, avoid high dose)</p> <p>Aminoglycosides (except in life threatening infection)</p> <p>Co-amoxiclav (associated with NEC in certain groups, local decision to avoid where possible – discuss with microbiology if no alternative)</p>

Appendix 3: When to send an MSU in pregnancy⁹

Bacteriuria is the presence of bacteria in urine. In the absence of signs or symptoms of urinary tract infection this asymptomatic state *should* be treated in pregnancy when usually it is considered as normal.

Pregnancy is associated with physiological pyuria and treatment should not be used based on this alone.

The predictive values of urine dipsticking are useful in symptomatic disease in the non-pregnant but are not adequate for use in pregnancy. Urine culture is the standard for screening for ASB and diagnosis of symptomatic disease. Confirmatory MSU is required in ASB. Blind empirical therapy is not indicated in ASB ie wait for confirmation prior to treatment.

Symptoms to enquire about include:

- Dysuria
- Frequency
- Urgency
- Polyuria
- Supra-pubic tenderness
- Haematuria
- Flank pain

Presence of fever is suspicious for upper urinary tract involvement.

Urine from antenatal patients is to be sent in the following scenarios:

- The first antenatal visit to screen for asymptomatic bacteriuria (ASB). If present on 1st sample, repeat MSU and then commence treatment as necessary after the second sample has been analysed
- Suspected pyelonephritis
- Symptoms of UTI/pyelonephritis regardless of urinalysis

- Following treatment of ASB or symptomatic disease, culture one week after treatment and on all subsequent clinic visits
- Where the antenatal care plan notes that frequent MSU's are required (e.g. recurrent UTI, renal disease, persistent symptoms)

In the event that urine is dipped (do not dip looking specifically for bacteriuria) then send a sample for culture (investigation of ASB) only if nitrites are identified

All urines should be reviewed at 24-48 hours and antibiotics changed or stopped accordingly.

Monitoring and Audit

Auditable standards:

Documentation and administration of antibiotics
Requirement and timing of blood cultures been taken

Reports to:

Clinical Effectiveness Committee – responsible for action plan and implementation of recommendations audit

Frequency of audit:

Annual

Responsible person:

Senior labour ward midwife

Cross references

Antenatal Guideline 31 - Maternity Hand Held Notes, Hospital Records and Record Keeping
Intrapartum Guideline 10 The monitoring of fetal well-being during labour
Postnatal Guideline 8 Postnatal care
Antenatal Guideline 44 – Guideline development within the maternity services

References

Specific (numbered in text)

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4. Existing models fail to predict sepsis in an obstetric population with intrauterine infection. *Am J Obstet Gynaecol* 2010; **203**: e1-5.
5. The relationship between intrapartum maternal fever and neonatal acidosis as risk factors for neonatal encephalopathy. AUImpy LW, *Am J Obstet Gynecol*. 2008;198(1):49.e1.
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7. Single additional dose post-partum therapy for women with chorioamnionitis *Obstet Gynaecol* 2003; **102**: 957.
8. A randomized, double blind, placebo controlled trial of oral antibiotic therapy following intravenous antibiotic therapy for post-partum endometritis *Obstet Gynaecol* 1991; **77**: 60-62. (check green top etc)
9. NICE UTI - clinical knowledge summaries

General background

RCOG green top guideline Sepsis in pregnancy Guideline 64

The Maternal-Fetal Medicine Units cesarean registry: chorioamnionitis at term and its duration-relationship to outcomes. AURouse, National Institute of Child Health And Human Development, Maternal-Fetal Medicine Units Network, *Am J Obstet Gynecol*. 2004;191(1):211.

Diagnosis and Management of Clinical Chorioamnionitis
(www.ncbi.nlm.nih.gov/pmc/articles/PMC3008318)

Diagnosis of UTI, simple algorithm

www.gov.uk/government/uploads/system/uploads/attachment_data/file/345784/UTI_quick_ref_guidelines.pdf

<http://cks.nice.org.uk/urinary-tract-infection-lower-women#!scenario:4>

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Version	6

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