Companions to Management Series

FEVER/SEPSIS IN PREGNANCY

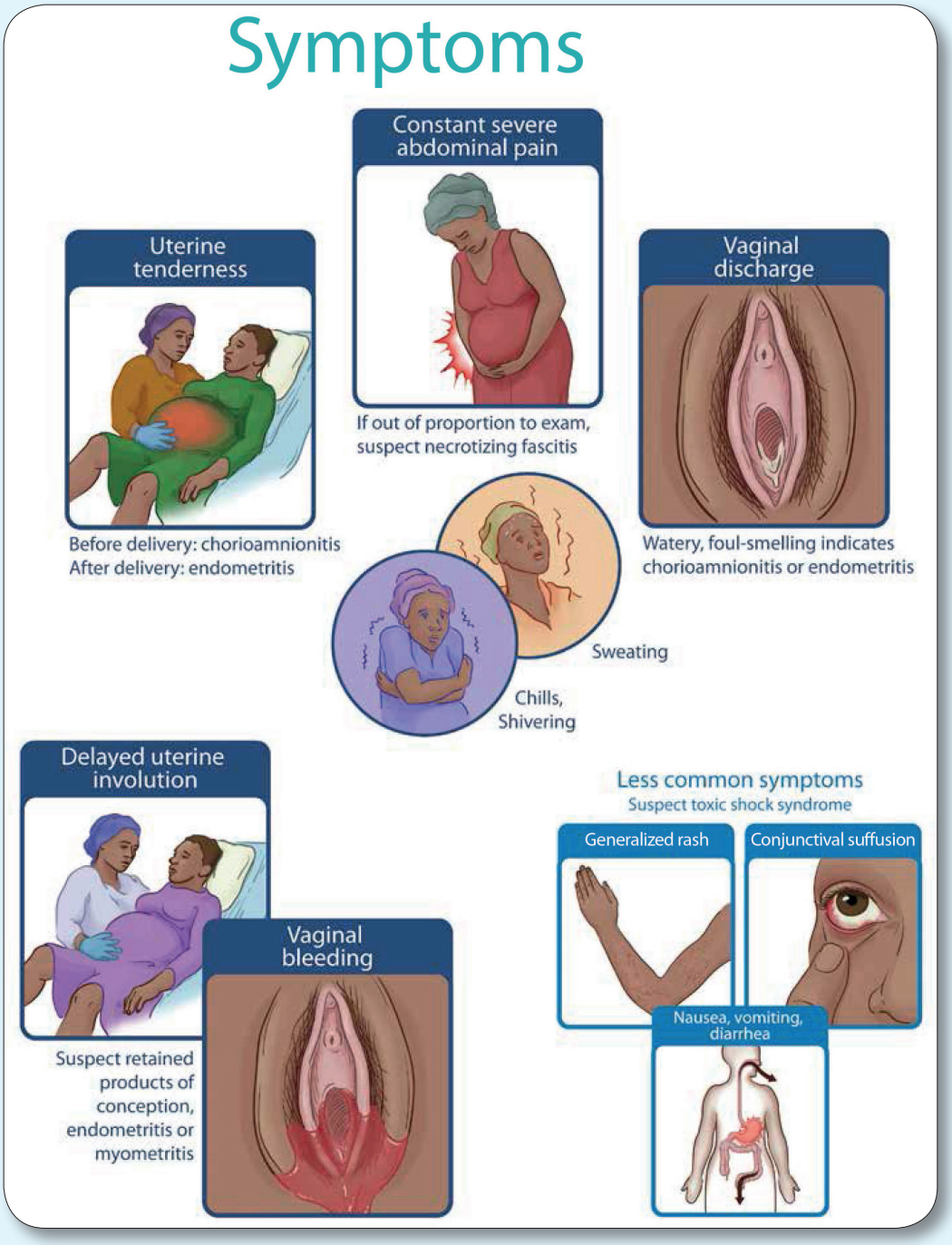
The Welfare of Women

Fever/Sepsis in Pregnancy

Infections both during and shortly after pregnancy are the cause of about 1 in 10 maternal deaths. They may also cause neonatal morbidity and mortality through either direct infections of the newborn baby or through pre-term labour. This Companion to Management provides guidance on infections in early pregnancy, during pregnancy, peripartum, and postpartum.

The key to managing sepsis is:

- Timely recognition
- Resuscitation
- Antimicrobial therapy
- Source control
- Continued monitoring and assessment



Clinical Relevance

Sepsis is an infection with systemic manifestations, where the body's own organ systems can be damaged by chemicals it produces to fight the infection. It is a leading cause of maternal morbidity and mortality – around 11 women per 1000 live births have an infection that contributes to their death, or near death. It is therefore essential to be able to rapidly identify patients who may have sepsis and treat them quickly and effectively.

The following clinical features are associated with sepsis:

- Fever (>38°C) or rigors
- Low temperature (<36°C)
- Tachycardia (heart rate >100)
- Tachypnoea (respiratory rate >20)
- Hypoxia (cyanosis or oxygen SpO2 <92%)
- Hypotension (systolic BP <90 mmHg)
- Poor urine output (no output in 18 hours)
- Reduced level of consciousness
- Rash
- Pelvic pain
- Abnormal vaginal discharge

The table below identifies risk factors for infection in pregnancy.

Risk Factors	
Pre-existing factors	**Pregnancy-specific factors**
• Malnutrition	• Prolonged rupture of membranes
• Diabetes	• Multiple vaginal examinations
• Severe anaemia	• Manual removal of placenta
• Obesity	• Operative vaginal birth
• HIV	• Caesarean section
	• Obstructed labour
	• Termination of pregnancy
	• Miscarriage and procedures to empty the uterus

Control of each of the medical conditions in the left column should ideally be optimised before pregnancy. But intervening during routine antenatal care with iron and nutritional supplementation, improving diabetic control, and optimising antiretroviral treatment are all beneficial.

The following specific interventions can help to reduce the risk of infections:

- Provision of safe termination of pregnancy (abortion)
- Screening for urinary tract infections in pregnancy

- 10 days of oral antibiotics (e.g. amoxicillin or erythromycin) following pre-term pre-labour rupture of membranes
- Cleaning the vagina with iodine prior to Caesarean section
- Prophylactic antibiotics for
  - Manual removal of placenta (ampicillin or first-generation cephalosporin)
  - 3rd and 4th degree perineal tears (ampicillin or first-generation cephalosporin)
  - Instrumental delivery (one dose of broad-spectrum IV antibiotics within 6 hours of delivery)
  - Caesarean section (one dose of broad-spectrum IV antibiotics given prior to skin incision)

Potential Differential Diagnoses

It is important to consider the possible source of infection because different organisms are more likely in certain types of infection and this will affect the choice of antibiotic.

The idea of controlling the source of the infection is important in sepsis, for example it may be necessary to remove retained pregnancy tissue after a miscarriage.

Early pregnancy

Septic Miscarriage	
Clinical Features	**Notes**
• Cervical os may be open • Pelvic tenderness • Foul smelling discharge	• Antibiotics are necessary, but it is essential to empty the uterus to remove the source of infection – this can be achieved with manual vacuum aspiration

Unsafe Termination of Pregnancy	
Clinical Features	**Notes**
• As above • May be very unwell	• Antibiotics are necessary, but it is essential to empty the uterus to remove the source of infection – this can be achieved with manual vacuum aspiration • Women may be very unwell with severe infections – there may be uterine perforation with pelvic abscess

Antenatal

Chorioamnionitis	
Clinical Features	**Notes**
• History of ruptured membranes • May be foul smelling discharge or pus draining vaginally	• A fever in a woman with ruptured membranes should be considered due to chorioamnionitis unless there is a clear alternative diagnosis

• Uterine tenderness • Fetal tachycardia	• Avoid vaginal examination in women with pre-term pre-labour rupture of membranes as this may cause infection – where assessment is required, a sterile speculum is safer than a digital examination • Often infection will lead to spontaneous labour, but if not induction of labour is indicated • The baby will require close monitoring and probably antibiotics as there is a high risk of neonatal infection

Intrapartum

Chorioamnionitis	
Clinical Features	**Notes**
• As above	• A fever that develops in labour should be considered due to chorioamnionitis unless there is a clear alternative diagnosis • If the woman is in early labour, give broad-spectrum IV antibiotics and consider if she needs to be transferred to a higher level of care (whether for her or the baby)

Postpartum

Endometritis	
Clinical Features	**Notes**
• Lower abdominal pain • Worsening bleeding • May be foul smelling discharge or pus draining vaginally	• Consider also retained pregnancy tissues

Wound Infection (perineal tears, Caesarean section scar, IV access sites)	
Clinical Features	**Notes**
• Localised redness and swelling • Increasing pain • Discharge from the wound	• Breakdown of a Caesarean wound should be referred to hospital – it is important to investigate how deep this goes • It is unclear whether perineal wounds are best re-sutured or allowed to heal by secondary intention; infection must be treated before considering any re-suturing or the wound will break down again

Mastitis	
Clinical Features	**Notes**
• Breast pain, redness, and swelling	• Requires careful monitoring as can easily develop into a breast abscess (which needs incision and drainage) • In addition to antibiotic therapy, it is important to avoid milk stasis – the patient should be encouraged to continue feeding (or hand expressing) from the affected breast if possible; warm compresses can help

Other Infections Associated with Pregnancy

Urinary Tract Infections

- These are more common in pregnancy
- May present with lower abdominal pain or vomiting, as well as dysuria and urinary frequency
- Can lead to premature labour so should be regularly screened for, and treated quickly and effectively

Respiratory Tract Infections

- Include a range of viral and bacterial infections of the upper and lower respiratory tract
- Can be more severe in pregnancy, so appropriate treatment and careful observation are required
- See separate GLOWM information on Covid-19 in pregnancy

Malaria

- All pregnant women should be admitted and treated as 'severe' malaria with IV therapy

  1st trimester:

  - Quinine (20 mg/kg loading dose, then 10 mL/kg 8-hourly) [dilute in 5% glucose to correct hypoglycaemia], plus . . .
  - Clindamycin (450 mg 8-hourly)

  2nd and 3rd trimester:

  - Artesunate (2.4 mg/kg IM/IV at 0, 12, and 24 hours)
  - Then once daily until able to take oral artesunate 2 mg/kg/day
  - Total course 7 days

Management Algorithm

This includes suggestions for antibiotics; however, these should be adjusted according to availability, local guidelines, and sensitivity data.

At every step, consider what resources you have available and whether this woman and baby need to be referred to a higher level of care. Sepsis kills and a patient's condition can deteriorate quickly. It is essential to be proactive in assessment and treatment, and to consider referral early.

1. Resuscitate the patient

Sepsis can make some patients very unwell. Acting quickly to stabilise them can be life-saving.

- **Give oxygen (if available) to maintain oxygen saturations of 94–98%**
- **Obtain IV access and give IV fluids**
  - Use fluids to correct hypotension
  - The optimal rate is difficult to specify, but in severe cases 1 L of fluid should be given as quickly as possible, and certainly within 1 hour
  - Give fluids with caution if hypertension (and possible pre-eclampsia) is present
- **Control any obvious source**
  - Empty the uterus, or drain a collection/abscess, if appropriate
  - Consider delivery in antenatal or intrapartum cases

2. Obtain further information that might help determine the cause/location of the infection

- **Take a comprehensive history focused on risk factors and symptoms of sepsis**
- **Undertake an appropriate examination, to look for a potential focus of infection**

  As discussed above, consider if any of the following may apply:
  - Recent miscarriage or pregnancy termination
  - Intra-uterine infection (chorioamnionitis or endometritis)
  - Wound infections (perineal, Caesarean section, or other)
  - Mastitis
  - Urinary tract infection
  - Respiratory tract infection (viral or bacterial)
  - Gastro-intestinal tract tract infection
  - Malaria
- **Undertake investigations to determine (a) a potential cause for the infection and (b) its severity**

  Consider, as available:

  Microbiology samples
  - Blood cultures
  - Vaginal swab

- Wound swab
- Urine culture
- Throat swab
- Sputum sample
- Blood film

Haematology and biochemistry samples

- Full blood count
- CRP
- Renal function tests
- Liver function tests
- Lactate (the higher the level the more concerning the clinical picture; a level >2 mmol/L is significant)

While it is preferable to obtain these samples beforehand, it is very important that doing so does not delay the early administration of antibiotics

3. Administer appropriate antibiotics as soon as possible (always within 1 hour)

Antibiotics are a key element of treatment, and patient mortality rises directly in relation to increasing delays in administering the first (and subsequent) doses of these.

Therefore, where sepsis is suspected **it is vital to administer antibiotics as soon as possible**.

The suspected source of sepsis will determine which antibiotic combination will be most effective, which is why it is important to undertake step 2 efficiently.

Suggested treatment choices:

Complicated abortion, or chorioamnionitis

Ampicillin 2 g IV/IM (then 1 g 6-hourly)

+

Gentamicin 80 mg IM (then 80 mg 8-hourly)

Any severe febrile illness (e.g. postpartum endometritis)

Clindamycin 150 mg IV/IM/PO (then 150 mg 6-hourly)

+

Gentamicin 80 mg IM (then 80 mg 8-hourly)

Mastitis

Cloxacillin 500 mg PO (then 500 mg 6-hourly)

Lower urinary tract infection

Amoxicillin 500 mg PO (then 500 mg 8-hourly)

Malaria

As listed above

All treatment choices should be guided by local protocols and availability.

Determine any history of allergy prior to administering and choose safe options where these exist.

The patient may also benefit from paracetamol 1 g IV/PO (4–6 hourly) to reduce her temperature, plus any additional analgesia required.

4. Use an Early Warning Score (EWS) system to monitor the patient's progress

Regularly monitor blood pressure, pulse, temperature, respiratory rate, oxygen saturation, urine output, conscious level.

Try to correct persistently adverse readings – do not just keep monitoring without action!!

For example, if the blood pressure is low → consider an IV fluid challenge; if oxygen saturations are low → give supplemental oxygen; if temperature remains high → give paracetamol, and physically cool with a fan +/– cold compresses.

(See Companion to Management – 'Early Warning Scores' CTM for further information)

If the EWS is increasing (i.e. getting worse) then the patient's condition is deteriorating.

In such cases:

- Reassess whether the correct source is being treated and consider other potential alternatives
- Consider **early** referral and transfer to a higher-level health facility – do not wait until the patient is too ill to travel

5. When a mother has fever (and suspected sepsis), consider the risk of infection to her newborn and ensure that they are appropriately monitored, treated, and/or referred

Newborns have relatively weak immune systems and infection is the main cause of neonatal mortality.

If a mother has developed an infection before, during, or shortly after labour then her baby will be also be at risk of sepsis.

It is essential to monitor the baby closely for signs of infection and maintain a low threshold for treatment, based on local protocols.

Always seek a second opinion (ideally from a paediatrician) with any concerns or uncertainties.

Associated GLOWM Resources

- Sepsis wall chart
  https://www.glowm.com/pdf/Maternal_Sepsis_WallChart_Single_Pages_WEB.pdf
- Advances in labour and risk management textbook
  https://www.glowm.com/resource_contents/page/sepsis/title/advances-in-labor-and-risk-management---chapter-7/resource_doc/635
- Infection in maternal-fetal medicine
  https://www.glowm.com/section_view/heading/infection-in-maternal-fetal-medicine-an-overview/item/173

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