Section 2.8

— may follow a head injury if there is damage to the dura and/or meninges.

There is a risk of coning and death if a diagnostic lumbar puncture is performed in a patient with significantly raised intracranial pressure.

**Diagnosis of meningitis or encephalitis**

Classic signs and symptoms include the following:

- headache
- vomiting
- neck stiffness
- opisthotonus
- photophobia
- rash
- altered consciousness.

Poisoning (see Section 7.4).

Malaria in pregnancy (see Section 2.8.D).

Eclamptic coma (see Section 2.5.E).

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2.8 Infections complicating pregnancy, delivery and after birth

### 2.8.A Pneumonia

**BOX 2.8.A.1 Minimum standards**

- Oxygen.
- Antibiotics (IV and oral).
- Chest X-ray.

**Clinical findings**

A high fever is usually associated with pneumonia and bacterial tracheitis. In the absence of stridor and wheeze, breathing difficulties in association with a significant fever are likely to be due to pneumonia.

Examination of the chest may show reduced air entry, bronchial breathing and crepitations. Pleuritic chest pain, neck stiffness and abdominal pain may be present if there is pleural inflammation. Pleural effusions and empyema are complications.

Always consider HIV infection and TB.

**Emergency treatment of pneumonia**

- Assess ABC.
- Give oxygen through nasal cannulae or mask depending on flow rate required to maintain saturation (if available) as below.
- Attach a pulse oximeter (if available).
- Maintain $\text{SaO}_2$ in the range 94–98%, with nasal cannulae at a flow rate usually up to 5 litres/minute or if necessary by face mask with higher flow rates.
- Give antibiotics for 7 days:
  - ampicillin 2 grams IV/IM 6-hourly plus gentamicin 80mg IV/IM 8-hourly or 5mg/kg IV/IM every 24 hours for most cases of community-acquired pneumonia
  - cefuroxime 500mg IV/IM 8-hourly or flucloxacillin 500mg IM or IV slowly every 6 hours for suspected or bacteriologically diagnosed *Staphylococcus aureus*
  - erythromycin 500 mg every 6 hours orally for *Chlamydia* or *Mycoplasma pneumoniae*
  - or whatever is available locally and appropriate.
- Sit the patient upright.
- Maintain hydration.
  - Extra fluid may be needed to compensate for fluid loss from fever.
  - Fluid restriction may be needed because of inappropriate ADH secretion, revealed by oliguria < 30mL per hour or rising blood urea levels.
- Chest X-ray is indicated.
- Large pleural effusions/empyemas should be diagnosed where possible by ultrasound, and pleural drainage undertaken under ultrasound cover (do not place a chest drain into the heart, liver or an undiagnosed tumour or hydatid cyst) (see Section 8.3). **Remember that in advanced pregnancy the diaphragm is elevated.**
  - Effusions/empyemas adjacent to the heart on the left side may cause pericarditis and cardiac arrhythmias. (Listen regularly for a pericardial rub, and ideally monitor an ECG if available until the patient is stable.)
2.8.B Severe dehydration and gastroenteritis

**BOX 2.8.B.1 Minimum standards**
- IV fluids containing appropriate amounts of sodium.
- Low-osmolarity oral rehydration solution (ORS).
- Nasogastric tubes.
- Urea and electrolyte measurements.
- Accurate weighing scales.

**Introduction**

Dehydration is loss of water, sodium and other essential electrolytes from the body. It causes death as a result of shock and electrolyte emergencies (see Section 2.5.A). Dehydration is a common cause of hospital admission, most commonly due to acute gastroenteritis and diabetic ketoacidosis (see Section 2.7.D).

A rapid clinical assessment (with support from biochemical tests, if rapidly available) in the very sick is the basis for treatment. The majority of patients can be treated with low-osmolarity oral rehydration solution (ORS) (by mouth or by nasogastric tube).

In patients with coincidental severe malnutrition, it is safer to use ORS with a lower sodium content, such as ReSoMal.

**Classification of dehydration**

Dehydration is classified according to clinical criteria. This may not apply in severe malnutrition, where caution is needed as signs may overlap and be misleading (see Section 5.10.B).

**No dehydration (<3% weight loss)**

There are no clinical signs with this degree of dehydration, although there will be thirst in the fully conscious patient. The woman or girl who is not fully conscious will not feel thirsty.

**FIGURE 2.8.B.1 Pathway of care for gastroenteritis with severe dehydration (10% or more). ORS, oral rehydration solution.**
Some dehydration (3–9% weight loss)
The following clinical signs are seen:
- increased thirst
- dry mucous membranes
- loss of skin turgor, tenting when pinched
- sunken eyes
- restless or irritable behaviour.

Severe dehydration (= 10% weight loss)
The following clinical signs are seen:
- more pronounced effects of the signs seen in moderate dehydration
- lack of urine output
- hypovolaemic shock, including:
  - rapid and feeble pulse (radial pulse may be undetectable)
  - low or undetectable blood pressure
  - cool and poorly perfused extremities
  - decreased capillary refill time (> 3 seconds); test this on the sternum of patients with light skins and on the thumb of those with dark skins
  - peripheral cyanosis
- rapid deep breathing (from acidosis)
- altered level of consciousness or coma.

Emergency treatment of severe dehydration
- Treat shock with an initial bolus of 1000 mL of Ringer-lactate or Hartmann’s solution (see Section 2.5.A).
- Decide on the cause (e.g. acute gastroenteritis, diabetic ketoacidosis).
- Classify the extent of dehydration (see above).
- Calculate the fluid deficit (see below), add this to the maintenance and ongoing losses and give over 24 hours.
- The major danger in rehydration (once shock has been treated) is causing the plasma sodium level to fall rapidly. This may increase the transfer of water into the brain and result in cerebral oedema.
- Before the electrolyte results are known, or if such testing is not available, the safest fluid to give is Ringer-lactate or Hartmann’s solution.

If the serum sodium level is higher than 155 mmol/litre, aim to lower it slowly over 48 hours or longer.

Calculating fluid requirements
**Deficit**
If an accurate recent pre-illness weight is available, subtract the current weight to estimate lost fluid (1 kg = 1 litre of fluid).

For example, a mother who weighed 70 kg is seen with diarrhoea and a weight of 65 kg.

In this case the estimated fluid loss is (70 – 65) kg = 5 kg = 5000 mL deficit (i.e. 7% dehydrated).

If no recent weight is available, or the weight value given is considered to be unreliable:
- Decide the degree of dehydration.
- Weigh the patient.
- Use the formula: percentage dehydration × weight (kg) × 10 = deficit (in mL).

For example, a mother whose weight is estimated to be 70 kg is 8% dehydrated.

In this case the estimated fluid loss is 8 × 70 × 10 = 5600 mL (233 mL/hour if replaced over 24 hours).

**Maintenance**
Estimated maintenance fluid requirements are 2400 mL/day and 100 mL/hour.

**Ongoing losses**
- **For each diarrhoeal stool:** 500 mL of ORS after each stool.
- **For each vomit:** 200 mL of ORS after each vomit. Give small frequent volumes (e.g. 20 mL every minute) with a spoon or syringe or cup.

Add deficit to maintenance and ongoing losses and aim to replace these over 24 hours.

For example, for a 70 kg mother who is 8% dehydrated, maintenance is 100 mL/hour, if there are no ongoing losses. Total fluids needed per hour = 233 mL/hour (deficit) + 100 mL/hour (maintenance) = 333 mL/hour.

**Severe acute gastroenteritis in pregnancy**
Gastroenteritis is a common cause of dehydration and shock. Management starts with ABC, followed by assessment of the fluid deficit (extent of dehydration) and ongoing losses of fluid. Weigh the patient and keep an accurate fluid balance chart.

It is important to give fluids that:
- correct the deficit
- provide maintenance
- replace ongoing losses.

**Differential diagnosis**
Look for an abdominal mass or abdominal distension.

Consider the following:
- HIV infections
- surgical conditions, such as acute appendicitis, peritonitis or bowel obstruction (if suspected, resuscitate and call for surgical opinion)
- typhoid (high-grade fever, rash, hepatosplenomegaly and toxicity)
- antibiotic-associated colitis
- (rarely) inflammatory bowel disease.

**Treatment if not shocked**
- Start low-osmolality oral rehydration solution (ORS) with 1–2 litres over 2–4 hours.
- The carer should give small amounts of ORS (e.g. using a small cup) frequently.
- Gradually increase the amount as tolerated, using a tablespoon, cup or glass.
- After 12–24 hours, review progress with regard to rehydration and progress to the maintenance phase or continue rehydration.

**Severe dehydration (= 10% fluid deficit with or without clinical signs of shock**
- If the patient is shocked, assess and manage ABC, give oxygen if available, and start IV fluids immediately (use two intravenous lines if possible: use long saphenous vein cut-down or the external jugular vein if venous access is difficult).
Give a 500 mL or 1-litre bolus of Ringer-lactate or Hartmann’s solution IV as rapidly as possible.

- Reassess pulse, perfusion (capillary refill time) and mental status, and repeat the bolus if these are still abnormal.
- Do not use low-sodium-containing IV fluids such as 0.18% saline with 4% glucose, which can be dangerous (they can cause hyponatraemia and cerebral oedema). Instead use Ringer-lactate or Hartmann’s solution, ideally also containing 10% glucose (obtained by adding 100 mL of 50% glucose to each 500 mL).

Hypokalaemia is a major complication which needs urgent attention. Ideally measure serum K+ levels frequently. Provided that the patient is passing urine and IV potassium can safely be given, it should be added to the IV fluids given subsequent to the boluses given to treat shock. Ideally and if tolerated, potassium should be corrected by giving low osmolality ORS enterally as soon as possible.

If it is necessary to add potassium to IV fluids given to correct dehydration, particularly if diarrhea is continuing and if measured serum K+ is < 2.0 mmol/litre or there are ECG signs of hypokalaemia, namely ST depression, T-wave reduction and prominent U waves, and only if safe to do so, great care must be taken.

In acute depletion, an infusion at the rate of 0.1 to 0.2 mmol/kg/hour (6 to 12 mmol/hour for a woman weighing 60 kg) of IV potassium can be used and the serum K+ level checked after 3 hours. The potassium for injection must be diluted before use and thoroughly mixed before being given. The maximum concentration of potassium that can be given through a peripheral vein is 40 mmol/litre. The maximum infusion rate of potassium is 0.5 mmol/kg/hour.

Remember that Ringer-lactate or Hartmann’s solution both already contain 5 mmol/litre of potassium.

Note: The injectable form of KCl usually contains 1.5 grams (i.e. 20 mmol) of potassium in 10 mL, and can be given orally. The daily potassium requirement is 1–2.5 mmol/kg.

When shock has resolved, and the patient’s level of consciousness has returned to normal, the remaining estimated deficit must be taken by mouth or by gastric tube, especially if severe malnutrition and/or anaemia is present (giving large fluid volumes IV can precipitate heart failure).

Assess the patient’s hydration status frequently.

**Oral fluids**

Recommendations for oral replacement therapy in gastroenteritis are as follows:

- Give low-osmolality ORS (containing 75 mmol/litre of sodium) or, if the latter is unavailable, ORS containing 90 mmol/litre of sodium with an additional source of low-sodium fluid (e.g. water).
- The amount given should be in the range 300–500 mL/hour.
- Giving high-osmolality fluids may contribute to hypernatraemia, whereas giving water alone, or low-salt drinks, may cause hyponatraemia.
- Oral glucose within ORS enhances electrolyte and water uptake in the gut.
- “Home-made” ORS can be prepared by adding a pinch of salt (1 mL) and a handful of sugar (5 mL) to a glass of clean potable water (250 mL).

**Intravenous fluids**

- Even in patients who are drinking poorly, try to give enteral fluids by mouth or by gastric tube until the IV infusion is running.
- Use Ringer-lactate or Hartmann’s solution, which contains Na+ 131 mmol/litre, K+ 5 mmol/litre, HCO3− 23 mmol/litre and Ca2+ 2 mmol/litre.
- Hartmann’s solution has no glucose to prevent hypoglycaemia. This can be corrected by adding 100 mL of 50% glucose to 500 mL of Ringer-lactate or Hartmann’s, giving approximately a 10% glucose solution (adding 50 mL to 450 mL of Ringer-lactate or Hartmann’s gives a 5% solution).
- Ringer-lactate or Hartmann’s solution with 5% dextrose added has the advantage of providing glucose to help prevent hypoglycaemia.
- See above regarding potassium supplementation.

- It is dangerous to use plain 5% glucose solutions, or 0.18% saline plus 4% glucose. They do not contain adequate electrolytes, do not correct the acidosis or hypovolaemia, and can cause dangerous hyponatraemia.

All patients should start to receive some ORS (at the rate of about 300 mL/hour) when they can drink without difficulty, which is usually within 1–2 hours. This provides additional base and potassium, which may not be adequately supplied by the IV fluid. Alternatively, give as soon as possible by gastric tube.

**Over-hydration**

Signs of over-hydration include the following:

- Oedematous eyelids and generalised oedema, particularly ankle, facial and sacral oedema
- Cardiac failure, especially in severe malnutrition or protein-losing enteropathy.
- Respiratory distress (raised rate and some chest wall recession)
- Tachycardia out of proportion to respiratory difficulty
- Raised jugular venous pressure
- Gallop rhythm/murmur
- Enlarged liver
- Basal lung crepitations.

A chest X-ray may be helpful for showing pulmonary plethora or oedema.

**Management of over-hydration**

- Stop giving ORS, but give plain water and food.
- Do not give a diuretic unless the patient is in cardiac failure.

When the oedema has resolved, resume giving ORS.

**Reassess the following:**

- ABC
- Circulatory and hydration status
- Plasma electrolytes if possible
- Urine output and urine electrolytes
- Give fluid according to plan; do not forget ongoing losses
- Reassess regularly (including biochemistry if possible)
- Do not forget glucose.

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2.8.C HIV/AIDS

Introduction
Prevention of mother-to-child transmission (PMTCT) of the human immunodeficiency virus (HIV) is possible, even in resource-limited settings, and the World Health Organization guidance (Recommendations for a Public Health Approach) published in 2010 on antiretroviral drugs for treating pregnant women and preventing HIV infection in infants suggests that elimination of mother-to-child transmission of HIV (MTCT) is a realistic public health goal. Since the previous WHO guidance was published in 2006, new evidence has emerged on the use of antiretroviral prophylaxis to prevent MTCT, on the optimal time to initiate antiretroviral therapy (ART), and on safe feeding practices for HIV-exposed infants. This section draws heavily from the WHO 2010 and 2013 guidelines, which should be used and adapted within local settings. Once implemented, these recommendations could reduce the risk of MTCT to less than 5% in breastfeeding populations (from a background risk of 35%), and to less than 2% in non-breastfeeding populations (from a background risk of 25%), and will ensure increased maternal and child survival.

A woman will only know her HIV status if she has had an HIV test. HIV tests may be performed as a bedside point of care test (using capillary blood) or within a laboratory. An HIV-positive mother will pass her antibodies to her baby. These are harmless and are usually cleared by 18–24 months of age. It is transmission of the HIV virus that causes infection. An infant will have circulating maternal antibodies until 18–24 months of age, so the HIV antibody test is often not useful before this time, as it remains positive until the maternal antibodies have cleared.

When HIV infection is recent or the CD4 count is high, and a pregnant woman has no symptoms, HIV has little effect on pregnancy, and pregnancy has little effect on HIV. However, when HIV infection is advanced or the CD4 count is low, a woman is at risk of opportunistic infections, and HIV can directly affect the pregnancy, including increasing the risk of premature delivery, severe malaria and perinatal sepsis.

MTCT can occur when the baby is in the uterus, during delivery or during breastfeeding. Pregnant women should be encouraged to be tested for HIV because, if they are found to be HIV-positive, there are interventions at each of these stages that reduce the risk of MTCT, and there is also treatment to preserve the mother’s own health. A negative HIV test provides an opportunity for health education, including promoting safer sex (e.g. use of condoms) to avoid the woman becoming HIV infected, particularly during pregnancy. Acquiring HIV during pregnancy carries a high risk of transmitting HIV to an unborn baby. HIV-negative women should be offered a repeat HIV test in the third trimester.

Box 2.8.C.1 Minimum standards
- Prevention of mother-to-child transmission (PMTCT).
- Antiretroviral therapy (ART) for HIV-infected women.
- Health education and community support.

‘Adult-to-child transmission’ or ‘vertical transmission’ are other ways of describing MTCT, and are sometimes felt to imply less blame.

Prevention of mother-to-child transmission and ART in pregnancy
The WHO 2010 guidelines state that a woman with a CD4 count of ≤350 cells/mm³ (regardless of WHO clinical staging) or WHO clinical stage 3 or 4 (irrespective of CD4 count) [WHO Case Definitions of HIV for Surveillance and Revised Clinical Staging and Immunological Classification of HIV-Related Disease in Adults and Children, published in 2007] requires lifelong ART.

Updated consolidated ART guidelines published by the WHO in 2013 (www.who.int/hiv/pub/guidelines/2013/ art/africa.pdf) recommend that all pregnant and breastfeeding women should be commenced on ART (one simplified triple regimen), and that this should be maintained for at least the duration of MTCT risk (i.e. throughout breastfeeding). They suggest that, particularly in generalised epidemics, all pregnant and breastfeeding women with HIV should initiate ART as lifelong treatment. In pregnancy the focus is no longer on ‘when or what to start’ but on ‘whether to stop’ treatment after delivery. Ideally, a CD4 count should be obtained before deciding whether ART for PMTCT only (i.e. stopping after delivery) is an option.

As most women should continue ART following delivery, an effective link with HIV treatment programmes is essential.

The WHO 2013 guidelines are simplified, and they harmonise the approach to ART in adults and pregnancy. National programmes are encouraged to move from the previous Option ‘A’ to Option ‘B’ or ‘B+’.

Option B+: all pregnant and breastfeeding women infected with HIV should be started on ART as lifelong treatment. This is particularly important in generalised epidemics where high fertility, long duration of breastfeeding, limited access to CD4 to determine ART eligibility, and high partner serodiscordance rates all increase the risks of transmission to the woman’s partner and babies.

Option B: in some countries (e.g. where CD4 counts are available), in the case of women who are not eligible for ART for their own health, consideration can be given to stopping the ARV regimen after the period of risk of mother-to-child transmission has ended. Single-dose nevirapine (sdNVP) for women in labour is no longer recommended (unless it is combined with other ART) because it causes the virus to develop high levels of drug resistance.

Option A (from the 2010 WHO guidelines) is no longer recommended, although some countries may not have the resources necessary to use options B or B+.

The treatment focus is shifting to consider ART for the mother’s health, to utilise more effective ART drugs, and to extend coverage throughout the MTCT risk period. All women should be started on ART in pregnancy.
TABLE 2.8.C.1 WHO guidelines for ART in pregnancy for HIV-infected women who have not had previous ART

<table>
<thead>
<tr>
<th>For pregnant women for PMTCT only</th>
<th>For infants of mothers given a short course of ART for PMTCT</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Option A</strong> (WHO 2010 guidelines)</td>
<td>Baby being breastfed: daily NVP from birth until at least 4–6 weeks of age and until 1 week after breastfeeding has stopped</td>
</tr>
<tr>
<td>AZT twice a day from 14 weeks  sdNVP at onset of labour, and start AZT + 3TC for 7 days</td>
<td>Baby being bottle-fed: daily NVP or sdNVP + AZT twice a day until 4–6 weeks</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Option B</strong></th>
<th>Baby being breastfed: daily nevirapine (NVP) for 6 weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preferred regimens: TDF + 3TC (or FTC) + EFV (as fixed-dose combination)</td>
<td>Baby being bottle-fed: daily nevirapine (NVP) for 4–6 weeks</td>
</tr>
<tr>
<td>Alternative regimens: AZT + 3TC + EFV or TDF + 3TC (or FTC) + EFV</td>
<td>or AZT twice a day for 4–6 weeks</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Option B+</strong></th>
<th>Baby being breastfed: daily nevirapine (NVP) for 6 weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preferred regimens: TDF + 3TC (or FTC) + EFV (as fixed-dose combination)</td>
<td>Baby being bottle-fed: daily nevirapine (NVP) for 4–6 weeks</td>
</tr>
<tr>
<td>Alternative regimens: AZT + 3TC + EFV or TDF + 3TC (or FTC) + NVP</td>
<td>or AZT twice a day for 4–6 weeks</td>
</tr>
</tbody>
</table>

Women diagnosed with HIV during labour or immediately postpartum

If a woman is diagnosed with HIV infection during labour or immediately postpartum, ART should be commenced immediately for PMTCT. This regimen can be modified later when the woman has been assessed (with CD4 count) with regard to whether she requires lifelong ART for herself.

TABLE 2.8.C.2 WHO guidance for ART for women diagnosed with HIV in labour/immediately postpartum

<table>
<thead>
<tr>
<th>For the mother</th>
<th>For the infant</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Option A</strong></td>
<td>Baby being breastfed: Daily NVP from birth for 6 weeks, consider extending to 12 weeks</td>
</tr>
<tr>
<td>sdNVP in labour and AZT + 3TC twice a day for 1 week</td>
<td>Baby being bottle-fed: Daily NVP from birth for 6 weeks</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Option B</strong></th>
<th>Baby being breastfed: Daily NVP from birth for 6 weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Start (triplet) ART immediately. Continue until 1 week after exposure to breast milk has ended</td>
<td>Baby being bottle-fed: Daily NVP from birth for 6 weeks</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Option B+</strong></th>
<th>Baby being breastfed: Daily NVP from birth for 6 weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Start (triplet) ART immediately. Continue lifelong</td>
<td>Baby being bottle-fed: Daily NVP from birth for 6 weeks</td>
</tr>
</tbody>
</table>

If a woman is diagnosed with HIV infection postpartum and plans replacement (formula or bottle) feeding, refer her for HIV care and evaluation for treatment.

HIV-exposed infants (children born to women with HIV) should be given co-trimoxazole prophylaxis from 4–6 weeks of age, and this should be continued until HIV infection has been excluded and the infant is no longer at risk of acquiring HIV through breastfeeding (World Health Organization, Guidelines on Co-Trimoxazole Prophylaxis for HIV-Related Infections among Children, Adolescents and adults: recommendations for a public health approach, published in 2006).

Delivery

Labour can be a worrying time for the HIV-positive woman, particularly because of possible underlying fears about her own HIV infection and the risk of infecting her baby. She will need reassurance and support, and it is important to ensure she knows that with all of the interventions that are given her baby is more likely to be HIV-negative than infected.

Get close to her, greet her and be seen to shake hands with her, to help to reduce the stigma around touching those infected with HIV. Support her relatives, and encourage her to tell her partner so that he can be tested for HIV. Promote safer sex and advise her to use condoms to prevent transmission of HIV.

Standard precautions should be used when caring for women in labour, whether or not they have HIV infection. Always wear gloves when touching body fluids, and dispose of single-use syringes and needles safely.

During delivery, to reduce MTCT:
- avoid artificial rupture of membranes
- avoid prolonged rupture of membranes
- avoid unnecessary episiotomy, but also avoid a tear.

Both blood and placenta will contain HIV, so wear gloves, an apron and eye protection. Avoid direct contact of blood on your skin. Blood on intact skin should be washed off
immediately. HIV-positive blood on an open wound or splashed into the eye can transmit HIV and should be washed immediately (use soap and water for a wound, and water for an eye) and managed in the same way as a needlestick injury (with post-exposure prophylaxis with ART).

Other considerations for managing HIV infection in pregnancy

Anaemia
Screening for and treatment of anaemia should be routine in antenatal care for all pregnant women (World Health Organization, Pregnancy, Childbirth, Postpartum and Newborn Care: a guide for essential practice, 2nd edn, published in 2009). Iron supplements and folate supplements in areas with a high prevalence of iron deficiency are indicated for all pregnant women regardless of haemoglobin levels. Iron should be continued for 3 months after delivery. If possible, antenatal screening for anaemia should include laboratory measurement of haemoglobin levels, but anaemia can be assessed clinically if this is not available.

In women with severe anaemia, AZT should be avoided, and TDF or stavudine (d4T) should be used instead.

Malaria and worm infestations
The prevention and treatment of malaria and worm infestations is necessary in high-prevalence areas (see Sections 2.8.D and 6.3.C).

HIV-2 infection
HIV-2 is much less transmissible than HIV-1 (the MTCT risk is 0–4%).

Non-nucleoside reverse transcriptase inhibitors (NNRTIs) such as NVP and EFV are not effective against HIV-2, and a triple nucleoside reverse transcriptase inhibitor (NRTI) combination is recommended.

BOX 2.8.D.2 Treatment of HIV-2 infection
Mother requires treatment: AZT + abacavir (ABC) + 3TC
PMTCT only: AZT from 14 weeks and continued until delivery
Infant of mother with HIV-2: AZT twice a day until 4–6 weeks

Tuberculosis
The risk of active TB increases in pregnancy, and is around 10 times higher in HIV-infected women. It is associated with increased maternal mortality, premature labour, low birth weight and tuberculosis in the infant. HIV-infected women must be assessed for TB at each visit; any woman with a cough, fever, night sweats and weight loss should be evaluated for TB and started on TB treatment. ART is also required regardless of the CD4 count. Commence TB treatment first, followed by ART as soon as clinically possible (within 8 weeks of starting TB treatment).

Rifampicin interacts with many antiretroviral drugs, especially the boosted protease inhibitors. As is the case for all adults, EFV is the preferred NNRTI for HIV/TB co-infected pregnant women (starting after the first trimester).

For those women on TB therapy who are unable to tolerate EFV, give a NVP-based regime or a triple NRTI regimen such as AZT + 3TC + ABC or AZT + 3TC + TDF. In the presence of rifampicin, start full-dose NVP (a lead-in dose is not required).

Summary
Interventions during pregnancy, labour and delivery and postpartum can all significantly reduce the risk of MTCT of HIV. Therefore all pregnant women should be tested for HIV. The WHO 2007 guidelines (www.who.int/hiv/pub/mctct_scaleup2007/en/index.html) summarise the essential services required for good-quality antenatal care, and these are listed below.

package of routine quality antenatal and postpartum care for all women, regardless of HIV status

1 Health education, information on HIV and sexual transmitted infection (STI) prevention and care including safer sex practices, pregnancy including antenatal care, birth planning and delivery assistance, malaria prevention, optimal infant feeding; family planning counselling and related services.

2 Provider-initiated HIV testing and counselling, including HIV testing and counselling for women of unknown status at labour and delivery, or postpartum.

3 Couple and partner HIV testing and counselling, including support for disclosure.

4 Promotion and provision of condoms.

5 HIV-related gender-based violence screening.

6 Obstetric care, including history taking and physical examination.

7 Maternal nutritional support.

8 Infant feeding counselling.

9 Psychosocial support.

10 Birth planning, birth preparedness (including pregnancy/postpartum danger signs), including skilled birth attendants.

11 Tetanus vaccination.

12 Iron and folate supplementation.

13 Syphilis screening and management of STIs.

14 Harm reduction interventions for injecting drug users.

Additional package of services for HIV-positive women

1 Additional counselling and support to encourage partner testing, adoption of risk reduction and disclosure.

2 Clinical evaluation, including clinical staging of HIV disease.

3 Immunological assessment (CD4 cell count) where available.

4 ART when indicated.

5 Infant feeding counselling and support based on knowledge of HIV status.

6 ART prophylaxis for PMTCT provided during the antepartum, intrapartum and postpartum periods.

7 Co-trimoxazole prophylaxis where indicated.

8 Additional counselling and provision of services as appropriate to prevent unintended pregnancies.

9 Supportive care, including adherence support.

10 TB screening and treatment when indicated; preventive therapy (INH prophylaxis) when appropriate.
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11 Advice and support on other prevention interventions, such as safe drinking water.
12 Supportive care, including adherence support, and palliative care and symptom management.

**Essential postnatal care for HIV-exposed infants**
1. Completion of ART prophylaxis regimen.
2. Routine newborn and infant care, including routine immunisation and growth monitoring.
4. Early HIV diagnostic testing and diagnosis of HIV-related conditions.
5. Continued infant feeding counselling and support, especially after early HIV testing.

**2.8.D Malaria**

**Introduction**
Malaria, particularly falciparum malaria, is an important cause of maternal mortality and postpartum morbidity, severe anaemia, miscarriage, intrauterine growth retardation, intrauterine death, stillbirth, premature delivery, low birth weight (LBW), and perinatal and neonatal morbidity. Plasmodium falciparum malaria is the most dangerous type. *P. vivax* malaria is less dangerous. Malaria destroys red blood cells and can harm the placenta. The main danger with falciparum malaria is cerebral malaria, which causes coma and death.

In most endemic areas of the world, pregnant women are the main adult risk group for malaria. The burden of malaria infection during pregnancy is chiefly caused by *Plasmodium falciparum*, the most common malaria species in Africa. The impact of the other three human malaria parasites (*P. vivax*, *P. malariae* and *P. ovale*) is less clear. Every year at least 30 million pregnancies occur among women in malarious areas of Africa, most of whom reside in areas of relatively stable malaria transmission.

In sub-Saharan Africa, poor nutrition, micronutrient imbalances (particularly vitamin A, zinc, iron and folate), HIV co-infection, poverty and limited access to effective primary healthcare and emergency obstetric services exacerbate the impact of pregnancy-associated malaria.

In Africa, perinatal mortality due to malaria is around 1500 deaths per day. In areas where malaria is endemic, 20–40% of all babies born may have a low birth weight, increasing the likelihood of infant mortality.

Malaria in pregnancy is a particular problem for women in their first and second pregnancies, and for women who are HIV-positive.

Studies have shown that in high transmission zones more than 50% of women have placental malaria infections at birth. This increases the risk of HIV vertical transfer (especially if the parasite load is high), and prevents the transfer of maternal antibodies protecting against measles.

**Malaria in pregnancy in low versus high transmission areas**
The clinical presentation and severity of malaria in pregnancy differ in areas of high and low transmission due to differences in the level of immunity of the population. Although these settings are presented as two distinct epidemiologic conditions, in reality the intensity of transmission and immunity in pregnant women occurs on a continuum, with potentially diverse conditions occurring within a country.

In areas of epidemic or low (unstable) malaria transmission, adult women have not acquired any significant level of immunity and usually become ill when infected with *P. falciparum* malaria. Pregnant women resident in areas of low or unstable malaria transmission are at a two- or three-fold higher risk of developing severe disease as a result of malaria infection than are non-pregnant adults living in the same area. In these areas, maternal death may result either directly from severe malaria or indirectly from malaria-related severe anaemia. In addition, malaria infection of the mother may result in a range of adverse pregnancy outcomes, including spontaneous abortion, neonatal death, and low birth weight (LBW).

In areas of high and moderate (stable) transmission of malaria, most adult women have developed sufficient immunity that, even during pregnancy, *P. falciparum* infection does not usually result in fever or other clinical symptoms. In these areas, the principal impact of malaria infection is associated with malaria-related anaemia in the mother, and with the presence of parasites in the placenta. The resulting impairment of foetal nutrition contributing to low birth weight is a leading cause of poor infant survival and development. In areas of Africa with stable malaria transmission, *P. falciparum* infection during pregnancy is estimated to cause as many as 10,000 maternal deaths each year, 8–14% of all low-birth-weight babies, and 3–8% of all infant deaths.

The strategy for management of malaria in the pregnant population in areas of high transmission should include screening and treating of positive cases, intermittent presumptive treatment (IPTp) for rapid diagnostic test (RDT)-negative cases and use of insecticide-treated bed nets (ITNs).

In high transmission areas, in women who are known to be HIV-positive, or where the prevalence of HIV exceeds 10%, IPTp should be given monthly (and at least four times during pregnancy), see below.
In areas of low transmission the risk of malaria infection during pregnancy is greater, and can result in maternal death, and in spontaneous abortion in up to 60% of cases. Silent malaria is rare. The strategy in these areas involves ITNs, screening and treatment of positive cases, chemoprophylaxis if possible, and early diagnosis and prompt effective treatment of malaria.

### TABLE 2.8.D.1 Comparison of occurrence of complications in areas of high and low transmission

<table>
<thead>
<tr>
<th>Complication</th>
<th>Hyper-endemic areas</th>
<th>Low transmission</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypoglycaemia</td>
<td>–</td>
<td>++</td>
</tr>
<tr>
<td>Severe anaemia</td>
<td>+++</td>
<td>+++</td>
</tr>
<tr>
<td>Pulmonary oedema</td>
<td>–</td>
<td>++</td>
</tr>
<tr>
<td>Acute renal failure</td>
<td>–</td>
<td>++</td>
</tr>
<tr>
<td>Hyperpyrexia</td>
<td>+</td>
<td>+++</td>
</tr>
<tr>
<td>Placental malaria</td>
<td>+++</td>
<td>+++</td>
</tr>
<tr>
<td>LBW babies</td>
<td>+++</td>
<td>+++</td>
</tr>
<tr>
<td>Abortions</td>
<td>–</td>
<td>+++</td>
</tr>
<tr>
<td>Congenital malaria</td>
<td>–</td>
<td>+++</td>
</tr>
</tbody>
</table>

A pregnant woman who has not lived in a malarious area has no immunity. Therefore if she goes to a malarious area she is at risk of developing severe malaria. She must take tablets to prevent malaria before she goes to that area and throughout her pregnancy, and sleep under a bed net when she gets there.

If a mother has had malaria before, she will have some immunity. Unfortunately, pregnancy reduces immunity. She is at risk from severe anaemia, but the other complications are unusual. Often her blood film will be negative, and she will have few symptoms. If she has fits they will probably be caused by eclampsia or meningitis, not malaria.

Partially immune primigravida mothers are at particular risk, especially during the last trimester. Early teenage primigravida are at greatest risk. This risk decreases with further pregnancies.

### Screening and treating pregnant women during antenatal care

Since in most African countries over 70% of pregnant women make multiple antenatal clinic visits, these provide a major opportunity for prevention of malaria, along with other important diseases that affect pregnant women.

The rationale for screening and treating all pregnant women for malaria during routine antenatal care is that even one attack at any time during pregnancy can have serious consequences (i.e. low birth weight and maternal anaemia).

There is a four-pronged approach to malaria prevention and control during pregnancy:

1. **Intermittent preventive treatment (IPTp)**
2. Insecticide-treated bed nets (ITNs), or preferably long-lasting insecticide-treated bed nets (LLINs).
3. Indoor residual spraying (IRS) with insecticides

### Intermittent preventive treatment (IPTp)

This involves providing all pregnant women with preventive treatment doses of an effective antimalarial drug during routine antenatal clinic visits. This approach has been shown to be safe, inexpensive and effective. A study in Malawi evaluating IPT showed a decline in placental infection (from 32% to 23%) and in the number of low-birth-weight babies (from 23% to 10%). It also found that 75% of all pregnant women took advantage of IPTp when it was offered.

The drug recommended at present is sulphadoxine/pyrimethamine (SP, also called Fansidar). Starting as early as possible in the second trimester, IPTp-SP is recommended for all pregnant women in Africa at each scheduled antenatal care (ANC) visit (four visits are recommended by WHO during every pregnancy) until the time of delivery, provided that the doses are given at least one month apart. SP should not be given during the first trimester of pregnancy; however, the last dose of IPTp-SP can be administered up to the time of delivery without safety concerns.

IPTp-SP should ideally be administered as directly observed therapy (DOT) of three tablets sulfadoxine/pyrimethamine (each tablet containing 500mg/25mg SP) giving the total required dosage of 1500mg/75mg SP.

In areas where malaria is very common and antenatal clinic attendance is poor, all mothers, especially all primigravida, should be given a dose of SP when they first come to the antenatal clinic after quickening (when the mother first feels the fetus moving).

Although high levels of resistance to SP occur in many countries, it is not known at what level of SP resistance IPTp still gives a positive outcome in terms of improved haemoglobin levels in the mother and higher birth weights. A preventative effect provided by SP seems to exist even at relatively high levels of resistance.

For pregnant women who are HIV-positive, the dosage schedule for IPT should be augmented to at least four doses of SP, starting in the second trimester, the doses being given at least 1 month apart. This increased frequency is also recommended for all pregnant women with unknown HIV status living in areas of high HIV prevalence (over 10%).

Women who are HIV-positive experience increased vulnerability to malaria in all pregnancies, not just the first two pregnancies.

**Note:** HIV patients who are receiving co-trimoxazole preventive therapy should not take IPTp as adverse effects can occur.

Research to assess the safety, efficacy and programme feasibility of other antimalarial drugs for use in IPTp is ongoing.
Weekly chloroquine has in the past been shown to be effective in preventing malaria in pregnancy, especially in the case of *P. vivax* malaria. Adherence to this regime and loss of efficacy in the case of *P. falciparum* malaria make this regime less appropriate.

**Insecticide-treated bed nets (ITNs) and long-lasting insecticide-treated bed nets (LLINs)**

Nets decrease both the number of malaria cases and the malaria death rates in pregnant women. A study in an area of high malaria transmission in Kenya has shown that women who are protected by ITNs every night during their first four pregnancies produce 25% fewer underweight or premature babies. In addition, ITN use benefits the infant who sleeps under the net with the mother, by decreasing their exposure to malaria infection. ITNs should be provided to pregnant women as early in pregnancy as possible, and their use should be encouraged for women throughout pregnancy and during the postpartum period. Health education programmes, social marketing and lobbying to reduce the prices of ITNs and re-treatments are helping to encourage the use of ITNs by pregnant women.

**Indoor residual spraying (IRS) with insecticides**

IRS involves applying a long-lasting (residual) insecticide to the inside walls of houses and other structures where people sleep, to kill mosquitoes when they rest on the walls. It is a highly effective malaria prevention method in settings where it is epidemiologically and logistically appropriate. IRS must be applied prior to the transmission season (either annually, or twice a year if there are continuous or multiple seasons of transmission), and is carried out by a trained cadre of workers who move through a community spraying all appropriate structures. Its full potential is realised when at least 80% of houses in targeted areas are sprayed. Indoor spraying is effective for 3–6 months, depending on the insecticide used and the type of surface on which it is sprayed. DDT can be effective for 9–12 months in some cases. Longer-lasting forms of IRS insecticides are under development. The WHO approves the following pyrethroid class of pesticides; lambda-cyhalothrin, bifenthrin, alpha-cypermethrin, deltamethrin, cyfluthrin and etofenprox.

**Case management of malarial illness**

In areas of unstable (infrequent) *P. falciparum* malaria transmission, non-immune pregnant women exposed to malaria require prompt case management of febrile illness. Although at present there are no fully effective tools to prevent malaria among non-immune women, ITNs will decrease exposure to infective mosquito bites, and thus would be expected to be of benefit in decreasing symptomatic infections. Essential elements of the antenatal care package should therefore include malaria diagnosis, where available and needed, and treatment with antimalarial drugs that have an adequate safety and efficacy profile for use in pregnancy.

In view of the increasing evidence of the severe effects of malaria in pregnancy on both the woman and her unborn child, even when asymptomatic, all pregnant women presenting for antenatal care or delivery should be tested using an RDT. Since the sensitivities of both RDT and smear to detect low parasitaemias in pregnancy are not infallible, both are recommended where this is programmatically possible. Where this is not possible, RDTs are to be preferred.

All women who are found to be positive should receive an effective antimalarial drug, namely quinine in the first trimester and artemisinin-combination therapies (ACT) in the second and third trimesters. If they are found to be negative, they should receive a dose of SP as IPTp. Women should not be screened more often than monthly in the absence of signs or symptoms of malaria.

Patients with severe anaemia (haemoglobin < 7 g/dL) in a high transmission zone are in all probability infected, and should be treated with an effective antimalarial drug as well as iron/folic acid even if there are no other signs of malaria and negative smear or RDT, or if laboratory tests cannot be undertaken.

All patients with a positive biological test (RDT and/or microscopy) should be treated with an effective antimalarial drug. If you suspect malaria, but cannot examine a blood film or do an RDT, treat the mother anyway.

**Asymptomatic (placental) malaria** has the same implications in pregnant women as symptomatic malaria. Asymptomatic women should be routinely tested and treated.

In high transmission zones, many women suffer minor attacks of malaria for which they do not seek treatment. However, the placenta can still be infected. Women should be advised at each antenatal visit to come for treatment even if their symptoms are minor. Both RDTs and smears may miss cases of placental malaria. Because of the inability of biological tests to reliably detect placental malaria, patients with a negative biological test should receive SP as IPTp both to treat an undetected infection and to prevent further infection.

In low transmission zones, anaemia without a positive biological test and without symptoms or signs of malaria such as fever is probably due to other causes, and such patients should not automatically receive an antimalarial drug, but should be treated for the underlying cause (including treatment with iron and folate tablets).

**RDTs versus microscopy in pregnancy**

There is indirect evidence that only 30% of cases with placental malaria show peripheral parasitaemias. Although there is little evidence, it is more likely that RDTs will detect sequestered parasites because of accumulated antigenic product.

In Thailand and Assam, studies found that RDTs missed cases of parasitaemia found on slides (2.5% of patients in Assam). This is a much lower number of cases than the number missed by smears.

Ideally, use of both RDT and microscopy would detect most cases. However, this is usually impractical in the field setting. RDTs are preferable to microscopy in this setting for the detection of subclinical infections.

In cases of *P. vivax* malaria, placental malaria is difficult to detect. However, placental *P. vivax* malaria occurs infrequently because vivax malaria does not sequestrate. Detection of parasites in vivax is best done by microscopy.

**Treatment of malaria**

**Drug safety in pregnancy**

Guidelines on the treatment of malaria in pregnancy are made difficult by the lack of evidence about the safety of ACTs in pregnancy.

The recommendation is to ask the woman if she is...
pregnant, and if she is not, to treat her with ACT. This is a pragmatic recommendation based on the fact that no serious adverse effects have yet been recorded in women who were inadvertently given ACT in the first trimester, and the fact that a 7-day course of quinine is rarely adhered to.

As a change from previous recommendations, the combination of artesunate and lumefantrine (AL) is now considered as safe (or as unsafe) as the other combinations of AS + AQ, AS + SP and AS + MQ.

Drug resistance of P. falciparum to chloroquine and the antifolates has arisen throughout malaria-endemic areas. Combination therapy (artesinin combination therapies, or ACTs) is considered best for malaria management (artesinin-based compounds in combination with other classes of antimalarial drugs).

ACTs are highly effective and may help to delay development of resistance. It is important to ensure wide access to these drugs through effective delivery systems and affordable cost.

The risks of ACT in the second and third trimester are low. During these phases of pregnancy, ACTs should be used to treat both clinical and subclinical infections, due to the serious outcomes of these infections.

Quinine should always be used in the first trimester. However, if the life of the woman is threatened (i.e. when the risk to the mother outweighs the theoretical risk to the fetus), an ACT should be prescribed. Malaria is less often resistant to quinine than it is to other drugs, and this drug may be safely used throughout pregnancy if ACTs are not available.

ACTs in pregnancy: the use of ACTs in pregnancy has not been widely studied, but all of the current evidence points to their relative safety, even in the first trimester. Research into the safety and pharmacokinetics of antimalarial drugs in pregnancy is ongoing. The following ACTs (arranged in alphabetical order) are currently recommended by the WHO for the treatment of uncomplicated P. falciparum malaria:

- **artemether (ATM) + lumefantrine (LM):** combined (fixed-dose combination, FDC) tablets ATM 20 mg/LM 120 mg in blister packs.
  - **Dose:** On day 1 give 4 tablets and then repeat 4 tablets between 8 and 12 hours later. Then give 4 tablets twice daily in the morning and evening on days 2 and 3.
  - Advise the patient to take dosages with food, preferably fatty food. Consider supplying dried milk powder or Plumpy’Nut® to take with tablets.
- **artesunate (AS) + amodiaquine (AQ):** combined (fixed-dose combination, FDC) tablets AS 100 mg/AQ 270 mg in colour-coded blister packs.
  - **Dose:** 2 tablets per day for 3 successive days.
- **artesunate (AS) + mefloquine (MQ):** AS = 50 mg tablets, MQ = 250 mg tablets as base.
  - **Dose:** give 4 tablets of AS on days 1, 2 and 3, and 6 tablets of MQ on day 1 and 2 tablets of MQ on day 2 (or 8 tablets on day 1 only).
- **artesunate (AS) + sulfadoxine + pyrimethamine (SP):** AS = 50 mg tablets, SP = 25 mg (S) + 500 mg (P).
  - **Dose:** give 4 tablets of SP on days 1, 2, 3 and 4 and 3 tablets of SP on day 1.
- **dihydroartemisinin (DHA) + piperaquine (PQP):** combined (fixed-dose combination, FDC) tablets DHA 40 mg/PQP 320 mg.
  - **Dose:** mother weighing 50–60 kg, 1 tablet three times a day for 1 day; mother weighing 60–70 kg, 1 tablet three times a day for 1 day plus additional ½ tablet at onset of day 1.
  - quinine = usually 200 mg and 300 mg tablets.
  - **Dose:** give 600 mg 8-hourly over the first 24 hours or 30 mg/kg/day in three divided doses at 8-hourly intervals.
  - In South-East Asia where quinine sensitivity appears to be reduced, add clindamycin 7–13 mg/kg every 8 hours for 5 days.

Most pregnant women with malaria also lack folate, so give them folate tablets 5 mg daily.

If a pregnant woman is not immune, that is if she comes from an area without malaria transmission, she must have regular malaria tablets throughout pregnancy, especially in the last trimester.

**Severe complicated malaria**

This is usually **P. falciparum** malaria.

**Severe malaria is a complex multi-system disease, and is a medical emergency.**

Mortality approaches 100% without treatment, and death often occurs within the first few hours. Prompt initiation of antimalarial treatment in peripheral healthcare facilities and comprehensive management in hospital are necessary to prevent deaths.

Care should be provided within 15 minutes of arrival at a healthcare facility. **Triage systems** should be in place to pick up severely ill patients, referral should be rapid, and emergency facilities should be instituted in hospitals, with a high standard of medical and nursing care available 24 hours a day.

Any seriously ill or unconscious patient in a malaria endemic area must be tested for malaria by RDT (remember that parasites may not be present in the peripheral blood of a patient with cerebral malaria).

Even if a diagnostic test is not available, the patient should be given an antimalarial drug (IV, IM or rectally, depending on the skill of the staff in the facility) before transfer to the hospital. This can be repeated if transfer is impossible or is delayed for more than 12 hours. **A note of what has been given should be sent with the patient as soon as transfer can be arranged.**

**Clinical features of severe malaria (WHO 2013)**

- Impaired consciousness (including unrousable coma)
- Prostration, i.e. generalised weakness so that the patient is unable to sit, stand or walk without assistance
- Multiple convulsions: more than two episodes within 24 hours
- Deep breathing and respiratory distress (acidotic breathing)
- Acute pulmonary oedema and acute respiratory distress syndrome
- Circulatory collapse or shock, systolic blood pressure < 80 mmHg in adults and < 50 mmHg in children
- Acute kidney injury
- Clinical jaundice plus evidence of other vital organ dysfunction
- Abnormal bleeding.
If any doubt exists about the diagnosis, it is safer to treat than not to treat before transfer.

**Immediate measures (in hospital)**
- **Vital signs:** temperature, pulse, blood pressure, and rate and depth of respiration.
- **State of hydration.**
- **Estimation or measurement of body weight.**
- **Level of consciousness (AVPU or Glasgow Coma Scale scores).**
  - The depth of coma may be assessed rapidly by observing the response to standard vocal or painful stimuli (rub your knuckles on the woman’s sternum; if there is no response, apply firm pressure on the thumbnail bed).
- **RDT and malaria smear (thick and thin film) for diagnosis and for continued monitoring of the progress of the disease. Do not wait for a malaria smear result before initiating treatment, as it can take up to an hour. If the RDT is positive, commence treatment immediately.**
- **Perform a lumbar puncture if the patient is unconscious, to eliminate meningitis.**
- **Measurement of glucose (finger prick test), haemoglobin, haematocrit and packed cell volume (PCV).**
- **Group and cross-match blood and search for a suitable donor if there are no blood banking facilities.**
- **Parenteral treatment (see below for details):**
  - **First choice:** IV artemesinin (2.4 mg/kg by slow IV injection at 0, 12 and 24 hours).
  - **Second choice:** IM artesunate (loading dose of 3.2 mg/kg followed by 1.6 mg/kg every 24 hours).
  - **If artemisinins are not available or the Ministry of Health has not authorised their use, commence with a loading dose of quinine 20 mg/kg (generally given in 10% dextrose to reduce the risk of hypoglycaemia) by slow infusion over 4 hours, followed by 10 mg/kg over 4 hours, every 8 hours for a minimum of 3 doses and continued until the patient is able to tolerate oral drugs. A full course of oral antimalarials must be completed once IV quinine has been discontinued. The loading dose of quinine may be omitted if the patient has definitely received a treatment dose of quinine within the previous 12 hours.**

Every effort should be made to convince the Ministry of Health to allow the use of artemisinins to treat severe malaria in hospital, as mortality may be reduced by up to 30% over the use of quinine.

**Additional measures where needed**
- **Insert a nasogastric tube to minimise the risk of aspiration pneumonia if the patient’s level of consciousness is low. This can also be used to give food to prevent hypoglycaemia if the patient is unconscious for a long period and is unable to eat.**
- **Monitor for hypoglycaemia by laboratory or bedside testing if available (see below for more detailed advice).**
- **Insert an IV cannula and restore circulating volume.**
  - Fluids should be given with caution and the need for them assessed on an individual basis after ascertaining the nutritional status and degree of dehydration present (see below for more details).
  - In general, patients with metabolic acidosis who have not previously received parenteral fluids are dehydrated and should be managed accordingly (see below for more details).
- **Give oxygen, especially if metabolic acidosis is suspected or shock is present.**
- **Treat severe anaemia with a safe blood transfusion if the patient is showing signs of decompensation.**
- **Give anticonvulsants (diazepam is preferred initially, then phenytoin if convulsions persist) if the patient is fitting, to prevent long-term neurological damage (see below for more details).**
- **Convolusions are common before or after the onset of coma. They are significantly associated with morbidity and sequelae. They may present in a very subtle way. Important signs include intermittent nystagnus, salivation, minor twitching of a single digit or a corner of the mouth, and an irregular breathing pattern.**
- **Prophylactic anticonvulsants have been recommended in the past, but recent evidence suggests that phenobarbital is harmful.**
- **IV broad-spectrum antibiotics should be given routinely in an unconscious patient.**
- **The patient will need intensive nursing care at least until they regain consciousness. They may urgently need glucose or a blood transfusion if hypoglycaemia or haemolysis is severe.**

**Special issues with regard to severe malaria in pregnancy**
Severe malaria is malaria with severe drowsiness, coma, vomiting, inability to walk, jaundice, fits or pulmonary oedema. These women are usually non-immune multi-gravid, or semi-immune primigravida, with *P. falciparum* malaria.

Severe malaria in pregnancy may be misdiagnosed as eclampsia. If a pregnant woman living in a malarial area has fever, headaches or convulsions and malaria cannot be excluded, it is essential to treat the woman for both malaria and eclampsia. Pregnant women with severe malaria are particularly prone to hypoglycaemia, pulmonary oedema, anaemia and coma.

Malaria is especially dangerous during the last trimester.

**Malaria drug treatment in pregnancy**
Treat malaria in pregnancy urgently and early!
Calculate the dose in mg/kg. If you cannot weigh the patient, an average pregnant woman weighs about 60 kg, a small woman weighs around 50 kg and a large woman in resource limited settings around 80 kg.

Where available, artesunate IV/IM or artemether IM are the drugs of choice in the second and third trimesters. Their use in the first trimester must balance their advantages over quinine (better tolerability and less hypoglycaemia) against the limited documentation of pregnancy outcomes. Artemesinin and artesunate may be given rectally.

**IV/IM artesunate**
Artesunate IV/IM: 2.4 mg/kg by direct IV injection (over 5 minutes) or IM injection at 0, 12 and 24 hours, then once daily until oral therapy is possible.
A solution for parenteral use should be prepared for either IV (10 mg/mL) or IM (20 mg/mL) use, following the
manufacturer’s instructions, using the sodium bicarbonate and saline solution supplied to dilute the concentrated artesunate.

For a small pregnant woman (estimated body weight 50kg), each dose would be 12 mL IV (10 mg/mL) or 6 mL IM (20 mg/mL).

Artesunate IM should be administered in the anterolateral thigh, drawing back before injection to ensure that the needle is not in a vein.

**IM artemether**

Artemether IM: loading dose is 3.2 mg/kg on day 0, followed by 1.6 mg/kg daily for at least two more doses; then continue until oral therapy is possible. A full course of oral therapy should be taken once IM therapy is discontinued.

An 80 mg/mL presentation is preferred to reduce the volume of the injection.

For a small pregnant woman (estimated body weight 50 kg) each dose would be 2 mL IM (80 mg/mL).

Artemether IM should be administered in the anterolateral thigh, drawing back before injection to ensure that the needle is not in a vein.

Artemether is not well absorbed in shock, and in this situation an alternative treatment (parenteral or rectal artesunate, or IV quinine) should be chosen.

**Rectal artesunate**

- It is recommended that this should be available in all rural settings, including those with trained village healthcare workers.
- It can be given at 12-hourly intervals.
- The minimum dose is 10 mg/kg. Larger doses are not harmful, but are not more effective.
- It can also be given to vomiting patients, or those unable to tolerate oral drugs.
- Rectal artesunate must always be followed by a full course of ACT when the patient is able to take oral drugs.

At present the WHO only recommends rectal artesunate as a pre-referral treatment. Where referral is not possible, ensure a full course of ACT is given as soon as the patient is able to take oral treatment.

Artesunate is available as a rectal capsule: Rectocaps (Mephy), 50 mg and 200 mg.

A WHO-approved rectal capsule is to be available soon, as 100 mg and 400 mg presentation.

The dose is 10 mg/kg, and therefore an average-sized mother needs 600 mg per dose. Give three 200 mg rectal suppositories at 0, 12, 24, 36, 48 and 60 hours.

**Follow-on treatment**

When the patient has received at least three parenteral doses of artesunate or artemether, and is able to tolerate oral intake, give a full course (3 days) of ACT orally.

**Quinine dihydrochloride**

**Always give quinine with glucose.**

Do not confuse doses of salt and base. Quinine is usually prescribed as the salt (10 mg of quinine dihydrochloride = 8.3 mg of base).

**Loading dose**

Infuse quinine dihydrochloride 20 mg/kg body weight (usually 1.2 grams for the average 60 kg pregnant woman) in 500 mL of IV fluids (Ringer-lactate or Hartmann’s solution plus 5% or 10% glucose) over 4 to 8 hours. Do not let it go in too quickly. Quinine is usually available in 2-mL ampoules of 150 mg/mL, where 1.2 g thus corresponds to 8 mL.

Do not give quinine in 5% dextrose solutions, as there is a danger of hyponatraemia. Add 50 mL of 50% glucose to 500 mL of Ringer-lactate or Hartmann’s solution to produce Ringer-lactate or Hartmann’s plus 5% glucose solutions. Add 100 mL of 50% glucose to 500 mL of Ringer-lactate or Hartmann’s solution to give 10% glucose solutions.

**Never give an IV bolus injection of quinine, as it is likely to cause cardiac arrest.**

- If it is definitely known that the mother has taken an adequate dose of quinine (1.2 grams) within the preceding 12 hours, do not give the loading dose. Proceed with the maintenance dose (see below).
- If the history of treatment is not known or is unclear, give the loading dose of quinine.

Alternatively, omit the loading dose if the patient has received three or more doses of oral quinine in the last 48 hours, or mefloquine or halofantrine within the last 3 days.

- Wait 8 hours before giving the maintenance dose.

**Maintenance dose**

Infuse quinine dihydrochloride 10 mg/kg body weight (usually 600 mg for the average pregnant woman) in 500 mL of fluids (as above) IV over 4 hours. Repeat every 8 hours (i.e. quinine infusion for 4 hours, no quinine for 4 hours, quinine infusion for 4 hours, etc.) for 24 hours and then change to oral medication if the woman is conscious and able to swallow safely.

For follow-on oral treatment, give a 3-day course of ACT or 7 days of oral quinine. If the combination AS + MQ is used, wait 12 hours after the last dose of quinine before giving MQ. Do not use AS + MQ if the patient developed neurological signs during the acute phase.

The dose of oral quinine dihydrochloride or quinine sulphate is 10 mg/kg body weight (usually 600 mg for the average size of pregnant woman) by mouth every 8 hours to complete 7 days of treatment. Ask the patient to swallow the tablets quickly with milk.

Monitor blood glucose levels for hypoglycaemia every hour while the patient is receiving quinine IV.

Quinine may increase the risk of hypoglycaemia, and it may cause haemolysis in patients with glucose-6-phosphate dehydrogenase (G6PD) deficiency, which may result in the passage of haemoglobin in the urine (this is called blackwater fever).

Make sure that plenty of fluids are given so that the urine output is adequate. Keep a strict fluid balance chart. Monitor the volume of fluid that you give, and the urine output. Do not overload with fluid.

If the haemoglobin level falls below 6 g/dL try to give blood, but observe closely for fluid overload. When the patient is improving, give iron and folic acid tablets.

**Intramuscular quinine**

If you cannot place an IV line, you can give quinine IM, at a strength of not more than 60 mg/mL. Some ampoules are 60 mg/mL (usually 10-mL ampoules), Some ampoules are 300 mg/mL or 600 mg/mL. Dilute these in 0.9% saline or Ringer-lactate or Hartmann’s solution to a concentration of
60 mg/mL (e.g. 600 mg of quinine in 10 mL of saline). If you do not dilute quinine, the mother may develop an injection abscess. Use the same dose as you would give IV. Give half the dose into each anterior thigh.

When giving quinine by IM injection, regularly draw back to ensure that the needle is not in a vein, as an IV injection of quinine is likely to cause cardiac arrest.

**Fluid replacement**

If the patient is unable to drink, maintain daily fluid requirements using the nasogastric (preferred) or IV (greater risk of fluid overload) route. Do not use 0.9% saline as it is an acid solution: use Ringer-lactate or Hartmann’s solution. Measure urine output (a Foley catheter should be used in unconscious patients).

<table>
<thead>
<tr>
<th>Weight</th>
<th>Daily fluid requirement</th>
<th>Hourly fluid requirement</th>
</tr>
</thead>
<tbody>
<tr>
<td>In pregnancy</td>
<td>50 mL/kg</td>
<td>2.0 mL/kg</td>
</tr>
</tbody>
</table>

**IV fluids**

A Ringer-lactate or Hartmann’s solution plus glucose mix is commonly recommended. Use a 10% glucose mix with Ringer-lactate or Hartmann’s solution if hypoglycaemia is identified. Monitor carefully for fluid overload, especially when the IV route is used. Switch to the oral route as soon as possible. Fluids given should be included in the daily fluid requirement totals to avoid over-hydration.

**Antibiotics**

All patients who are in shock or who remain severely ill following resuscitation should receive a presumptive treatment with broad-spectrum IV antibiotics. Unconscious patients should have a lumbar puncture to exclude meningitis. Where this is not possible a presumptive treatment with broad-spectrum IV antibiotics. Unconscious patients.

**Continuing hospital care of pregnant women with severe malaria**

This should include the following:

- Nurse in the lateral position if the woman is more than 20 weeks’ pregnant, to avoid inferior vena caval compression.
- If the patient is unconscious, nurse her in the recovery position, alternating sides frequently.
- Observe hourly pulse, blood pressure, respiratory rate and level of consciousness (using the AVPU scale: see Section 1.11).
- Frequently measure blood glucose levels (every hour if the patient has a reduced conscious level, especially when they are receiving quinine and/or where the level of consciousness does not improve).
- If the patient is conscious, regularly (4-hourly) determine blood glucose levels to exclude hypoglycaemia particularly if the patient is not eating well. This is especially important in pregnant women, particularly those receiving quinine therapy.
- A daily microscopic blood slide to determine the level of parasitaemia and to follow treatment efficacy.
- Regular haemoglobin measurement. The frequency will depend on the rate of red blood cell breakdown. This may be very rapid in cases of high parasite density.

- Blood transfusion where necessary with careful monitoring to prevent fluid overload. Packed cells should be used where possible. If overload is suspected, give a single dose of 20 mg IV.
- If the patient is unconscious or in shock, administer IV broad-spectrum antibiotics to manage septicaemia, pneumonia or meningitis, which are often associated with cerebral malaria.
- Oxygen is needed for patients in respiratory distress.
- Blood gases and urea and electrolytes should be measured where possible.
- Controlled IV fluids.
- Fluid balance charts: unconscious patients should be catheterised to measure urine output, facilitate correct fluid balance and detect possible renal failure.

**Management of life-threatening complications of severe malaria**

**Severe anaemia (due to haemolysis)**

Monitor haemoglobin levels daily.

- Severe haemolytic anaemia: haemoglobin < 5 g/dL or haematocrit < 15%.
- Severe anaemia may be the presenting feature in malaria. Patients with severe anaemia, especially pregnant women, should be tested for malaria.

- Establish safe transfusion as soon as possible.
- Transfuse with screened blood only if the patient is severely symptomatic. For patients with haemoglobin < 5 g/dL or haematocrit < 15%, recheck haemoglobin levels at least every 4 hours. Transfuse if haemoglobin levels start to fall or symptoms develop.
  - Packed cells are preferred for transfusion in pregnancy. Allow red blood cells to settle at the bottom of the bag, and stop the infusion when all of the cells have been used.
  - Perform microscopy following transfusion, and repeat or extend antimalarial treatment if parasitaemia is increasing.
- Transfusion rates may depend on the status of the patient. Exercise caution with malnourished patients.
- Suggested rates: two 500-mL units over 4–6 hours giving IV 20 mg of furosemide with each 500 mL.
- If the patient shows signs of fluid overload, give additional furosemide 20 mg IV, and repeat after 1–2 hours if indicated.

Give ferrous sulphate or fumarate 60 mg by mouth plus folic acid 5 mg by mouth once daily upon discharge.

**Hypoglycaemia**

This is defined as glucose levels of less than 2.5 mmol/litre (< 45 mg/dL).

Check for hypoglycaemia in patients who are unconscious, in shock or deteriorating, especially if they are malnourished, and in all patients receiving quinine. Often hypoglycaemia causes no symptoms until it results in coma and death. Watch for abnormal behaviour, sweating and sudden coma. Always give glucose with quinine. If the mother is drowsy, delirious or unconscious, do not assume that she has cerebral malaria; she is probably hypoglycaemic.

Treat with an IV glucose infusion over 15 minutes.
- If you give 50% glucose it irritates the veins, so dilute
50 mL of 50% glucose with 50 mL of Ringer-lactate or Hartmann’s solution to make a 25% solution.

- Then give 500 mL of 5% dextrose in Ringer-lactate or Hartmann’s solution over 8 hours (see above for details of how to prepare this).

If you do not have IV glucose, give sugar water by mouth or by nasogastric tube. Dissolve 4 level teaspoons (20 grams) in a 200 mL cup of clean water.

Retest 15 minutes after completion of infusion, and repeat the infusion if blood glucose levels remain low. Repeat until blood glucose levels recover, and then infuse with 5–10% glucose in Ringer-lactate or Hartmann’s solution (according to hypoglycaemia risk) to prevent recurrence. Ensure regular feeding when oral intake can be sustained. Fluids used to treat hypoglycaemia must be included in the daily fluid requirements.

Hypoglycaemia is a major cause of death in patients with severe malaria, especially those who are pregnant. Remember that quinine will potentiate hypoglycaemia. Patients should receive regular feeding, including by nasogastric tube, when they are unable to take oral foods.

Fluid balance problems
Maintain a strict fluid balance chart and monitor the amount of fluids administered and urine output to ensure that there is no fluid overload. Assess the patient’s clinical status regularly.

**Note:** Pregnant women with severe malaria are prone to fluid overload.

Acute renal failure (ARF)
This is defined as an abrupt decline in the renal regulation of water, electrolytes and acid–base balance, and continues to be an important factor contributing to the morbidity and mortality of malaria patients.

Oliguria or anuria is often associated with jaundice, anaemia and bleeding disorders.

**Note:** Dehydration is a common cause of low urine output.

- The basic principles of management are avoidance of life-threatening complications, maintenance of fluid and electrolyte balance, and nutritional support.
- The patient must be catheterised so that urine output can be accurately measured.
- A level or more accurate measurement is obtained when the hourly urine output is < 30 mL/hour (over 4 hours). Blood concentrations of urea and creatinine are usually raised (> 2.9 mg/dL that is > 256 mmol/litre).
- Make sure that the patient is adequately hydrated, but avoid overload.
- If possible, monitor plasma electrolytes, especially serum potassium levels.

If urine output continues to be low despite adequate hydration, peripheral perfusion and normal blood pressure, give furosemide 40 mg IV.

If renal failure is established, restrict fluid to insensible loss (30 mL/hour) plus urine output. If possible, refer the mother to a tertiary care centre for management of renal failure. Consider peritoneal dialysis (if available).

**Convulsions**
If there are convulsions, consider whether the mother has eclampsia. Test the urine for protein and measure the blood pressure (see Section 2.5.E).

If the mother has eclampsia, treat this with magnesium sulphate. If she does not have eclampsia, prevent more convulsions with anticonvulsants.

**Note:** seizure activity in cerebral malaria needs to be looked for carefully, as it may just appear as a twitching of the thumb or mouth.

Give diazepam, 10 mg rectally or by slow IV injection over 2 minutes.

Do not exceed 10 mg per dose. Always have a bag-valve-mask of a suitable size available in case the mother stops breathing.

Alternatively, paraldehyde 0.1 mL/kg of body weight may be given by deep IM injection (usually 6 mL total dose) or 0.4 mL/kg of body weight (usually 24 mL) intra-rectally using a sterile glass syringe (a disposable plastic syringe may be used provided that the injection is given immediately after the paraldehyde is drawn up, and the syringe is never reused). Consider preventing subsequent convulsions with phenytoin (see below).

**Phenytoin**

**Loading dose**
Infuse phenytoin 1 gram (approximately 18 mg/kg body weight) in 50–100 mL of 0.9% saline over 30 minutes (the final concentration should not exceed 10 mg/mL).

**Note:** Only 0.9% saline can be used to infuse phenytoin. All other IV fluids will cause crystallisation of phenytoin.

Flush the IV line with 0.9% saline before and after infusing phenytoin.

Do not infuse phenytoin at a rate exceeding 50 mg/minute, due to the risk of irregular heartbeat, hypotension and respiratory depression. Complete administration within 1 hour of preparation.

**Maintenance dose**
Give phenytoin 100 mg IV slowly over 2 minutes or by mouth every 8 hours beginning at least 12 hours after the loading dose.

**Respiratory distress**

**Rapid laboured breathing:** check for and treat secondary pneumonia (give antibiotics and oxygen) or anaemia (transfuse), or pulmonary oedema, which may occur with or without fluid overload. Check the fluid balance (reduce IV fluids), supply oxygen, nurse the patient in a semi-sitting position, and do a trial of furosemide, 40 mg IV, repeating this after 1–2 hours if indicated.

**Slower laboured breathing (acidotic)** (Kussmaul breathing): ensure appropriate fluid replacement (plus transfusion if indicated), and treat associated conditions and infections.

**Metabolic acidosis**

Deep breathing with a clear chest is a sensitive and specific sign for the presence of metabolic acidosis. It is the single most important determinant of survival, and can lead to respiratory distress syndrome. Metabolic (lactic) acidosis has been identified as an important cause of death in severe malaria.

Metabolic acidosis in severe malaria has been attributed to the combined effects of several factors that reduce oxygen delivery to tissues:
Pulmonary oedema is very dangerous. The mother may have it on admission, or it may develop after several days. Fast difficult breathing is the first sign. Frothy (bubbly) fluid may be coming from the mouth. Pulmonary oedema causes hypoxia, fits, coma and death. It can also be caused by too much fluid. Sometimes it is caused by malaria and too much hypoxia, fits, coma and death. It can also be caused by too much fluid. Sometimes it is caused by malaria and too much hypoxia, fits, coma and death. It can also be caused by too much fluid. Sometimes it is caused by malaria and too much hypoxia, fits, coma and death.

Management
- Maintain airway patency and oxygen delivery; intubate if the patient is unconscious, in severe shock, or otherwise unstable.
- Establish an IV line; replace an adequate intravascular fluid volume if the patient has tachycardia, hypotension or other signs of poor tissue perfusion, such as poor capillary refill time. IV normal (0.9%) saline can be harmful in severe malaria, when there is frequent acidosis. Normal saline is a strongly acidic solution and can make the acidosis much worse. Therefore use Ringer-lactate or Hartmann’s solution for IV fluid replacement or in shock.
- Monitor for cardiac arrhythmias.
- The use of sodium bicarbonate is controversial and generally should be avoided.

Shock
Although severe malaria alone may cause shock (algid malaria), it is uncommon and bacterial sepsis often coexists, which must be treated.

Coexisting infections
- Treat any associated pneumonia, dysentery or endometritis (see Sections 2.8.A, 2.8.B and 2.5.G).
- Congenital malaria
  - Congenital malaria is relatively rare; it occurs in up to 10% of affected pregnancies. This is because the placental barrier and maternal IgG antibodies that cross the placenta protect the fetus to some extent. All four species can cause congenital malaria, but *P. malariae* causes proportionately more than the other species.
  - Congenital malaria is much more common in non-immune populations, and the incidence increases during epidemics of malaria.
  - Fetal plasma quinine levels are about one-third of simultaneous maternal levels, and this sub-therapeutic drug level does not cure the infection in the fetus.
  - The newborn child can manifest with fever, irritability, feeding problems, hepatosplenomegaly, anaemia and jaundice. The diagnosis can be confirmed by a smear from cord blood or a heel prick, any time within 1 week after birth (HRP2 tests may not be relevant in the early days after birth, as the infant blood may include HRP2 from the mother). The risk of congenital malaria is higher in children born to mothers who have malaria during or shortly before delivery.

Prevention, diagnosis and treatment of non-*falciparum* malaria
Other forms of malaria are found all over the world and need to be prevented, diagnosed and treated.

*P. vivax* and *P. ovale* malaria
*P. vivax* and *P. ovale* malaria are recurrent due to the fact that the parasites can conceal themselves as the hypnozoite form in the liver. They can emerge and cause new attacks of malaria at regular intervals for up to 30 years. Most medications (except primaquine) only act on the erythrocyte stage of the parasite and therefore do not affect the hypnozoites.

Prevention
Long Lasting Impregnated Bednets (LLINs) with appropriate information should be supplied to prevent initial infection (and co-infection with other parasite species), but they will not prevent recurrent attacks once the infection is established. *Indoor residual spraying* should be used.

Diagnosis
The following methods can be used:
- microscopy
- RDTs: HRP2 tests such as Paracheck will only detect *P. falciparum*. pLDH tests such as CareStart will detect
other species. At present the sensitivity and specificity of pLDH in detecting *P. vivax* and other species of malaria are not clearly defined.

- **Polymerase chain reaction (PCR)** can be used to distinguish between new and recurrent infections.

### Treatment

At present, the treatment for *P. vivax* malaria (and the other non-falciparum species) is **chloroquine (CQ)**.

**This should only be used for CQ-sensitive non-falciparum malaria.**

It is available in the following formulations:

- 100 mg base tablets (chloroquine phosphate)
- 150 mg base tablets
- 50 mg base/5 mL syrup.

Chloroquine is sometimes found as a salt, but the WHO recommends use of the base product.

The regime described below is recommended by the WHO for use in settings where compliance may be difficult and dosing regimes need to be simplified.

**Dose:**

- 6 tablets 100 mg on days 1 and 2, then 3 tablets 100 mg on day 3 or 4 tablets 150 mg on days 1 and 2, then 2 tablets 150 mg on day 3. **Total dose = 1500 mg base (= 2500 mg salt).**

There is some evidence of resistance to chloroquine in India and Indonesia, but it is difficult to determine whether apparent failure of the treatment is due to recurrence from hypnozoites or to drug failure. There has been little evidence from efficacy studies.

**Note:** ACTs cure all types of malaria, but chloroquine is still effective (and cheaper) for treating most cases of *P. vivax*, *P. malariae* and *P. ovale*.

As mentioned above, chloroquine only kills the parasites in the red blood cells, and does not kill the pre-erythrocyte forms or the hypnozoites of the recurrent malaria *P. vivax* and *P. ovale* in the liver.

At present **primaquine** is the only drug available to tackle the hypnozoites and prevent recurrence.

### Treatment with primaquine

Primaquine is the only drug at present available to prevent recurrent attacks of *P. vivax* and *P. ovale*. However, it is not recommended for pregnant women, so treatment with this drug should wait until the pregnancy has ended.

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### 2.8.E Acute appendicitis

#### Introduction

Appendicitis should be suspected in any woman or girl with abdominal pain, whether she is pregnant or not. The diagnosis of appendicitis can be more difficult in pregnancy, due to the possibility of pregnancy-related conditions, including ectopic pregnancy, abruptio placenta, torsion of an ovarian cyst and pyelonephritis.

As pregnancy advances, the enlarging uterus displaces the appendix from its usual position, shifting the site of maximal tenderness towards the right upper quadrant (see Figure 2.8.E.1). In the third trimester, it may consequently mimic cholecystitis. The site of an incision for appendicectomy should be over the point of maximum tenderness.

#### Clinical management

If appendicitis is suspected clinically, give a combination of antibiotics before surgery, and continue until the woman is post-operative and fever-free for 48 hours:

- ampicillin 2 grams IV every 6 hours
- plus gentamicin 80 mg IV/IM every 8 hours or 5 mg/kg body weight IV/IM once every 24 hours
- plus metronidazole 500 mg IV every 8 hours.

Morphine 10 mg IV or IM may be administered as analgesia (see Section 1.16).

Immediate surgical exploration is required, regardless of the stage of gestation. Appendicectomy should be performed even if the appendix does not look infected.

**Delaying diagnosis and treatment can result in rupture of the appendix, which may lead to generalised peritonitis.** This has a high maternal mortality in pregnancy, as well as a significant risk of miscarriage or preterm labour.

If there are signs of peritonitis (fever, rebound tenderness and guarding), give antibiotics above as for peritonitis but continue until the infection has fully resolved (usually following surgery) and there has been no fever for 48 hours.

If appendicitis occurs in late pregnancy, the infection may be walled off by the gravid uterus. As the uterus rapidly decreases in size (involutes) after delivery, the infection may spill into the peritoneal cavity. In these cases, appendicitis then presents as generalised peritonitis.

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**Figure 2.8.E.1** The changes in position of the appendix as pregnancy advances. Adapted from McGraw-Hill Companies, Inc. Reproduced with the permission of Chris Paschalidis.
2.8.F Cystitis and acute pyelonephritis

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**Acute cystitis**
Cystitis is a common complication of pregnancy, and is characterised by dysuria, frequency, urgency and, if severe, by haematuria. Severe cystitis can progress to pyelonephritis if not treated. The presence of loin pain and tenderness, along with fever, suggests a diagnosis of pyelonephritis. Asymptomatic cystitis is more common in pregnancy, carries a risk of progression to pyelonephritis, and is associated with an increased risk of premature delivery.

**Diagnosis**
- Use a dipstick leucocyte esterase test to detect white blood cells, and a nitrate reductase test to detect nitrites.
- Microscopy of a urine specimen (see Section 8.5) may show white blood cells in clumps, bacteria and sometimes red blood cells. Urine examination requires a clean-catch midstream specimen of urine to minimise the possibility of contamination. The results of bacterial culture, although not necessary before starting treatment, are helpful if there is treatment failure, and also for monitoring bacterial sensitivity in the population.

**Treatment with antibiotics for uncomplicated cystitis**
- Amoxicillin 500 mg by mouth three times a day for 5 days or cephalaxin (or alternative available cephalosporin) 500 mg three times a day for 5 days.
- Trimethoprim/sulfamethoxazole 1 tablet 160/800 mg by mouth twice a day for 3 days. **This drug is best avoided in pregnancy** unless there is no alternative. It must be completely avoided in the first trimester. This antibiotic is a folate antagonist and therefore promotes congenital abnormalities, and in the third trimester it may cause haemolysis in the neonate.
- If treatment fails, check urine culture and sensitivity (if available), and treat with an antibiotic appropriate for the organism.

**Acute pyelonephritis**
Acute pyelonephritis is an acute infection of the upper urinary tract, mainly of the renal pelvis, which may also involve the renal parenchyma. It can precipitate premature labour.
- If shock is present or suspected, initiate immediate ABC treatment.
- Check urine culture and sensitivity (if available), and treat with an antibiotic appropriate for the organism.
- If urine culture is unavailable, treat with antibiotics until the woman has been fever-free for 48 hours:
  - ampicillin 2 grams IV every 6 hours
  - plus gentamicin 80 mg IM/IV every 8 hours or 5 mg/kg body weight IV/IM once every 24 hours.
- Once the woman has been fever-free for 48 hours, give amoxicillin/ampicillin 500 mg by mouth three times a day to complete 14 days of treatment.
- If there is no clinical response within 72 hours, review the results and antibiotic coverage.
  - Alternative and/or second line treatment is with IV cephalosporins, e.g. cefuroxime 750 mg to 1.5 g 8-hourly.
- Perform a renal ultrasound scan. If any significant malformation of the kidneys or renal tract is noted, refer the patient for specialist advice.

2.8.G Tuberculosis in pregnancy

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for TB. This includes a tuberculin skin test, sputum for acid-fast bacilli (AFB) stain and culture for mycobacterium TB. A chest X-ray may have harmful effects on the fetus in the first trimester of pregnancy, but may be done with an abdominal lead shield. If clinically indicated a Chest X-ray is recommended as the risk to the fetus is very small and the mother’s health a priority.

Additional newer tests, namely interferon gamma release assay (IGRA) or polymerase chain reaction (PCR) identification (if available), may complement diagnosis.

Extra-pulmonary TB is much more difficult to diagnose during pregnancy. After delivery, the placenta should be sent for histopathology, AFB stain and AFB culture to contribute to a diagnosis. The neonate should be evaluated thoroughly and treated accordingly.

Antituberculous treatment during pregnancy

During pregnancy, tuberculosis represents a greater hazard to the pregnant woman and her fetus than does its treatment. Therefore treatment should be commenced as soon as possible after a diagnosis has been made. Treatment for new patients with pulmonary TB is the same in pregnancy as it is for all other adults (see WHO guidelines 4th edition 2010 for full details: www.who.int/tb/publications/2010/9789241547833/en/).

In summary, new patients with pulmonary TB should be treated with a regime containing isoniazid (H) and rifampicin (R) for 6 months (see Table 2.8.G.1 for doses). There is an initial 2-month intensive phase of HRZE and then a 4-month continuation phase of just HR.

The optimal dosing frequency is daily throughout the 6-month course. However, provided directly observed therapy is practiced and the patient is not living with HIV a 3-month course is an option. Provided directly observed therapy is practiced and the patient is not living with HIV the last 4 months of treatment can be given three times a week.

Isoniazid, ethambutol and rifampin are relatively safe for pregnancy. The effects of other second-line drugs on the fetus are unknown, and their use during pregnancy must be undertaken only after a careful risk and benefit analysis.

The WHO-recommended two-, three- and four-drug FDC schemes are simplified for clinical use according to body weight, and ensure that the doses remain within the therapeutic margins, and that underlying liver and renal impairment is considered (see Tables 2.8.G.1 and 2).

Table 2.8.G.1 Commonly used drugs for the treatment of TB in pregnancy

<table>
<thead>
<tr>
<th>Drug</th>
<th>Daily dose (mg/kg/when given daily)</th>
<th>Daily dose when given three times weekly</th>
<th>Potential adverse reactions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Isoniazid (H) tablet, 100 mg, 300 mg</td>
<td>5 mg/kg (4–6 mg/kg) Maximum 300 mg</td>
<td>10 mg/kg (8–12 mg/kg) Maximum 900 mg</td>
<td>Mild hepatic enzyme elevation, hepatitis, peripheral neuritis, hypersensitivity</td>
</tr>
<tr>
<td>Rifampin (R) tablet, 150 mg, 300 mg, 450 mg</td>
<td>10 mg/kg (8–12 mg/kg) Maximum 600 mg</td>
<td>10 mg/kg (8–12 mg/kg) Maximum 600 mg</td>
<td>Orange discoloration of urine and other body fluids, vomiting, hepatitis</td>
</tr>
<tr>
<td>Pyrazinamide (Z) tablet, 500 mg</td>
<td>25 mg/kg (20–30 mg/kg)</td>
<td>35 mg/kg (30–40 mg/kg)</td>
<td>Hepatotoxicity, hyperuricaemia</td>
</tr>
<tr>
<td>Ethambutol (E) tablet, 100 mg, 400 mg</td>
<td>15 mg/kg (15–20 mg/kg)</td>
<td>30 mg/kg (25–35 mg/kg)</td>
<td>Optic neuritis, decreased visual acuity, gastrointestinal disturbance, hypersensitivity</td>
</tr>
<tr>
<td>Four-drug FDC tablet, R 150 mg + H 75 mg + Z 400 mg + E 275 mg</td>
<td>Dosage recommendations are more straightforward, and adjustment of dosage is done according to patient weight category</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Three-drug FDC tablet, R 150 mg + H 75 mg + Z 400 mg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Two-drug FDC tablet, R 300 mg + H 150 mg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Two-drug FDC tablet, H 150 mg + E 400 mg</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

H = isoniazid, R = rifampicin, Z = pyrazinamide, E = ethambutol, S = streptomycin, FDC = fixed drug combination.
A three- to four-drug regimen of isoniazid, rifampin and pyrazinamide with or without ethambutol is recommended for uncomplicated pulmonary TB (see Table 2.8.G.1).

If pyrazinamide treatment is included in the initial drug regimen, after an initial 2 months of three to four drugs, therapy is continued with two drugs (isoniazid and rifampin) to complete at least 6 months of therapy.

If pyrazinamide is not used, the two-drug period should be extended to at least 9 months.

Prompt initiation of therapy is mandatory to protect the mother and the fetus.

Streptomycin should not be used in pregnancy, as it crosses the placenta and can cause auditory nerve impairment and nephrotoxicity in the fetus.

Vitamin K should be administered at birth to the infant of a mother taking rifampicin because of the risk of postnatal haemorrhage.

Pyridoxine (vitamin B6) 10 mg daily is recommended for pregnant or breastfeeding women who are taking isoniazid-containing regimens.

Extra-pulmonary TB in pregnant women requires the same regimens as uncomplicated pulmonary TB. Some forms (e.g. meningitis, bone, joint) require a longer duration (9–12 months) of TB drugs.

If a woman has suspected resistant TB, attempts must be made to confirm drug resistance by appropriate cultures and therapy based on susceptibility results. Regimens are complicated and depend on susceptibilities, previous drug therapy, local susceptibility data, availability of second-line drugs and tolerability. An expert in infectious disease must be consulted in such cases. Pregnant women with resistant TB have a less favourable prognosis. They may sometimes require treatment with second-line drugs, including cycloserine, ofloxacin, amikacin, kanamycin, capreomycin and ethionamide. The safety of these drugs is not well established in pregnancy.

Breastfeeding and TB

The low concentrations of anti-TB drugs in breast milk do not produce toxicity in the nursing newborn. Therefore breastfeeding should not be discouraged for an HIV-seronegative woman who is planning to take or is taking anti-TB drugs. Anti-TB treatment is the best way to prevent transmission of tubercle bacilli to the baby. Mother and baby should stay together and the baby should continue to breastfeed. After active TB in the baby is ruled out, the baby should be given 6 months of isoniazid preventive therapy, followed by BCG vaccination (for advice on breastfeeding and HIV, see Section 6.2.D). Breastfed infants do not require pyridoxine supplementation unless they are receiving isoniazid.

Treatment of LTBI

In most pregnant women, treatment of latent TB infection (LTBI) – that is, treatment of asymptomatic pregnant women with a positive tuberculin test or IGRA result and normal chest X-ray – should be delayed until 2 or 3 months after delivery, even though no harmful effects of isoniazid (INH, the standard treatment regimen for LTBI) on the fetus have been documented.

However, in the following situations where there is a high risk of progressing to active disease, treatment for LTBI with isoniazid (INH), 300 mg daily should begin during pregnancy.

Treatment of LTBI should be started during the first trimester of pregnancy for:

- Pregnant women who have HIV infection or behavioural risk factors for HIV infection, but who refuse HIV testing
- Pregnant women who have been in recent close contact with an individual with smear-positive pulmonary TB.

Treatment of LTBI should be started after the first trimester of pregnancy for pregnant women who have had a documented tuberculin skin test conversion in the past 2 years.

Treatment of LTBI, if indicated, should be started 2 to 3 months after delivery for all other pregnant women, including those with radiographic evidence of old healed TB. The recommended duration of LTBI therapy is 9 months. If a woman who is taking isoniazid and/or rifampin for treatment of LTBI becomes pregnant, treatment should be interrupted and started again 2 or 3 months after delivery, unless one or more of the above risk factors are present.

Perinatal TB

Women who have only pulmonary TB are not likely to infect the fetus, but can infect their infant after delivery. Although protection of the infant from exposure and infection is of paramount importance, continuous close contact between infant and mother should be encouraged. Congenital TB is rare, but in-utero infections can occur after maternal bacteraemia. If a newborn infant has suspected congenital TB, a full evaluation should be done and treatment initiated based on individual circumstances and specific recommendations. Management of the newborn infant is based on categorisation of the maternal (or household contact) infection as follows:

- If the mother has completed TB chemotherapy during pregnancy, or has inactive disease, her infant should be given BCG at birth.
- If the mother has active disease or still requires treatment, the infant should be given isoniazid 10 mg/kg once daily for 3 to 6 months.
- Once the mother and infant are on appropriate treatment, the infant may be breastfed only if the mother has multidrug-resistant TB. A tuberculin test and chest X-ray are then performed on the neonate. If these are negative, BCG is given. If they are positive, full investigations for TB are undertaken. If no evidence of disease is detected, isoniazid is continued for another 3 to 4 months. If TB is suspected, full treatment is given at standard doses.

Monitoring

All pregnant women with TB must be carefully followed up monthly. At each visit, the patient needs to be checked for compliance, response to therapy, adverse effects and adjustment for any clinical event.

Directly observed treatment

Directly observed treatment: short-course (DOTS) remains an important WHO strategy for reducing the TB burden worldwide. In DOTS, healthcare workers observe patients as they take their medicine. DOTS is practised even for children, and parents can be asked to supervise treatment in the communities where DOTS is used. This is especially true for HIV-infected children, patients with multi-drug-resistant (MDR) TB or those with complicated TB, and has been shown to be successful.
The WHO has developed a new six-point **Stop TB Strategy**, which builds on the successes of DOTS. One of these is to ‘pursue high-quality DOTS expansion and enhancement’ through the following steps.

1. Secure political commitment, with adequate and sustained financing.
2. Ensure early case detection and diagnosis through quality-assured bacteriology.
3. Provide standardised treatment with supervision and patient support.
4. Ensure effective drug supply and management.

## 2.8.H Syphilis in pregnancy and the newborn infant

### Introduction

Syphilis is a dangerous bacterial infection caused by *Treponema pallidum* which, when it occurs in pregnancy, can cause early fetal death, stillbirth, preterm birth, neonatal death or congenital infection. Mother-to-child transmission is a major problem, especially in resource-limited countries.

In a recent analysis, it was estimated that in 2008 worldwide there were between 1.2 and 1.6 million pregnant women with active syphilis, of whom 39% were living in Africa. In the absence of screening and treatment this would have resulted globally in 707,000 adverse pregnancy outcomes, including 286,000 stillbirths or early fetal deaths, 122,000 neonatal deaths, 82,000 preterm or low-birthweight babies and 218,000 infected newborn infants. Additional mortality after the first month of life was estimated to be 10% by 1 year of age.

The cost of diagnosis and treatment per individual is US$2.

All countries must ensure that all pregnant women have access to antenatal care that includes diagnostic screening and treatment for syphilis.

### Clinical features

Infection is either congenital (through in-utero transfer) or acquired (through sexual transmission or blood transfusion). The average time between acquired infection and the appearance of symptoms and signs is 21 days, but this period can range from 10 to 90 days.

Acquired syphilis has early and late phases. The early phase has primary, secondary, early latent (hidden and < 1 year), late latent (hidden > 1 year) and tertiary stages. The early stages are more infectious and respond best to penicillin treatment.

The symptoms and signs can resemble those of many other diseases.

#### Primary stage

The chancre is firm, round, painless and usually single, but may be multiple at the location where syphilis entered the body. Chancre may not be visible in the vagina or anus. The chancre lasts for 3 to 6 weeks, and heals whether or not it is treated. If untreated, the infection progresses to the secondary stage.

#### Secondary stage

A non-itchy skin rash and/or mucous membrane lesions (sores in the mouth, vagina or anus) occur. This stage typically starts with the development of a rash on one or more areas of the body. The characteristic rash is rough red or reddish brown spots on the palms of the hands and the soles of the feet. However, rashes with a different appearance may occur on other parts of the body, sometimes resembling rashes caused by other diseases. Sometimes the rashes are visibly rare. Large raised grey or white lesions, known as condylomata lata, may develop in warm moist areas such as the mouth, underarm or groin region.

In addition, there may be fever, swollen lymph glands, sore throat, patchy hair loss, headaches, weight loss, muscle aches and fatigue. The symptoms will resolve with or without treatment, but if not treated the infection will progress to the latent and possibly late stages of disease.

#### Late (hidden) and late stages

Without treatment, syphilis infection can persist without showing any signs or symptoms. **Early latent syphilis** is latent syphilis where infection occurred within the past 12 months. **Late latent syphilis** is latent syphilis where infection occurred more than 1 year ago.

**Late stages (tertiary syphilis)** develop in around 15% of people who have not been treated, and can appear 10–20 years after infection was first acquired. In the late stages of syphilis, the disease may damage the internal organs, including the brain, nerves, eyes, heart, blood vessels, liver, bones and joints. Symptoms of the late stages of syphilis include difficulty coordinating muscle movements, paralysis, numbness, gradual blindness and dementia.

When it invades the nervous system, at any stage of infection, syphilis causes headache, altered behaviour, and movement disorders that occur in Parkinson’s and Huntington’s disease.

HIV infection modifies the symptoms and signs described above, including hypopigmented skin rashes. There is also a greater likelihood of neurological involvement.

Where disease is prevalent, most cases are asymptomatic. At least 50% of women with acute syphilis have adverse pregnancy outcomes. The more recent the maternal infection, the more likely it is that the fetus and infant will be infected.

Congenital syphilis is divided into early (becoming apparent in the first 2 years of life) and late (becoming apparent after the first 2 years of life) types. At birth the following can be present: low birth weight, hepatosplenomegaly, pallor, jaundice and purpura, blisters or peeling of palms and soles. There can be difficulties in feeding and rhinorrhea. If not treated immediately, the newborn baby may remain asymptomatic but more commonly develops serious problems within a few weeks affecting many body systems. Untreated babies may become developmentally delayed, have seizures or die.

Late congenital syphilis can present with the following: blunted upper incisor teeth known as Hutchinson’s teeth,
inflammation of the cornea known as interstitial keratitis, deafness from auditory nerve damage, frontal bone bossing, a saddle nose (collapse of the bony part of nose), defects of the hard palate, swollen knees, saber like shins, short maxillae and protruding mandible. A frequently-found group of symptoms is Hutchinson’s triad, which consists of Hutchinson’s teeth (notched incisors), keratitis and deafness and occurs in 63% of cases.

Treatment (with penicillin) before the development of these late symptoms is essential.

Congenital syphilis may occur if the expectant mother has syphilis, but the risk is minimal if she has been given penicillin during pregnancy. Congenital syphilis does not cause congenital malformations as infection of the fetus in early pregnancy is lethal.

Treatment with penicillin is extremely effective (98% success rate) in preventing mother-to-child transmission.

**Diagnosis**

There are two types of blood tests available, namely non-treponemal tests and treponemal tests.

**Non-treponemal tests** (e.g. VDRL and RPR) are simple, inexpensive, and are often used for screening. Ideally, women with a reactive non-treponemal test should receive a treponemal test to confirm a syphilis diagnosis.

Their sensitivity increases from primary to secondary syphilis, and their specificity is high in the absence of another chronic condition.

The on-site RPR card test is quick and simple to use, allowing immediate treatment to be given. A simple strip of paper impregnated with treponemal antigen is used to test a finger-prick sample of blood.

**Treponemal tests** such as the *Treponema pallidum* haemagglutination assay (TPHA) and Rapid Syphilis Test have higher sensitivity and specificity and measure antibodies that are specific for syphilis. Treponemal antibodies appear earlier than non-treponemal antibodies and usually remain detectable for life, even after successful treatment, and therefore do not correlate with disease activity.

All pregnant women should be screened for syphilis at their first antenatal visit with an on-site RPR or other rapid test and to prevent congenital infection, preferably before 16 weeks’ gestation and again in the third trimester.

All women who were not screened or tested during pregnancy should be screened at or immediately after delivery.

All infants born to mothers who have positive non-treponemal and treponemal test results should be evaluated for congenital syphilis.

Advise women who test positive that their partner(s) must also be investigated and treated if positive.

Test all women with a history of adverse pregnancy outcome (e.g. abortion, stillbirth, syphilitic infant) for syphilis.

Screen all women with syphilis for other sexually transmitted and HIV infections.

**Treatment of pregnant women with syphilis**

**Early syphilis (primary, secondary or latent syphilis of not more than 2 years’ duration)**

Give benzathine benzylpenicillin, 2.4 million IU intramuscularly (check that it is not injected into a vein), in a single session. Because of the high volume, this is usually given as two injections at separate sites.

Alternatively, give procaine benzylpenicillin 1.2 million IU intramuscularly (check that it is not injected into a vein) daily for 10 consecutive days.

If the patient is allergic to penicillin, give ceftriaxone 500 mg IM/IV daily for 10 days. Erythromycin does not cross the placenta to treat the fetus.

**Late latent syphilis (infection of more than 2 years’ duration)**

Give benzathine benzylpenicillin, 2.4 million IU intramuscularly (check that it is not injected into a vein), once weekly for 3 consecutive weeks.

Alternatively, give procaine benzylpenicillin, 1.2 million IU intramuscularly (check that it is not injected into a vein), once daily for 20 consecutive days.

If the patient is allergic to penicillin, give ceftriaxone 500 mg IM/IV daily for 14 days or (although this is less effective) erythromycin, 500 mg orally, four times a day for 30 days.

**Treatment of congenital syphilis**

All asymptomatic newborn infants born to seropositive mothers should be treated with a single IM dose of benzathine benzylpenicillin, 50 000 IU/kg, whether or not their mothers were treated during pregnancy. Routine CSF examination is not required.

Newborn infants with any signs of congenital syphilis should receive:

- aqueous benzylpenicillin, 100 000–150 000 IU/kg/day administered as 50 000 IU/kg/dose IV every 12 hours, during the first 7 days of life, and every 8 hours thereafter for a total of 10 days or
- procaine benzylpenicillin, 50 000 IU/kg by IM injection, as a single daily dose for 10 days (ensure that it is not injected into a vein).

Early congenital syphilis generally responds well to penicillin. Recovery may be slow in seriously ill children with extensive skin, mucous membrane, bone or visceral involvement.

For older infants up to 2 years of age with confirmed congenital syphilis the treatment is the same as above.

If the patient is allergic to penicillin (this is unusual), give ceftriaxone 80 mg/kg IM/IV once daily for 10 days or give erythromycin, 7.5–12.5 mg/kg orally, four times a day for 14 days but erythromycin is less effective.

For infants older than 2 years, give aqueous benzylpenicillin, 200 000–300 000 IU/kg/day by IM/IV administered as 50 000 IU/kg/dose IV every 4–6 hours for 10–14 days.

An alternative regimen for penicillin-allergic patients after the first month of life is to give erythromycin, 7.5–12.5 mg/kg orally, four times a day for 30 days.

**Jarisch–Herxheimer reaction**

After starting penicillin treatment in some patients, the death of the bacteria results in the release of mediators that produce the adverse symptoms and signs such as myalgias, fever, headache and tachycardia, sometimes with exacerbation of whatever current syphilitic lesions are manifested (e.g. rash, chancre).

This reaction develops within several hours after
beginning antibiotic treatment, and usually clears within 24 hours after its onset. It is very rare in newborn infants.

Management consists of symptomatic treatment (e.g. antipyretics, analgesics) and observation. In pregnancy, treatment may induce early labour or cause fetal distress. Patients should be informed of the possibility of this reaction before undergoing antibiotic therapy. However, this risk should not preclude or delay therapy for syphilis. Women are advised to seek obstetric care after treatment if they notice any fever, uterine contractions, or a decrease in fetal movement.

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2.8.1 Varicella zoster (chickenpox) in pregnancy

**Introduction**

Pregnant women and newborn infants are at risk of severe disease from varicella, involving serious effects on organs such as the lungs.

Varicella is transmitted from respiratory aerosols and skin lesions in chickenpox itself, and from the skin lesions but not aerosols in shingles (which is not infectious until the skin lesions appear).

In chickenpox, patients are infectious for 48 hours prior to emergence of the rash and until all of the skin lesions are crusted over.

The incubation period is 10–21 days.

Non-immune patients are those without a history of chickenpox or shingles or a completed vaccination profile. Immune status can be checked with blood varicella IgG measurement (if available).

**Clinical features in pregnancy**

*Congenital varicella syndrome (CVS)*

In the first or early second trimester infection may result in stillbirth, or the neonate may be born with a group of physical abnormalities known as congenital varicella syndrome (CVS). This is rare, occurring in 1–2.8% of women infected with chickenpox in the first 20 weeks of gestation (the period of maximum risk is between 12 and 20 weeks’ gestation). There may be dermatical scarring, limb hypoplasia, ocular abnormalities, low birth weight and early death. Survivors may have long-term developmental problems. An infant with CVS has a 30% risk of mortality in the first few months of life, and a 15% risk of developing herpes zoster between 2 months and 3 years of life.

*Varicella pneumonia*

Pregnant women with chickenpox may be more likely than non-pregnant women to develop severe pneumonitis. The risk is greatest in the third trimester, especially if lung disease is already present, or if the patient is a smoker or is immunocompromised (e.g. due to HIV infection).

Symptoms start as a non-productive cough, which can rapidly progress to respiratory failure within 36–48 hours. The cough becomes increasingly productive, with tachypnoea, dyspnoea, cyanosis and chest pain.

*Perinatal infection*

If a neonate is exposed (mother has a rash) around the time of birth (from 5 days before to 2 days after delivery), there is a 17–30% risk of dangerous perinatal infection. This is characterised by skin lesions, disseminated intravascular coagulation, pneumonitis and hepatitis, and it has a mortality of up to 30%.

**Management**

*Maternal contact with varicella during pregnancy*

If the patient is immune (see above for definition), no treatment or isolation is required.

If she is non-immune and an IgG test is not available and affordable, then if she has had a significant contact with chicken pox or shingles then give varicella zoster immunoglobulin (VZIG) (see below for details) within 4 days of contact if possible (maximum of 10 days after contact). Avoid contact with other pregnant women. The patient should be counselled regarding the signs of infection so that she can be treated early if it occurs.

Significant exposure to chicken pox occurs after very limited contact with an infected person (any face to face contact and as little as 15 minutes in the same room as an infectious patient). The risk of contracting chicken pox from exposure to shingles is very low if the infection is not in an exposed area.

*Chickenpox during pregnancy*

If this is mild, give oral aciclovir (see below for dose regimen) for 7 days, starting within 24 hours of the appearance of vesicles, and avoid contact with other pregnant women. In mild cases, aciclovir leads to little improvement. It is most important in women at risk of severe disease (immuno-compromised, HIV infected, history of respiratory disease or smoking).

If it is severe, give IV aciclovir for 7 days. High-dependency care should be provided if available, as appropriate.

*Prevention of neonatal chickenpox if the mother is infected from 7 days before to 7 days after birth*

Give VZIG to the neonate as soon as possible after delivery. Isolate the mother and infant.

In addition, give IV aciclovir to the neonate if the onset of maternal symptoms was between 4 days before, and 2 days after the birth.

*Infant in contact with chickenpox other than from mother, or from mother who develops chickenpox more than 7 days after the birth*

If the mother is immune and the infant is full term at birth, no prophylaxis is needed. Mild illness may occur.
If the mother is not immune and the infant is less than 4 weeks of age, and full term at birth, give varicella zoster immunoglobulin (VZIG) (if available).

If the infant is preterm, and regardless of maternal immunity, give VZIG.

Regardless of whether VZIG is given, monitor the baby for signs of infection to enable early treatment should infection occur.

Shingles is very rare in infants and, if present, suspect HIV infection.

Doses of VZIG and aciclovir

**In pregnancy**

Aciclovir is of no benefit if commenced more than 24 hours after the appearance of chickenpox vesicles.

**Oral route:** 800 mg five times daily for 7 days (mildly ill cases only).

**IV route:** 10 mg/kg/dose every 8 hours for 7 days.

Side effects include nausea, vomiting, diarrhoea, headache and nephrotoxicity. Reduce the dose or dosage interval in patients with impaired renal function.

**Varicella zoster immunoglobulin (VZIG):** 1 gram IM.

Anaphylaxis is rare, but ensure that adrenaline is available.

**In the neonate**

Aciclovir 10–20 mg/kg IV every 8 hours for at least 7 days.

Side effects are as described above.

Varicella zoster immunoglobulin (VZIG): 250 mg by deep IM injection.

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**2.9 Mental health problems associated with pregnancy and the postnatal period**

**BOX 2.9.1 Minimum standards**

- Screening tools for depression, such as the Edinburgh Postnatal Depression Scale (EPDS).
- Selective serotonin reuptake inhibitor (SSRI) antidepressants.
- Ideally, an inpatient hospital facility for mothers and babies when the mother has puerperal psychosis.
- Antipsychotic drugs.

**Introduction**

Childbirth poses a risk to a woman’s mental health. This applies to all women and girls who become pregnant in all countries, irrespective of their social and cultural background. However, the background will influence how a mother presents and how quickly she receives appropriate care.

Much of the research about pregnancy-related mental illness and its effects on the new baby has been done in high-income countries where it has been possible to develop specialised services. However, there is evidence that mental health problems in mothers are as common in low- and middle-income countries. A number of risk factors that have been suggested as underlying maternal depression are listed in Box 2.9.2.

Perinatal psychiatric services have developed in many high-income countries, and involve liaison between psychiatric and obstetric services. The specialty covers women with pre-existing mental health problems who want to have a family, as well as mental illness that is first diagnosed antenatally and postnatally. Maintaining the mental health of a pregnant woman benefits the family, and in some cases can prevent problems from developing postnatally. The onset of depression and anxiety in pregnancy or postnatally can be especially worrying for a woman and her family because it is contrary to their expectations that this will be a happy time. The woman may not want to admit how she is feeling, being ashamed both of her inability to feel joy about her newborn baby and of her perceived inability to cope, and fearing that she will be judged harshly for these feelings. This is especially important in countries and cultures where women and girls are not valued and their main role is perceived to be the production of healthy babies.

Mild antenatal and postnatal depression can be managed with minimal resources and does not require medication. Recognition of the condition and practical help from family and friends can be enough to prevent depression affecting the care of the baby. Reassurance from...