



Royal College of Obstetricians and Gynaecologists

Setting standards to improve women's health

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Management of HIV in Pregnancy



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This is the second edition of this guideline, which was originally published in 2004 under the same title.

This guidance was developed primarily for UK clinical practice. Certain recommendations will need to be adapted for specific settings; we encourage the use of the RCOG Clinical Governance Advice No. 1d: *Consensus Methods for Adaptation of RCOG Guidelines*.

EXECUTIVE SUMMARY: Management of HIV in pregnancy

Detailed guidance about the management of HIV in pregnancy has been published by the British HIV Association and can be accessed online at www.bhiva.org/PregnantWomen2008.aspx.

1. Antenatal HIV screening

- All pregnant women are recommended screening for HIV infection, syphilis, hepatitis B and rubella in every pregnancy at their booking antenatal visit, as part of the Infectious Diseases in Pregnancy Screening (IDiPS) Programme.
- If a woman declines an HIV test, this should be documented in the maternity notes, her reasons should be sensitively explored and screening offered again at around 28 weeks.
- If a woman tests HIV negative at booking but is judged by her clinician as being at continued high risk of acquiring HIV, offering a repeat HIV test should be considered.
- Midwives and doctors reviewing women during antenatal care should ensure that the HIV result is clearly documented.
- Fourth-generation laboratory assays are recommended as the first-line HIV test for antenatal screening. Where a woman books for antenatal care at 26 weeks of gestation or later, the test should be requested urgently and the result issued within 24 hours.
- Rapid HIV tests use rapid-test devices to deliver results within 20 minutes of the sample being taken. These tests are recommended for all women with unknown HIV status in labour and a reactive result should be acted on immediately.
- Further guidance about antenatal HIV testing can be found at the IDiPS website: <http://infectiousdiseases.screening.nhs.uk/>.

2. Professional approach to the antenatal care of women who are HIV positive

- Management should be by a multidisciplinary team, including an HIV physician, obstetrician, specialist midwife, health advisor and paediatrician.
- All women who are newly diagnosed HIV positive should have an early assessment of their social circumstances.
- Women should be reassured that their confidentiality will be maintained.
- Women should be encouraged to disclose their HIV status to their partner and given appropriate support.
- Care should be taken to avoid inadvertent disclosure to a woman's partner or family members, as they may be unaware of her HIV diagnosis, even though they may attend antenatal visits and be present at the delivery.
- Advice should be given about safer-sex practices and the use of condoms, to prevent transmission of HIV and other sexually transmitted infections to an uninfected partner.
- It is recommended that women with existing children of unknown HIV status should have them tested for HIV.
- In rare cases where women refuse interventions to reduce the risk of mother-to-child transmission, despite supportive guidance from the multidisciplinary team, a pre-birth planning meeting should be held with social services to discuss safeguarding issues.
- Each maternity unit in the UK and Ireland should have a named respondent who is responsible for notifying all HIV positive pregnancies to the National Study of HIV in Pregnancy and Childhood (details at www.nshpc.ucl.ac.uk).
- The pregnancies of all women taking anti-retroviral therapy should also be reported to the Antiretroviral Pregnancy Registry (details at www.apregistry.com).

3. Interventions to prevent disease progression in the mother

- Women who require HIV treatment for their own health should take highly active anti-retroviral therapy (HAART) and continue treatment postpartum. They may also require prophylaxis against *Pneumocystis carinii* pneumonia (PCP), depending on their CD4 lymphocyte count.
- Women already taking HAART and/or PCP prophylaxis before pregnancy should not discontinue their medication.

4. Interventions to prevent mother to child transmission of HIV

- Avoidance of breastfeeding, anti-retroviral therapy and appropriate management of delivery has reduced mother-to-child transmission rates from 25–30% to less than 1%.
- All women in resource-rich countries should be advised not to breastfeed.
- All women should be advised to take anti-retroviral therapy.
 - For women who require HIV treatment for their own health, their prescribed HAART regimen should be continued throughout pregnancy and postpartum.
 - For women who do not require HIV treatment for their own health, HAART should be initiated between 20 and 28 weeks and discontinued at delivery.
 - For women who do not require HIV treatment for their own health, have a plasma viral load of less than 10000 copies/ml and are prepared to be delivered by elective caesarean section, an acceptable alternative is zidovudine (ZDV) monotherapy initiated between 20 and 28 weeks, given orally, 250 mg twice daily, and intravenously at delivery.
- A decision about mode of delivery should be made by 36 weeks of gestation.
 - Delivery by elective caesarean section at 38 weeks to prevent labour and/or ruptured membranes is recommended for:
 - women taking HAART who have a plasma viral load greater than 50 copies/ml
 - women taking ZDV monotherapy as an alternative to HAART
 - women with HIV and hepatitis C virus coinfection.
 - A planned vaginal delivery can be offered to women taking HAART who have a plasma viral load of less than 50 copies/ml.
 - Delivery by elective caesarean section for obstetric indications or maternal request should be delayed until 39+ weeks in women whose plasma viral load is less than 50 copies/ml, to reduce the risk of transient tachypnoea of the newborn.

5. Antenatal care of pregnant women who are HIV positive

- Pregnant women who are HIV positive are recommended to have screening for syphilis, hepatitis B and rubella at their booking antenatal visit, in line with the general population.
- Pregnant women who are HIV positive should have additional blood tests for hepatitis C, varicella zoster, measles and toxoplasma.
- Women taking HAART at the time of booking should be screened for gestational diabetes.
- Hepatitis B and pneumococcal vaccination is recommended for all individuals who are HIV positive and can be safely administered in pregnancy. Influenza vaccination can also be safely administered in pregnancy and the decision to immunise depends on the time of year. Varicella zoster and measles, mumps and rubella vaccines are contraindicated in pregnancy.
- Women should be screened for genital infections at booking and again at 28 weeks. Any infection detected should be treated according to national guidelines, even if asymptomatic.
- Screening for aneuploidy should be offered to all women in accordance with national guidelines for the general population.
- Women who are HIV positive who are considering invasive diagnostic testing should be counselled in a fetal medicine unit and the advice of the HIV physicians sought about reducing the risk of HIV transmission.
- Dating and anomaly scans should be offered to all women in accordance with national guidelines for the general population.
- Monitoring of plasma viral load and drug toxicities should be undertaken as directed by the HIV physicians.
- A plan of care for anti-retroviral therapy and mode of delivery should be made at 36 weeks following detailed discussion with the mother. Only women with plasma viral loads of less than 50 copies/ml should be offered a planned vaginal delivery.

- This plan should be reviewed when the woman presents in labour, after confirming that any recently performed viral load results are less than 50 copies/ml. In the absence of a documented mode of delivery plan or, in the event of uncertainty about viral load results, urgent advice should be sought from the HIV physicians.

6. Management of antenatal complications

- For any woman who is HIV positive who becomes acutely unwell in pregnancy, close liaison between the obstetricians and HIV physicians is mandatory to avoid diagnostic error.
- HIV-related complications should also be considered as a cause of acute illness in pregnant women whose HIV status is unknown, particularly those who are not booked for antenatal care. In these circumstances, a rapid HIV test should be considered.

7. Management of preterm delivery and preterm prelabour rupture of membranes

- All women with threatened or established preterm labour and those with preterm prelabour rupture of membranes (PPROM) should have a genital infection screen performed and any infections, even if asymptomatic should be treated. The usual indications for steroids apply.
- Women should be counselled about the increased risk of preterm delivery associated with HAART.
- For women presenting with threatened preterm labour, multidisciplinary team advice (HIV physicians and paediatricians) should be sought so that, if preterm labour supervenes, there is a detailed plan of care.
- For women in preterm labour, urgent multidisciplinary team advice should be sought about the choice of anti-retroviral therapy. Infants born below 32 weeks of gestation may be unable to tolerate oral medication, so administering anti-retroviral therapy to the mother just before and during delivery will provide prophylaxis to the neonate.
- Where PPRM occurs after 34 weeks of gestation, delivery should be expedited. Augmentation may be considered if the viral load is less than 50 copies/ml and there are no obstetric contraindications. Consideration should be given to starting broad-spectrum intravenous antibiotics.
- Where PPRM occurs before 34 weeks of gestation, oral erythromycin should be started in accordance with national guidelines for the general population. Consideration should be given to starting broad-spectrum intravenous antibiotics. Evidence of chorioamnionitis and fetal distress are indications for prompt delivery. In other cases, the decision as to whether to expedite delivery should be made after multidisciplinary team consultation. Expert advice from outside the host institution may be helpful.

8. Management of delivery

- A plan of care for anti-retroviral therapy and mode of delivery should be made at 36 weeks, following detailed discussion with the mother.
- A maternal sample for plasma viral load and CD4 count should be taken at delivery.
- Women taking HAART should have their medications prescribed and administered before delivery and, if indicated, after delivery.
- Elective caesarean section:
 - If intravenous ZDV is indicated, the infusion should be started 4 hours before beginning the caesarean section and should continue until the umbilical cord has been clamped.
 - The surgical field should be kept as haemostatic as possible and care should be taken to avoid rupturing the membranes until the head is delivered through the surgical incision.
 - Peripartum antibiotics should be administered in accordance with national guidelines for the general population.
- Planned vaginal delivery:
 - Planned vaginal delivery should only be offered to women taking HAART who have a viral load of less than 50 copies/ml.
 - When a woman presents in labour, her plan of care for delivery should be reviewed and recent viral load results should be confirmed as less than 50 copies/ml.
 - HAART should be prescribed and administered throughout labour.
 - Invasive procedures such as fetal blood sampling and fetal scalp electrodes are contraindicated.
 - If labour progress is normal, amniotomy should be avoided unless delivery is imminent.
 - Amniotomy and possible use of oxytocin may be considered for augmentation of labour.
 - If instrumental delivery is indicated, low-cavity forceps are preferable to ventouse.

- Prelabour rupture of membranes at term:
 - In the case of prelabour ruptured membranes at term, delivery should be expedited. If the viral load is less than 50 copies/ml and there are no obstetric contraindications, augmentation may be considered.
 - Broad-spectrum intravenous antibiotics should be administered if there is evidence of genital infection or chorioamnionitis.
- Prolonged pregnancy:
 - For women on HAART with plasma viral load of less than 50 copies/ml, the decision regarding induction of labour for prolonged pregnancy should be individualised. There is no contraindication to membrane sweep or to use of prostaglandins.
- Vaginal birth after caesarean section:
 - A trial of scar may be considered for women on HAART whose plasma viral load is less than 50 copies/ml.
- HIV diagnosed in labour:
 - For women diagnosed HIV positive during labour, the paediatricians should be informed and urgent advice should be sought from the HIV physicians regarding optimum HAART.
 - Delivery should be by caesarean section and, where possible, this should be timed with respect to anti-retroviral administration.
 - Detailed guidance is available at: <http://www.bhiva.org/PregnantWomen2008.aspx>

9. Postpartum management of women who are HIV positive

- Women should be given supportive advice about formula feeding.
- An immediate dose of oral cabergoline should be given to suppress lactation.
- Women taking HAART should have their medication prescribed and administered.
- Guidance about contraception should be given in the immediate postpartum period.
- MMR and varicella zoster immunisation may be indicated, according to the CD4 lymphocyte count.

10. Management of the neonate

- All neonates should be treated with anti-retroviral therapy within 4 hours of birth.
- Most neonates should be treated with ZDV monotherapy but those at high risk of HIV infection should be treated with HAART.
- Prophylaxis against PCP is recommended only for neonates at high risk of HIV infection.
- Infants should be tested at 1 day, 6 weeks and 12 weeks of age. If all these tests are negative and the baby is not being breastfed, the parents can be informed that the child is not HIV-infected. A confirmatory HIV antibody test is performed at 18 months of age.
- Neonates born to women who are HIV infected are reported to the National Study of HIV in Pregnancy and Childhood <http://www.nshpc.ucl.ac.uk/>.

11. Prepregnancy management

- Couples who are serodiscordant choosing to have intercourse should be advised to use condoms.
- Couples who are serodiscordant where the female partner is HIV negative should be advised that assisted conception with either donor insemination or sperm washing is significantly safer than timed unprotected intercourse.
- Couples should be advised to delay conception until plasma viraemia is suppressed, prophylaxis against PCP is no longer required and any opportunistic infections have been treated.
- All women who are HIV positive are recommended to have annual cervical cytology.

1. Background and introduction

1.1 Aetiology, natural history and treatment

HIV is a complex chronic medical condition which, if untreated, is associated with high morbidity and mortality. Transmission is through sexual intercourse, injecting drug use, transfusion of blood or blood products and from mother to child during pregnancy and breastfeeding. HIV is a retrovirus containing reverse transcriptase. This enzyme allows the virus to transcribe its RNA genome into DNA, which then integrates into host cell DNA. HIV preferentially targets lymphocytes expressing CD4 molecules (CD4 lymphocytes), causing progressive immunosuppression. When CD4 lymphocytes fall below a critical level, infected individuals become more susceptible to opportunistic infections and malignancies. Treatment with a combination of three or more anti-retroviral drugs, known as highly active anti-retroviral therapy (HAART), has resulted in a dramatic decline in morbidity and an increase in life expectancy. However, these benefits are restricted to countries which can afford these drug regimens and have the infrastructure to deliver them safely and effectively. The three classes of anti-retroviral drug most commonly used in pregnancy are nucleoside reverse transcriptase inhibitors, non-nucleoside reverse transcriptase inhibitors and protease inhibitors.

1.2 UK epidemiology of HIV in pregnancy

The purpose of screening for HIV in pregnancy is to enable those diagnosed with HIV to take up interventions that reduce the risk of mother-to-child transmission and improve their own health. In 2003, the Department of Health Standards set an uptake target of 90% for HIV screening, which has been exceeded every year since 2005. Since the introduction of routine antenatal screening for HIV, there has been a dramatic reduction in HIV infection among children whose mothers were diagnosed in pregnancy, despite a marked increase in the number of women with HIV infection.¹ The prevalence of HIV infection in women giving birth in England and Scotland in 2008 was 1/486 (0.2%). This prevalence has been stable since 2004 and has remained highest in London (3.7/1000). The estimated proportion of exposed infants (born to both diagnosed and undiagnosed HIV-infected women) who became infected has decreased from 12% in 1999 to approximately 2% in 2007.²

1.3 Risks of mother-to-child transmission in untreated women

The risk of mother-to-child transmission of HIV is between 15% and 20% in non-breastfeeding women in Europe and between 25% and 40% in breastfeeding African populations.³ In the absence of breastfeeding, it is estimated that over 80% of transmissions occur perinatally, around the time of labour and delivery.⁴ In untreated women, the risk of transmission is determined by maternal health, infant feeding and obstetric factors. Overall, there is a close linear correlation between maternal viral load and the risk of transmission but rare transmissions have been reported even when plasma viraemia was less than 50 copies/ml at the time of delivery.^{5,6} The only obstetric factors that have consistently been associated with transmission are mode of delivery, duration of membrane rupture and delivery before 32 weeks of gestation. Sexually transmitted infections and chorioamnionitis have also been associated with perinatal HIV transmission in some studies. Breastfeeding doubles the risk of mother-to-child transmission from around 14% to 28%.

1.4 Risk of mother-to-child transmission in treated women

Transmission rates of less than 2% have been reported in studies from resource-rich countries in recent years, owing to effective HAART (leading to low or undetectable plasma viral loads), appropriate management of delivery and avoidance of breastfeeding. For non-breastfeeding women taking HAART, where plasma viral load was less than 50 copies/ml at delivery, mother-to-child transmission rates in two large European cohorts (UK/Irish and French) were less than 1%, irrespective of mode of delivery.^{5,6} In the UK/Irish cohort, among the 2117 infants born to women who were HIV positive and taking HAART who had a plasma viral load of less than 50 copies/ml at delivery, three babies were infected (0.1%).⁶ In the French cohort, 1338 women whom were HIV positive delivered at term with a plasma viral load at delivery of less than 50 copies/ml and five babies were infected (0.4%).⁵ For both cohorts, the principle risk factors for transmission were high

plasma viraemia at delivery, short duration of HAART and delivery at less than 32 weeks of gestation. In contrast to women who are untreated, the few transmissions that occur in women receiving HAART are likely to be as a result of *in utero* transmission occurring before treatment, rather than perinatal transmission.

1.5 *Inter-relationship between HIV, pregnancy and HAART*

In resource-rich countries, limited data from cohort studies suggest that pregnancy does not adversely affect HIV progression or survival, although long-term data are lacking. The decline in CD4 lymphocyte count during pregnancy usually resolves in the postpartum period and is attributed to haemodilution.⁷ Some studies have suggested women using HAART in pregnancy are at increased risk of obstetric complications, including gestational diabetes^{8,9,10} and pre-eclampsia.^{11,12} Further studies are required to confirm these associations. European studies have consistently demonstrated an association between HAART and preterm delivery but the mechanism by which this occurs is unclear.^{13,43}

1.6 *Viral load assays*

With increasing sensitivity of HIV RNA polymerase chain reaction (PCR) assays, the nature of an 'undetectable viral load' has changed over time. Many of the older studies of HIV transmission used assays with limits of detection of 400 copies/ml or higher. Current viral load assays can detect to between 10 and 40 copies/ml. However, 50 copies/ml is the cut-off point used in studies of mother-to-child transmission published in recent years. In the context of assessing transmission risk, the utility of detecting HIV at viral loads at levels lower than 50 copies/ml is unknown.¹⁵ To avoid confusion, the term 'undetectable viral load' is avoided in this guideline where possible.

1.7 *Further information*

Detailed guidance on HIV and pregnancy is published by the British HIV Association (BHIVA) and can be accessed online at www.bhiva.org/PregnantWomen2008.aspx.¹⁵ Further guidance about antenatal screening for HIV can be obtained from the Infectious Diseases in Pregnancy Screening (IDiPS) Programme. This is a collaboration between the Health Protection Agency, the UK National Screening Committee and the Department of Health (DH). The guidance can be accessed online at <http://infectiousdiseases.screening.nhs.uk>.

1.8 *Population and setting*

This guideline relates to the management of HIV in the UK and is likely to be applicable to other resource-rich countries. A comprehensive international perspective is provided by the World Health Organization (www.who.int/rhl/hiv_aids/en/).

In this guideline, we have used the term 'HIV' to refer to HIV-1. Guidance regarding HIV-2, which is of low prevalence in the UK and is less readily transmitted than HIV-1, can be found in the BHIVA guideline on the management of HIV in pregnancy.¹⁵

2. Identification and assessment of evidence

The Cochrane Library and Cochrane Register of Controlled Trials were searched for relevant randomised controlled trials, systematic reviews and meta-analyses. A search of Medline and PubMed electronic database from 1983 to 2009 was also carried out. The databases were searched using the relevant MeSH terms, including all subheadings, and this was combined with a keyword search using the terms 'HIV', 'pregnancy', 'mother-to-child transmission' and 'vertical transmission'. Reference lists of the articles identified were hand searched for additional articles. Articles relating specifically to management of HIV in pregnancy in resource-constrained settings were excluded (see above). Where possible, recommendations are based on and explicitly linked to the evidence that supports them. Areas lacking evidence are highlighted and annotated as 'good practice points'.

3. Antenatal HIV screening

3.1 What can be done to ensure continued high uptake of HIV screening?

All pregnant women are recommended to have screening for HIV infection in every pregnancy at their booking antenatal visit. This enables those diagnosed with HIV to take up interventions that can prevent mother-to-child transmission and significantly improve their own health.

A

All pregnant women who are HIV positive should be referred promptly for assessment and for their pregnancies to be managed within a multidisciplinary team.

D

If a woman declines screening, her reasons should be explored sensitively to ensure that she has received accurate information on which to base her decision. Involvement of a senior health professional should be considered. The decision to decline screening should be documented in the maternity notes and screening offered again at around 28 weeks.



All women booking for antenatal care should have one blood sample tested for HIV, syphilis, rubella and hepatitis B. All doctors and midwives should be competent to obtain consent for these tests and should request the tests according to local protocols.¹⁶

Evidence level 4

Those with HIV infection commonly remain asymptomatic for many years. HIV screening in pregnancy enables those diagnosed with HIV to take up interventions that can prevent mother-to-child transmission.^{5,6} Moreover, many will benefit from treatment that significantly reduces their risk of disease progression and death.¹⁷

Evidence level 2++

The current universal approach to screening has achieved a high uptake rate of 95%. Consequently, over 90% of pregnant women who are HIV infected have their infection diagnosed by the time of birth.²

Efforts to further improve these high screening uptake rates must be balanced by the risks of perceived coercion: one of the factors leading to the success of the HIV screening programme has been the element of choice. Recommendations for women who decline antenatal HIV screening at booking are currently being developed as part of Department of Health Standards for the IDiPS Programme and will be accessible online (<http://infectiousdiseases.screening.nhs.uk>). Discussion should include advice about safe sex and information on the availability of testing on request at any point in pregnancy. All women who declined screening at booking should be offered screening again at around 28 weeks. Involvement of a senior health professional should be considered, which may be an obstetrician, screening coordinator, genitourinary medicine physician or sexual health adviser.

Evidence level 4

3.2 What type of HIV test should be used?

Fourth-generation laboratory assays are recommended as the first-line HIV test for antenatal screening.

D

Where a woman has her HIV screening test at 26 weeks of gestation or later, an urgent request should be made and the result issued by the laboratory with 24 hours.

D

Rapid HIV tests are recommended for women with unknown HIV status who present in labour and a reactive result should be acted on immediately.

D

A handbook for laboratories is being developed by the IDiPS Programme and will be accessible online (<http://infectiousdiseases.screening.nhs.uk>). This should be referred to in the development of local laboratory protocols.

Evidence level 4

The time between acquiring HIV infection and testing HIV antibody positive is known as the window period, which is usually up to 3 months in duration (rarely up to 6 months). During this

period of seroconversion, an individual will test negative for HIV antibodies. The recommended first-line HIV tests for antenatal screening are fourth-generation assays that test for both HIV antibody and p24 antigen simultaneously. This type of assay reduces the diagnostic window to 1 month, as p24 antigen is detectable during seroconversion. Assays must have a high sensitivity (greater than 99.9%) and specificity (greater than 99.5%) and be able to detect all the major subtypes of HIV. A reactive result on initial testing is always confirmed as positive by testing the same sample with two further independent assays to confirm that the reactivity is specific for HIV. A confirmatory HIV test on a second sample is then made.¹⁸

For women having an HIV test at or beyond 26 weeks of gestation (in the event of late booking or delay in consenting to HIV screening), an urgent HIV test using a fourth-generation assay should be requested so that, in the event of a positive result, there is sufficient time for appropriate counselling, multidisciplinary team involvement and initiation of anti-retroviral therapy.¹⁵

Evidence level 4

Rapid HIV tests deliver results within 20 minutes of the specimen (finger-prick or mouth swab) being taken. Most of the rapid-test devices currently in use test for antibody only (not p24 antigen), so these tests are likely to test negative during seroconversion. Outside seroconversion, they are of equivalent sensitivity but lower specificity compared with screening assays.¹⁹ They are recommended in clinical situations where a rapid HIV diagnosis will affect the immediate management of the patient, such as in labour.¹⁵ Rapid HIV tests are often performed by hospital laboratories. However, they can be undertaken by appropriately trained delivery suite staff (point-of-care testing), provided that they are overseen by the local laboratory and a robust quality assurance programme is in place. All reactive rapid tests must be confirmed as positive by the laboratory.

3.3 How can seroconversions in pregnancy be prevented and identified?

All women testing HIV negative at booking should have access to information about safe sex and high-risk scenarios for HIV transmission. Repeat testing should be available at any time during pregnancy. Women judged to be at continued high risk of HIV acquisition may also be offered a repeat HIV test.

D

In an audit of perinatal HIV transmission in England between 2002 and 2005, at least 20% of the 54 infants born to undiagnosed women had a negative antenatal HIV test. The timing of maternal seroconversion in these cases is unknown. Although some will have occurred postnatally, others will have seroconverted during pregnancy.²⁰

Evidence level 2++

The significance of this with respect to subsequent paediatric HIV infection was highlighted in a retrospective case review of infants diagnosed with HIV in a tertiary referral centre in London over a 5-year period; five of these infants were born to mothers who had a negative antenatal HIV test. In all five cases, the HIV diagnosis of mother and child was made when the infants presented with severe infection (four of five with AIDS).²¹

Evidence level 3

For women testing HIV negative at booking but judged by their midwife or obstetrician to be at continued high risk of acquiring HIV, repeat testing should be considered on a case-by-case basis. Such cases may include individuals having unprotected sex with an HIV-positive partner or injecting drug users who share needles.¹⁵

Evidence level 4

3.4 How should HIV test results be recorded and communicated?

Midwives and doctors reviewing women during antenatal care should ensure that the HIV result is clearly documented.

D

Dates and details of test discussions, who was involved, decisions, samples taken and when results were available and were given should be recorded. Local protocols covering test turnaround times, receipt of results and referral of women with positive test results should be developed. These

Evidence level 4

should be based on Department of Health Standards currently being developed as part of the IDiPS Programme (<http://infectiousdiseases.screening.nhs.uk>). There should be a clear line of designated responsibility for communicating positive results and following up late results. Delivery suite staff must be aware of a woman's HIV status. Test results should be available on delivery suites to all clinical staff.¹⁵

Evidence level 4

4. Professional approach to the antenatal care of women who are HIV positive

4.1 What is the role of the multidisciplinary team and who should it include?

All antenatal care for women who are HIV positive should be managed by a multidisciplinary team, including (as a minimum) an HIV physician, obstetrician, specialist midwife, health advisor and paediatrician.

D

All women who are newly diagnosed as HIV positive should have an early assessment of their social circumstances.

D

Antenatal HIV care should be delivered by a multidisciplinary team, the precise composition of which will vary. Peer and voluntary sector support workers are particularly valuable. Disclosure of status to the general practitioner should be sensitively encouraged. Women with particular social difficulties, such as those with housing or immigration problems, will require considerable input from social workers. In addition, it may be necessary to involve some of the following: patient advocates, legal advocates, clinical psychologists, counsellors, drug-dependency specialists, interpreters and clinical nurse specialists.¹⁵

Evidence level 4

4.2 What are the psychosocial and ethical issues?

Pregnant women should be reassured that their confidentiality will be maintained.

D

Care must be taken to avoid inadvertent disclosure to a woman's partner or family members.

✓

It is important that all health professionals involved in the care of the pregnant woman are aware of her HIV diagnosis and plan of care, and this should be explained to the woman. She should also be reassured that her confidentiality will be respected.¹⁵

Health professionals should not assume that the woman's partner or family members are aware of her HIV diagnosis, even though they may attend antenatal visits and be present at the delivery. Care should be taken to avoid inadvertent disclosure in these situations.

Women who are HIV positive should be advised about safer-sex practices and the use of condoms, to prevent transmission of HIV and other sexually transmitted infections to an uninfected partner.

B

Among HIV serodiscordant couples, consistent use of condoms is associated with an 80% reduction in transmission of HIV.²²

Evidence level 2++

Individual counselling should be available for any individual who is HIV positive who wishes to consider unprotected sexual intercourse with a partner who is HIV negative or whose HIV infection status is not yet known. The availability of post-exposure prophylaxis should be discussed. A woman who is HIV positive whose partner is also HIV positive should be counselled about the low but possible risk of superinfection associated with unprotected sex.

Evidence level 4

Women should be encouraged to disclose their HIV status to their partner and should be given appropriate support. It is also recommended that women with existing children of unknown HIV status should have them tested for HIV.

D

The British HIV Association (BHIVA) has produced guidance on HIV testing,¹⁸ which can be accessed at www.bhiva.org/HIVTesting2008.aspx. Disclosure should be encouraged in all cases but is likely to take some time. Women should be given supportive guidance, taking into account their personal circumstances and any specific social or cultural issues. Reasons for refusing disclosure should be sensitively explored. These may include fear of domestic violence or relationship breakdown. Refusal to disclose can give rise to complex professional, ethical and legal dilemmas. There is a conflict between the duty of confidentiality to the patient and a duty to prevent harm to others. Breaking confidentiality to inform a sexual partner is sanctioned as a 'last resort' by the World Health Organization, General Medical Council and the British Medical Association.^{23,24,25} Difficult disclosure cases should be managed by the multidisciplinary team, with a low threshold for legal advice. Accurate recording of discussions and disclosure strategy is essential.

Evidence level 4

Detailed guidance about HIV testing of children whose parents are known to be HIV positive has been produced by BHIVA and can be accessed at www.bhiva.org/DontForgettheChildren.aspx.

In rare cases where women refuse interventions to prevent mother-to-child transmission of HIV, despite supportive guidance from the multidisciplinary team, a pre-birth planning meeting should be held with social services to discuss issues of safeguarding.

D

The input of the multidisciplinary team is crucial to support women who are reluctant to accept these interventions, as they are often the most isolated and unsupported. Despite all efforts, where the multidisciplinary team is unable to influence a mother's views antenatally, a pre-birth planning meeting with social services should be held. The mother should be informed that it is the paediatrician's role to advocate on behalf of the child's wellbeing and therefore to prevent, where possible, HIV infection. If the mother continues to refuse any intervention package, then legal permission should be sought at birth to treat the infant for 4 weeks with antiretroviral therapy and to prevent breastfeeding.¹⁵

Evidence level 4

4.3 *What is the notification process for HIV in pregnancy?*

Each maternity unit in England and Ireland should have a named respondent who is responsible for notifying all HIV positive pregnancies to the National Study of HIV in Pregnancy and Childhood (details at www.nshpc.ucl.ac.uk). In addition, the pregnancies of all women taking antiretroviral therapy should be reported to the Antiretroviral Pregnancy Registry (see section 6.6).



On reporting a case to the National Study of HIV in Pregnancy and Childhood, the respondent is asked to complete a standard notification form and subsequently an outcome-of-pregnancy form.¹⁵

Evidence level 4

5. Interventions to prevent disease progression in the mother and prevent mother-to-child transmission of HIV

A detailed description of interventions recommended in pregnancy is published by the British HIV Association guidelines and can be accessed at www.bhiva.org/PregnantWomen2008.aspx.¹⁵

5.1 *What interventions prevent disease progression in the mother?*

Women who require HIV treatment for their own health should take HAART and should continue treatment following delivery.

A

HAART regimens have become the standard of care for all individuals who are HIV positive who require antiretroviral therapy for their own health.²⁶ The timing of initiation of HAART is important; delaying treatment until the CD4 lymphocyte count has fallen below $200 \times 10^6/l$ is associated with a substantially greater risk of disease progression and death.¹⁷

Evidence level 2++

Current BHIVA guidelines for the general HIV population recommend initiation of HAART for those with symptomatic HIV infection and/or a falling or low CD4 lymphocyte count (less than $350 \times 10^6/l$). In addition, those with CD4 lymphocyte counts less than $200 \times 10^6/l$ are at risk of opportunistic infections; they should be given prophylaxis against *Pneumocystis carinii* pneumonia (PCP) and cotrimoxazole is usually the first-line agent.²⁶

Evidence level 4

In pregnancy, the criteria for initiating HAART for maternal health reasons and for PCP prophylaxis are the same as for the general population with HIV. However, it may be possible to delay treatment until after the first trimester.¹⁵

5.2 What interventions prevent mother-to-child transmission of HIV?

Women should be advised that, in the UK and other resource-rich settings, in the absence of breast feeding, the risk of mother-to-child transmission of HIV in women taking HAART during pregnancy is less than 1%.

B

In resource-rich settings, antiretroviral therapy, appropriate management of delivery and avoidance of breastfeeding are associated with mother-to-child transmission rates of less than 2%. In the large UK/Irish cohort of 4864 pregnant women who were HIV positive, the overall transmission rate was 1.2% and as low as 0.8% where at least 2 weeks of HAART had been given before delivery. Where the plasma viral load was less than 50 copies/ml at the time of delivery, the transmission rate was 0.1%.⁶

Evidence level 2++

5.2.1 Avoidance of breastfeeding

All women in resource-rich settings who are HIV positive should be advised to avoid breastfeeding.

B

In the absence of other interventions, large cohort studies have demonstrated around a two-fold risk of transmission associated with breastfeeding.²⁷

Evidence level 2++

The risk of transmission through breastfeeding where the mother has a viral load of less than 50 copies/ml is uncertain and current guidance states that all women who are HIV positive in resource-rich settings should avoid breastfeeding.¹⁵

5.2.2 Antiretroviral therapy

All pregnant HIV positive women should be advised to take antiretroviral therapy:

- For women who require HIV treatment for their own health, their prescribed HAART regimen should be continued throughout pregnancy and postpartum.**
- For women who do not require HIV treatment for their own health, HAART should be initiated between 20 and 28 weeks and discontinued at delivery.**
- For women who do not require HIV treatment for their own health, have a viral load less than 10 000 copies/ml and are prepared to be delivered by elective caesarean section, an acceptable alternative to HAART is zidovudine monotherapy initiated between 20 and 28 weeks, given orally twice daily, intravenously at delivery and discontinued immediately thereafter.**

A

B

A

Zidovudine (ZDV) monotherapy (ZDV given as a single agent) is the only anti-retroviral agent that has been shown to reduce significantly the risk of mother-to-child transmission in a randomised controlled trial.²⁸

Evidence level 1+

Currently in the UK, ZDV monotherapy is recommended as an option only for women with good CD4 lymphocyte counts and viral loads of less than 10 000 copies/ml and must be given in association with an elective caesarean section. According to this regimen, it is initiated between 20 and 28 weeks of pregnancy, administered orally twice daily and intravenously at delivery.

Evidence level 4

In the aforementioned large UK/Irish cohort study, there were no transmissions among 450 women taking this regimen.⁶

Evidence level 2++

With HAART now the standard of care for all individuals who are HIV positive requiring antiretroviral therapy for their own health and because of concerns about resistance to single-drug agents, ZDV monotherapy is less commonly used in pregnancy. However, ZDV has a well-established safety profile and, in light of emerging toxicity data associated with HAART, it may be used as an alternative to HAART for women who do not require HIV treatment for their own health and who are willing to be delivered by elective caesarean section.

5.2.3 Mode of delivery

Delivery by elective caesarean section at 38 weeks to prevent labour and/or ruptured membranes is recommended for:

- women taking HAART who have a plasma viral load greater than 50 copies/ml.
- women taking ZDV monotherapy as an alternative to HAART.
- women with HIV and hepatitis C virus co-infection.

A
A
D
B

A planned vaginal delivery (see section 8.2) can be offered to women taking HAART with plasma viral loads of less than 50 copies/ml.

Delivery by elective caesarean section for obstetric indications or maternal request should be delayed until after 39 completed weeks of gestation in women with plasma viral loads of less than 50 copies/ml, to reduce the risk of transient tachypnoea of the newborn.

D

An international multicentre randomised controlled trial performed before the widespread use of HAART showed a significant reduction in the mother-to-child transmission of HIV with elective caesarean section at 38 weeks compared with planned vaginal birth (relative risk 0.17; 95% confidence interval 0.05–0.55).²⁹ These findings were supported by a meta-analysis of 15 prospective cohort studies which included 8533 mother–infant pairs. The analysis reported a 50% reduction in the transmission rate in women who underwent elective caesarean section.³⁰

Evidence level 1++

For women who are HIV positive but not taking HAART and for women with a detectable plasma viral load, delivery by elective caesarean section is of clear benefit in reducing the risk of mother-to-child transmission. However, for women with plasma viral loads of less than 50 copies/ml who are taking HAART, data from a number of studies, including two large European cohorts, support the option of a planned vaginal delivery.^{5,6} In the UK/Irish cohort, 2117 infants were born to women who were HIV positive taking HAART who had plasma viral loads of less than 50 copies/ml. There were three infections (0.1%), two in infants born by elective caesarean section and one in an infant born by planned vaginal delivery.⁶ In the French cohort, among 1338 women who were HIV positive delivered at term whose plasma viral loads at delivery were less than 50 copies/ml, there were five transmissions (0.4%).⁵ In this cohort, elective caesarean section did not significantly reduce the rate of transmission compared with vaginal delivery if maternal viral load at delivery was less than 400 copies/ml.

Evidence level 2++

In women who are HIV negative but infected with hepatitis C virus (HCV) the risk of HCV transmission is approximately 5% and most studies have suggested that mode of delivery does not affect this risk.^{31,32}

Evidence level 2+

For women co-infected with HCV and HIV but not receiving antiretroviral therapy, a meta-analysis has demonstrated a three-fold increased risk in mother-to-child transmission of HCV.³³

Evidence level 1-

Furthermore, one cohort study of women co-infected with HCV and HIV has shown an increased risk of HIV transmission.³⁴

Evidence level 2-

Whether caesarean section is protective in women co-infected with HIV and HCV is uncertain and, until the results of larger studies are available, elective caesarean section is recommended for women who are HIV and HCV co-infected.¹⁵

6. Antenatal care for pregnant women who are HIV positive

6.1 What antenatal blood tests for infections are recommended for women who are HIV positive?

Women who are HIV positive are recommended to have a screening blood test for syphilis, hepatitis B and rubella in every pregnancy at their booking antenatal visit, in keeping with recommendations for the general population.

D

Additional recommended blood tests for women who are HIV positive include hepatitis C, varicella zoster, measles and toxoplasma.

D

Women who are HIV positive booking for antenatal care should have a blood sample tested for syphilis, rubella and hepatitis B, in keeping with recommendations for the general population.

Evidence level 4

Women who are HIV positive taking HAART at the time of booking should be screened for gestational diabetes.

D

Outside pregnancy, HAART regimens have been associated with a range of metabolic complications, including glucose intolerance, type-2 diabetes mellitus, dyslipidaemia, changes in body fat compartmentalisation (lipodystrophy) and insulin resistance. Protease inhibitors have been most commonly implicated.⁸

Evidence level 2+

In pregnancy, cohort studies investigating the association of HAART with gestational diabetes have yielded conflicting results.^{9,10}

Evidence level 2-

Until the results of large prospective studies are available, it seems prudent to ensure that all women who are HIV positive taking HAART regimens at the time of booking are screened for gestational diabetes.¹⁵

6.2 What immunisations should be undertaken?

Hepatitis B, pneumococcus and influenza immunisation are recommended for all individuals who are HIV positive; these immunisations can be safely administered in pregnancy.

D

Varicella zoster and measles, mumps and rubella vaccines are contraindicated in pregnancy. Women testing immunoglobulin G negative for these infections should be considered for immunisation postpartum, depending on their CD4 count (see section 9).

C

Comprehensive guidance about immunisation for individuals who are HIV positive is available at www.bhiva.org/Immunization2008.aspx.³⁵ Hepatitis B vaccination should be administered for all women who are HIV positive who are hepatitis B antibody negative at booking. Pneumococcal vaccination is indicated if the last vaccination was outside the recommended immunisation interval and influenza vaccination may be indicated, depending on the time of year.³⁵

Evidence level 4

6.3 When should screening for genital infections be undertaken?

Women who are HIV positive should be screened for genital infections at booking (or after multidisciplinary team referral if diagnosed HIV positive in pregnancy) and again at 28 weeks. Any infection detected should be treated according to UK national guidelines.

D

At present, the majority of pregnant women who are HIV-infected in the UK come from and mostly acquired HIV in sub-Saharan Africa, where the prevalence of genital infection, particularly in the HIV-infected population, can be high.³⁶

Evidence level 2+

Chorioamnionitis, prolonged rupture of membranes and preterm delivery have all been associated with perinatal transmission of HIV and may be interlinked.^{37,38,39}

Evidence level 2-

Bacterial vaginosis is associated with around a two-fold increased risk of preterm delivery.⁴⁰

Evidence level 1+

Organisms associated with bacterial vaginosis have been shown to stimulate HIV in vitro.^{41,42} European studies have consistently demonstrated a strong association between HIV and preterm delivery.^{14,43,44}

Evidence level 2++

Although, currently, there is no evidence that treatment of genital infections reduces mother-to-child transmission of HIV, these studies support the recommendation that all women who are HIV positive should be screened for genital infections. Moreover, any genital infection, even if asymptomatic, should be treated.¹⁵

Evidence level 4

6.4 How should screening for aneuploidy be undertaken?

Screening for aneuploidy should be offered to all pregnant women who are HIV positive in accordance with national guidelines.

D

First-trimester screening for Down syndrome should be offered in accordance with national guidelines.⁴⁵

Evidence level 4

Several small studies have shown that HIV infection and/or HAART are associated with changes in the values of the biochemical markers used for second-trimester screening for Down syndrome.^{46,47,48}

Evidence level 2-

Only one study, however, has evaluated first-trimester screening for Down syndrome using the combined test.⁴⁹ Brossard *et al.*, in a multicentre case-control study of 214 women who were HIV positive found no difference in the accuracy of the combined test in the estimation of Down syndrome risk between women who were HIV positive and controls who were HIV negative.⁴⁹

Evidence level 2+

6.5 How safe is invasive diagnostic testing?

Women who are HIV positive considering invasive diagnostic testing should be counselled in a fetal medicine unit and the advice of the HIV physicians sought concerning reducing the risk of HIV transmission.

D

Observational studies conducted in the pre-HAART era suggested an increased risk of HIV transmission associated with amniocentesis and other invasive procedures.^{50,51} More recently, a multicentre French cohort study found that, of 166 women who had amniocentesis, there was no transmission among the 81 mothers receiving HAART.⁵²

Evidence level 2+

Other smaller observational studies have also yielded reassuring results.⁵³ However, these studies are insufficiently powered to exclude a small increased risk of mother-to-child transmission associated with invasive procedures, even among women taking HAART. No studies have compared the risk of transmission of amniocentesis with chorionic villus sampling.

When any woman undergoes invasive diagnostic testing, the obstetrician carrying out the procedure should be aware of the woman's HIV antibody test result. For women known to be HIV positive who have started HAART but whose viral load is greater than 50 copies/ml, it may be advisable to delay the amniocentesis until the maternal viral load is less than 50 copies/ml. For women not already taking HAART, administration of anti-retrovirals to cover the procedure is advised. When performing amniocentesis, the placental route is absolutely contraindicated.¹⁵

Evidence level 4

6.6 When should ultrasound scanning be undertaken?

Many women who are HIV positive will have been exposed to potentially teratogenic drugs during the first trimester. Dating and anomaly scans should be offered according to national guidelines.

D

The Antiretroviral Pregnancy Registry, to which all women taking anti-retroviral therapy in pregnancy should be reported, contains a summary of relevant mutagenesis, carcinogenesis and teratogenesis data for each licensed antiretroviral (www.apregistry.com). Other than for didanosine (increased incidence of congenital malformations among babies exposed in utero) and efavirenz (increased risk of congenital abnormalities in animal studies), no anti-retrovirals have yet given cause for concern. Cotrimoxazole, a folate antagonist, is commonly used as prophylaxis against PCP for women with low CD4 lymphocyte counts, raising the possibility of neural tube defects. However, UK surveillance data collected between 1997 and 2007 are reassuring; the rate of reported major and minor congenital abnormality was 2.8%, with no significant difference according to timing of exposure or class of anti-retroviral. In particular, there was no increased risk of abnormalities in infants exposed to efavirenz or didanosine in the first trimester.⁵⁴

Evidence level 2++

6.7 What additional monitoring is necessary?

Monitoring of plasma viral load and drug toxicities should be undertaken as directed by the HIV physicians.

D

Comprehensive guidance is given in the BHIVA guideline.¹⁵ Resistance testing is performed at diagnosis. Maternal plasma viral load is the most important predictor of transmission. As a minimum, it is measured every trimester, at 36 weeks gestation and at delivery. Assessment of full blood count, urea and electrolytes and liver function is undertaken regularly to monitor for drug toxicities.

Evidence level 4

6.8 When should a decision regarding mode of delivery be taken?

A plan regarding mode of delivery should be made at around 36 weeks following detailed discussion with the mother.

D

Women taking HAART who have a viral load of less than 50 copies/ml at 36 weeks may be offered a planned vaginal delivery. A plan for intrapartum care should be clearly documented (see section 8.2). The decision for vaginal delivery should be reviewed when the woman presents in labour: the result of any plasma viral load sample taken after the documented plan should be checked and confirmed as less than 50 copies/ml.

For women taking HAART with a viral load of less than 50 copies/ml who do not wish to deliver vaginally, caesarean section should be scheduled for 39+ weeks, to minimise the risk of transient tachypnoea of the newborn. For women with a viral load greater than 50 copies/ml and those taking ZDV monotherapy as an alternative to HAART, caesarean section should be scheduled for 38 weeks; for these women, earlier delivery is justified because the risk of perinatal HIV transmission associated with labour and/or ruptured membranes is considered to outweigh the risk of transient tachypnoea.

Evidence level 4

7. Management of antenatal complications

7.1 What are the complications of HIV and adverse effects of HAART?

For any woman who is HIV positive who becomes acutely unwell in pregnancy, close liaison between the obstetricians and HIV physicians is mandatory to avoid diagnostic error.

D

HIV-related complications should also be considered as a cause of acute illness in pregnant women whose HIV status is unknown, particularly those who are not booked for antenatal care. In these circumstances, rapid HIV testing should be considered.

D

Pregnant women with advanced HIV are at increased risk of opportunistic infections, particularly PCP. Symptoms of PCP include fever, dry cough and shortness of breath and patients are typically hypoxic.

HAART regimens are commonly associated with gastrointestinal disturbances, skin rashes and hepatotoxicity. Lactic acidosis (including two fatal cases) has been reported in pregnant women taking HAART, most commonly where two particular anti-retrovirals (stavudine and didanosine) were included in the HAART regimen. As a consequence, these agents are now very rarely used. Symptoms of lactic acidosis are often non-specific but may include gastrointestinal disturbances, fever and breathlessness, and may cause diagnostic confusion.

In the pre-HAART era, HIV infection was associated with low rates of pre-eclampsia.⁵⁵ There are conflicting data on the risk of pre-eclampsia in women taking HAART. A case-control study from the UK found that the rate of pre-eclampsia among 214 women taking HAART was 11%, similar to that of HIV negative controls but higher than the rate in those taking ZDV monotherapy (1%) and those on no treatment (0%).¹¹ These data are supported by a cohort study from Spain (1985–2003), which showed a sharp rise in pre-eclampsia and fetal death in pregnant women who were HIV positive ($n = 472$) after the introduction of HAART in 2001. Pre-eclampsia was associated with preconception HAART (adjusted odds ratio 8.9; 95% CI 1.7–45.5) as was pre-eclampsia and/or fetal death (adjusted odds ratio 5.6; 95% CI 1.7–18.1).⁵⁶

Evidence level 2+

In a Brazilian study, however, despite high rates of HAART use, the rate of pre-eclampsia in women who were HIV positive was 0.8% compared with 10.6% in uninfected controls.¹²

Evidence level 2-

Presentation with symptoms suggestive of pre-eclampsia, cholestasis or other signs of liver dysfunction may indicate drug toxicity and early liaison with HIV physicians should be sought.

7.2 What is the risk of preterm delivery?

Women who are HIV positive should be counselled about the increased risk of preterm delivery associated with HAART.

B

European cohort studies have consistently demonstrated an increased risk of preterm delivery associated with HAART.^{13,43,57-59} Data from the UK and Ireland on 4445 pregnancies showed that the preterm delivery rate was higher in women taking HAART (14.1%) than in women on mono or dual therapy (10.1%), after adjusting for ethnicity, maternal age, clinical status and injecting drug use (adjusted odds ratio 1.51; 95% CI 1.19–1.93; $P = 0.001$). The association of HAART and prematurity was even stronger for deliveries before 32 weeks: 3.6% compared with 1.4% ($P = 0.001$).⁴³

Evidence level 2++

Data from the USA have been less consistent. In a meta-analysis of 13 cohorts performed by the US Centers for Disease Control, HAART compared with no therapy was not associated with preterm delivery but protease inhibitor-based compared with non-protease inhibitor-based HAART (odds ratio 1.24) and HAART started before or during the first trimester (odds ratio 1.71) were associated with preterm delivery.¹⁴

Evidence level 1-

At present, it is unclear whether the increased risk of preterm delivery demonstrated in UK and European studies is due to spontaneous labour, prelabour rupture of the membranes or obstetric intervention in response to antenatal complications.

7.3 How should preterm labour be managed?

For women presenting with threatened preterm labour, initial assessment is in accordance with guidelines for the general population. The multidisciplinary team should be involved so that a clear plan of care is in place should preterm labour supervene (see below).

D

The usual indications for steroids apply. A genital infection screen should be undertaken. Tocolysis may be initiated as appropriate. Close liaison with the HIV physicians and paediatricians will ensure that a clear plan of care is put into place.

Evidence level 4

For women in preterm labour, urgent advice should be sought from the HIV physicians and paediatricians about the choice of anti-retroviral therapy. Infants born below 32 weeks of gestation are at increased risk of HIV but may be unable to tolerate oral medication. Anti-retroviral therapy administered to the mother just before and during delivery will provide prophylaxis for the neonate.

C

In women taking HAART, French and UK cohorts have demonstrated increased risks of transmission in women delivering at gestations below 32 weeks, particularly if the duration of HAART is short.^{5,6,20}

Evidence level 2++

Furthermore, infants born below 30–32 weeks can be difficult to treat because they are unable to feed orally for the first few days and, currently, the only licensed intravenous anti-retroviral treatment available to them is ZDV. Thus, to optimise antiretroviral therapy for a neonate born at less than 32 weeks of gestation, appropriate anti-retroviral therapy should be administered to the mother before and during labour and delivery. For women in preterm labour, the choice of antiretroviral therapy will be influenced by maternal plasma viral load, gestational age, and pharmacokinetics (rapidity of placental transfer and persistence in the neonatal circulation). Detailed guidance is given in the BHIVA guidelines on management of HIV in pregnancy.¹⁵ Anti-retroviral drugs used in these circumstances include: a single dose of oral nevirapine (200 mg) given at least 2 hours before delivery, a double dose of oral tenofovir (600 mg) and intravenous ZDV.

Evidence level 4

7.4 How should preterm prelabour rupture of the membranes be managed?

Where preterm prelabour rupture of the membranes occurs after 34 weeks of gestation, delivery should be expedited.

D

A genital infection screen should be undertaken and consideration should be given to starting intravenous broad-spectrum antibiotics. At this gestation, the small risk of neonatal morbidity and mortality associated with prematurity is outweighed by the risk to both mother and neonate of chorioamnionitis and the risk of perinatal HIV transmission. If plasma viral load is less than 50 copies/ml and there are no obstetric contraindications, augmentation of labour may be considered.¹⁵

Evidence level 4

Where preterm prelabour rupture of the membranes occurs before 34 weeks of gestation, the decision as to whether to expedite delivery should be made after multidisciplinary team consultation, involving the HIV physicians and paediatricians.

D

Steroids should be administered in the usual way. A genital infection screen should be undertaken. Oral erythromycin should be started in accordance with national guidelines and consideration should be given to starting intravenous broad-spectrum antibiotics. Evidence of chorioamnionitis and fetal distress are indications for prompt delivery. In other cases, the multidisciplinary team discussion will consider the adequacy of maternal HAART, plasma viraemia and the presence of any other pregnancy or HIV-related comorbidities. The timing of delivery will take into consideration the risk of complications associated with prematurity, the availability of neonatal facilities and the risk of perinatal HIV transmission. Such complex decisions should involve the paediatricians and HIV physicians. Expert advice from outside the host institution may be helpful.

Evidence level 4

In untreated women, rupture of membranes for more than 4 hours is associated with a doubling of the risk of HIV transmission.⁶⁰

Evidence level 1+

In women taking HAART, delivery below 32 weeks of gestation is a risk factor for perinatal transmission, particularly if the duration of HAART is short.^{5,6,20}

Evidence level 2++

Limited case series data regarding transmission risk in women with PPRM taking HAART are reassuring.^{61,62}

Evidence
level 3

In selected cases, expectant management may be appropriate. Issues regarding choice of antiretroviral therapy in women delivering at less than 32 weeks of gestation are discussed in section 7.2.

7.5 How should pre-labour rupture of the membranes at term be managed?

In the case of prelabour rupture of the membranes at term, delivery should be expedited.

D

Broad-spectrum intravenous antibiotics should be administered if there is evidence of genital infection or chorioamnionitis.

D

In a meta-analysis of studies conducted before the advent of HAART, rupture of membranes for more than 4 hours is associated with a doubling of the risk of HIV transmission. These studies also demonstrated a 2% incremental increase in transmission risk for every hour of ruptured membranes up to 24 hours.⁶⁰

Evidence
level 1++

For women taking HAART with prelabour rupture of the membranes at term whose viral loads are low, the limited data regarding transmission risk are reassuring. One US study investigated the risk of perinatal HIV transmission in women taking HAART with viral loads less than 1000 copies/ml and membrane rupture of over 4 hours' duration at term. The study found that duration of membrane rupture was not a risk factor for transmission.⁶³ A prospective cohort study from Spain found that rupture of membranes of more than 6 hours' duration was associated with a three-fold increase in transmission in the absence of anti-retroviral treatment but there was no increased risk among the 19 women taking HAART.⁶⁴

Evidence
level 3

For all women with prelabour rupture of the membranes at term, delivery should be expedited. The aforementioned studies provide some data to support immediate augmentation rather than caesarean section where plasma viral load is less than 50 copies/ml, provided that there is no evidence of any genital infection or chorioamnionitis and no obstetric contraindications. Delivery should be led by a senior obstetrician with the advice of the HIV physicians.¹⁵

Evidence
level 4

7.6 How should prolonged pregnancy be managed?

For women on HAART with a plasma viral load of less than 50 copies/ml, the decision regarding induction of labour should be individualised. There is no contraindication to membrane sweep or to the use of prostaglandins.

D

If a woman remains undelivered beyond 41 weeks of gestation, is keen to achieve a vaginal delivery, is taking HAART and has a plasma viral load of less than 50 copies/ml, induction of labour may be considered, particularly if the cervix is favourable. Otherwise, an elective caesarean section should be performed.¹⁵

Evidence
level 4

7.7 What is the role of vaginal birth after caesarean section?

A trial of scar may be considered for women taking HAART whose plasma viral load is less than 50 copies/ml.

D

Scar rupture occurs in approximately 1/250 women who labour after a previous caesarean section.⁶⁵

Evidence
level 2+

Whether scar rupture in HIV infected women is associated with an increased risk of transmission from prolonged fetal exposure to maternal blood is unknown but, in women taking HAART with a plasma viral load of less than 50 copies/ml, this risk is likely to be very low indeed.

Evidence
level 4

7.8 *How should women diagnosed in late pregnancy but before the onset of labour be managed?*

Women diagnosed with HIV late in pregnancy should have a rapid multidisciplinary team assessment and HAART should be commenced as soon as possible.

D

With improved turnaround times for viral load testing, a woman diagnosed HIV positive beyond 32 weeks may still have her pregnancy managed with a view to planned vaginal delivery if she commences HAART and achieves a viral load of less than 50 copies/ml by 36 weeks. If the viral load is greater than 50 copies/ml at 36 weeks, she should be scheduled for an elective caesarean section at 38 weeks, should continue her HAART regimen and be given intravenous ZDV at delivery.

Evidence level 4

7.9 *How should women diagnosed with HIV during labour be managed?*

For women who are HIV positive who are diagnosed during labour, urgent advice should be sought from the HIV physicians regarding optimum HAART; delivery should be by caesarean section and, where possible, should be timed with respect to anti-retroviral administration.

D

If the woman's HIV status is unknown, a rapid test for HIV is recommended (see section 3.3) and a reactive result should be acted on immediately.¹⁹ Urgent advice should be sought from the HIV physicians about the choice of anti-retroviral therapy. In these circumstances, the HAART regimen is likely to include intravenous ZDV (the only licensed anti-retroviral available for parenteral use) and oral nevirapine (an anti-retroviral with rapid placental transfer and of proven benefit in reducing transmission). If delivery is not imminent, a caesarean section should be performed. Where possible, delivery should be timed to be at least 2 hours after administration of nevirapine. A confirmatory test should be taken, together with samples for CD4 count, viral load and resistance testing. The paediatricians should be informed so that neonatal care can be planned.¹⁵

Evidence level 4

8. Management of delivery

8.1 *How should caesarean section be managed?*

If intravenous ZDV is indicated, the infusion should be started 4 hours before beginning the caesarean section and should continue until the umbilical cord has been clamped.

D

The surgical field should be kept as haemostatic as possible and care should be taken to try to avoid rupturing the membranes until the head is delivered through the surgical incision. The cord should be clamped as early as possible after delivery.

D

A maternal sample for plasma viral load and CD4 lymphocyte count should be taken at delivery.

D

The decision for elective caesarean section will usually be made at or before around 36 weeks gestation. Details of which anti-retrovirals should be taken and whether they should be continued postpartum should be documented in that plan. For those women requiring intravenous ZDV, the infusion should be started 4 hours before beginning the caesarean section and continued until the umbilical cord has been clamped.

Evidence level 4

For all caesarean sections, whether elective or emergency, care should be taken to ensure that the surgical field is as haemostatic as possible and, where possible, that the membranes are left intact until the head is delivered through the surgical incision. The cord should be clamped as early as possible after delivery. Peripartum antibiotics should be administered in accordance with national guidelines for the general population.

Several studies have suggested that the complications of caesarean section are higher in women with HIV. The most frequent reported complication was postpartum fever.^{66,67}

Evidence level 2-

A more recent case-control study from the UK, where all women who were HIV-positive received antiretroviral therapy and prophylactic antibiotics ($n = 44$) did not demonstrate any differences in postoperative morbidity.⁶⁸ This is consistent with data from a Dutch cohort ($n = 143$).⁵⁹

Evidence level 2+

8.2 How should planned vaginal delivery be managed?

Only women with a plasma viral load of less than 50 copies/ml should be offered a planned vaginal delivery.

D

Invasive procedures such as fetal blood sampling and fetal scalp electrodes are contraindicated.

D

If labour progress is normal, amniotomy should be avoided unless delivery is imminent.

D

Amniotomy and possible use of oxytocin may be considered for augmentation of labour.

D

If instrumental delivery is indicated, the use of forceps is preferable to ventouse.

D

All women for planned vaginal delivery should have a clear plan for intrapartum care documented in their maternity notes by 36 weeks. The decision about mode of delivery should be reviewed when the woman presents in labour and her recent plasma viral load results should be checked. Only women with a viral load of less than 50 copies/ml at last measurement should be offered a planned vaginal delivery.

Evidence level 4

In the absence of a documented mode of delivery plan or in the event of uncertainty regarding viral load results, urgent advice should be sought from the HIV physicians. Management should be led by a senior obstetrician. Women taking HAART should continue their usual oral HAART regimen through labour.

Although the limited data on rupture of membranes in women taking HAART are reassuring (see section 7.4), until more robust data are available, it is recommended that the membranes are left intact for as long as possible.

Evidence level 3

Amniotomy and possible use of oxytocin may be considered for augmentation of labour.

Electronic fetal monitoring should be performed according to national guidelines.⁶⁸ HIV infection of itself is not an indication for continuous electronic fetal monitoring. Fetal blood sampling and fetal scalp electrodes are contraindicated.

Evidence level 4

If instrumental delivery is indicated, low-cavity traction forceps are the instruments of choice, as it is generally accepted that they are associated with lower rates of fetal trauma than ventouse. Mid-cavity and rotational instrumental deliveries should be avoided.

9. Postpartum care

9.1 What support should be given to women with respect to avoidance of breastfeeding?

Women in resource-rich countries who are HIV positive should be advised not to breastfeed.

B

In the absence of other interventions, breastfeeding has been shown to double the risk of mother-to-child transmission.²⁷

Evidence level 2++

The risk of transmission through breastfeeding where the mother has a viral load of less than 50 copies/ml is uncertain. Current guidance states that all women who are HIV positive in resource-rich settings should avoid breastfeeding.¹⁵

Evidence level 4

Women should be given appropriate support with regard to artificial (infant formula) feeding. This is particularly important for women whose families are unaware of their HIV status and where the cultural norm is to breastfeed.

One systematic review of randomised trials conducted in the general population found some evidence that pharmacological agents are better than no treatment at suppressing lactation in the first postpartum week.

Evidence level 1-

Cabergoline 1 mg orally given within 24 hours of birth is therefore recommended for all mothers in the UK who are HIV positive.

9.2 *What contraceptive advice should be given?*

All women who are HIV positive should receive guidance about contraception in the immediate postpartum period.

D

Contraceptive counselling requires specialist advice. There are many interactions between hormonal contraception and HAART. The BHIVA has issued comprehensive guidance on contraception (www.bhiva.org/UKGuidelines2008.aspx).⁶⁹

9.3 *What Immunisations should be offered to the mother?*

Measles, mumps and rubella and varicella zoster immunisation may be indicated. Advice of HIV physicians should be sought.

D

The BHIVA has produced comprehensive guidance about immunisation for people who are HIV positive,³⁵ which can be accessed at www.bhiva.org/Immunization2008.aspx. Measles, mumps and rubella and varicella zoster are live vaccines and are therefore contraindicated in pregnancy. However, they are recommended for susceptible individuals who are HIV positive with CD4 counts above 200 and 400, respectively, and they can therefore be considered postpartum for those found to be immunoglobulin G-negative on antenatal testing.

Evidence level 4

Hepatitis B and pneumococcal and influenza vaccines are recommended for all people who are HIV positive (between October and March). These vaccines can be safely administered in pregnancy or postpartum.

10. Care of the neonate

10.1 *What antiretroviral therapy should be administered to the neonate?*

All neonates born to women who are HIV positive should be treated with anti-retroviral therapy within 4 hours of birth.

A

Anti-retroviral therapy should be commenced as soon as possible after birth and certainly within 4 hours.¹⁵

Most infants will be given ZDV monotherapy twice daily for 4 weeks, as a modification of the postnatal component of the regimen shown to reduce mother-to-child transmission in a randomised controlled trial of non-breastfeeding women.²⁸ If a mother has resistance to ZDV, an alternative suitable monotherapy is given to the infant. HAART is given to infants at high risk of HIV infection; for example, infants of untreated mothers or mothers who have plasma viraemia greater than 50 copies/ml despite HAART. The only licensed antiretroviral drug available for intravenous use in sick or preterm infants is ZDV.

Evidence level 4

More detailed guidance is given in the BHIVA guideline on management of HIV in pregnancy. Expert advice from outside the host institution may be helpful.

10.2 Should prophylaxis against PCP be administered to the neonate?

Prophylaxis against PCP is recommended only for infants born to mothers at high risk of transmission.

C

Although primary PCP in infants with HIV carries a high mortality and morbidity, PCP prophylaxis is no longer routinely administered to infants of mothers who are HIV positive because the risk of mother-to-child transmission of HIV is so low. However, cotrimoxazole as PCP prophylaxis should still be prescribed for infants born to mothers at high risk of transmission.

Evidence level 4

10.3 How and when should the infant be tested for HIV?

Infants should be tested at 1 day, 6 weeks and 12 weeks of age. If all these tests are negative and the baby is not being breastfed, the parents can be informed that the child is not HIV-infected. A confirmatory HIV antibody test is performed at around 18 months of age.

D

A venous blood sample should be taken at the appropriate times. The gold-standard test for HIV in infancy is HIV DNA polymerase chain reaction on peripheral blood lymphocytes,⁷⁰ although some studies are now demonstrating equal or increased sensitivity with amplification of HIV RNA.⁷¹

Evidence level 4

Loss of maternal antibodies often occurs by 18 months of age but may take longer as newer, more sensitive tests are used. This can cause considerable anxiety.

10.4 What is the notification process for the child?

Children infected with HIV and those born to women who are HIV infected are reported to the National Study of HIV in Pregnancy and Childhood (details at www.nshpc.ucl.ac.uk).

✓

The paediatric reporting scheme is run by the National Study of HIV in Pregnancy and Childhood in collaboration with the British Paediatric Surveillance Unit of the Royal College of Paediatrics and Child Health.¹⁵

11. Prepregnancy management

For couples wishing to conceive where one or both partners is HIV positive, prepregnancy counselling should be undertaken by an appropriately trained health professional.

11.1 What interventions are there to minimise the risk of transmission between discordant couples at conception?

Couples who are serodiscordant for HIV infection and who choose to have sexual intercourse should be advised to use condoms.

B

Among couples who are HIV serodiscordant, consistent use of condoms is associated with an 80% reduction in transmission.²² These couples should be advised on the technique of self-insemination during the fertile time of the cycle using quills, syringes and sterile containers.⁷²

Serodiscordant couples where the female partner is HIV negative should be advised that assisted conception with either donor insemination or sperm washing is significantly safer than timed unprotected intercourse.

B

For these couples, assuming a stable relationship, the risk of transmission for each act of sexual intercourse is estimated to be between 0.03% and 0.001%.⁷³ This risk is significantly reduced, although not eliminated, if the male partner has a viral load of less than 50 copies/ml and is taking HAART.⁷⁴ The risk can be further reduced by limiting exposure to the fertile period of the cycle and ensuring that all genital infections have been treated.

Evidence level 2+

Sperm washing is a procedure during which live sperm that do not carry HIV are separated from HIV-infected seminal plasma and nongerminal cells by centrifugation before being used in an insemination or in vitro fertilisation (IVF) procedure.⁷⁴ The efficacy of the wash is then verified with a post-wash HIV RNA assay before the sperm are used in treatment.⁷⁶ The treatment is relatively simple and is significantly safer than timed unprotected intercourse, with no case of seroconversion in either female partner or child born in over 3000 cycles of sperm washing combined with intra-uterine insemination, IVF or intracytoplasmic sperm injection reported in the literature to date.^{72,77}

Evidence level 2++

11.2 How should the health of the mother who is HIV positive and her fetus be optimised periconceptually?

Couples are recommended to delay conception until plasma viraemia is suppressed, prophylaxis against PCP is no longer required and any opportunistic infections have been treated.

D

Folate supplementation should be administered in accordance with national guidelines. For women taking cotrimoxazole, higher dose folate (5 mg) should be administered.

D

Maternal health and HAART regimen should be optimised before conception. Folic acid should be commenced in accordance with national guidelines for the general population. For women taking cotrimoxazole for prophylaxis against PCP, a higher dose of folic acid is recommended because of the folate antagonist effect of cotrimoxazole. Ideally, couples should delay conception until PCP prophylaxis is no longer required and the HAART regimen is effectively suppressing viraemia.

Evidence level 4

All women who are HIV positive are recommended to have yearly cervical cytology.

B

Yearly cervical cytology screening is recommended for all women with HIV, because of the association of HIV, immunosuppression and cervical neoplasia.⁷⁸

Evidence level 2++

The same indications for referral to colposcopy apply as for the general population.

Evidence level 4

12. Auditable standards

- Percentage of women having an HIV test.
- Percentage of women with a birth plan in their notes at the time of delivery.
- Percentage of babies having their first dose of anti-retroviral medication given within 4 hours of delivery.
- Mother-to-child transmission rate.
- Mode of delivery.

13. Further research

- Preterm delivery, HIV and HAART.
- Pre-eclampsia, HIV and HAART.
- Gestational diabetes, HIV and HAART.

References

1. Health Protection Agency; UK National Screening Committee. *Infectious Diseases in Pregnancy Screening Programme 2007/08 Annual Report and 2005–2007 Surveillance Data*. London: HPA; 2009 [www.hpa.org.uk/web/HPAwebFile/HPAweb_C/1214464646883].
2. Health Protection Agency. *HIV in the United Kingdom: 2009 Report*. London: HPA; 2009 [www.hpa.org.uk/web/HPAweb&HPAwebStandard/HPAweb_C/1227515299695].
3. Working Group on Mother-To-Child Transmission of HIV. Rates of mother-to-child transmission of HIV-1 in Africa, America, and Europe: results from 13 perinatal studies. *J Acquir Immune Defic Syndr Hum Retrovirology* 1995;8:506–10.
4. Kourtis AP, Lee FK, Abrams EJ, Jamieson DJ, Bulterys M. Mother-to-child transmission of HIV-1: timing and implications for prevention. *Lancet Infect Dis* 2006;6:726–32.
5. Warszawski J, Tubiana R, Le Chenadec J. Mother-to-child HIV transmission despite antiretroviral therapy in the ANRS French Perinatal Cohort. *AIDS* 2008;22:289–99.
6. Townsend CL, Cortina-Borja M, Peckham CS, De Ruiter A, Lyall H, Tookey PA. Low rates of mother-to-child transmission of HIV


- following effective pregnancy interventions in the United Kingdom and Ireland, 2000–2006. *AIDS* 2008;22:973–81.
7. Tuomala RE, Kalish LA, Zorrilla C, Fox H, Shearer W, Landay A, *et al.* Changes in total, CD4+, and CD8+ lymphocytes during pregnancy and 1 year postpartum in human immunodeficiency virus-infected women. The Women and Infants Transmission Study. *Obstet Gynecol* 1997;89:967–74.
 8. Hitti J, Andersen J, McComsey G, Liu T, Melvin A, Smith L, *et al.* Protease inhibitor-based antiretroviral therapy and glucose tolerance in pregnancy: AIDS Clinical Trials Group A5084. *Am J Obstet Gynecol* 2007;196:331–7.
 9. Watts DH, Balasubramanian R, Maupin RT Jr, Delke I, Dorenbaum A, Fiore S, *et al.* Maternal toxicity and pregnancy complications in human immunodeficiency virus-infected women receiving antiretroviral therapy: PACTG 316. *Am J Obstet Gynecol* 2004;190:506–16.
 10. Tuomala RE, Watts DH, Li D, Vajaranant M, Pitt J, Hammill H, *et al.* Improved obstetric outcomes and few maternal toxicities are associated with antiretroviral therapy, including highly active antiretroviral therapy during pregnancy. *J Acquir Immune Defic Syndr* 2005;38:449–73.
 11. Wimalasundera RC, LARBalestier N, Smith JH, de RA, McG Thom SA, Hughes AD, *et al.* Pre-eclampsia, antiretroviral therapy, and immune reconstitution. *Lancet* 2002;360:1152–4.
 12. Mattar R, Amed AM, Lindsey PC, Sass N, Daher S. Preeclampsia and HIV infection. *Eur J Obstet Gynecol Reprod Biol* 2004;117:240–1.
 13. Thorne C, Patel D, Newell ML. Increased risk of adverse pregnancy outcomes in HIV-infected women treated with highly active antiretroviral therapy in Europe. *AIDS* 2004;18:2337–9.
 14. Kourtis AP, Schmid CH, Jamieson DJ, Lau J. Use of antiretroviral therapy in pregnant HIV-infected women and the risk of premature delivery: a meta-analysis. *AIDS* 2007;21:607–15.
 15. de Ruiter A, Mercey D, Anderson J, Chakraborty R, Clayden P, Foster G, *et al.* British HIV Association and Children's HIV Association guidelines for the management of HIV infection in pregnant women 2008. *HIV Med* 2008;9:452–502.
 16. NHS Infectious Diseases Screening Programme. *Infectious Diseases in Pregnancy Screening Programme Standards Including Requirements to Support the Management of Women with Positive Antenatal Screening Test Results Consultation Document*. London: NHS; 2009 [http://infectiousdiseases.screening.nhs.uk/cms.php?folder=2416].
 17. May M, Sterne JA, Sabin C, Costagliola D, Justice AC, Thiébaud R, *et al.* Prognosis of HIV-1-infected patients up to 5 years after initiation of HAART: collaborative analysis of prospective studies. *AIDS* 2007;21:1185–97.
 18. British HIV Association; British Association of Sexual Health and HIV; British Infection Society. *UK Guidelines for HIV Testing*. London: BHIVA; 2008 [www.bhiva.org/HIVTesting2008.aspx].
 19. British Association for Sexual Health and HIV Clinical Governance Committee. Guidance on the appropriate use of HIV point of care tests [www.bashh.org/groups/clinical_governance_committee].
 20. Children's HIV Association. *Perinatal Transmission of HIV in England: 2002–2005*. London: CHIVA; 2007 [www.chiva.org.uk/health/publications/perinatal].
 21. Struik SS, Tudor-Williams G, Taylor GP, Portsmouth SD, Foster CJ, Walsh C, *et al.* Infant HIV infection despite 'universal' antenatal testing. *Arch Dis Child* 2008;93:59–61.
 22. Weller SC, Davis-Beatty K. Condom effectiveness in reducing heterosexual HIV transmission. *Cochrane Database Syst Rev* 2002;(1):CD003255.
 23. Potterat JJ. Partner notification for HIV: running out of excuses. *Sex Transm Dis* 2003;30:89–90.
 24. World Health Organization. *Guidance on Provider-initiated HIV Testing and Counselling in Health Facilities*. Geneva: WHO; 2007 [www.who.int/hiv/pub/vct/pitc/en/index.html].
 25. General Medical Council. *Confidentiality Guidance*. London: GMC; 2009 [www.gmc-uk.org/guidance/ethical_guidance/confidentiality_contents.asp].
 26. Gazzard BG. British HIV Association Guidelines for the treatment of HIV-1-infected adults with antiretroviral therapy 2008. *HIV Med* 2008;9:563–608.
 27. Dunn DT, Newell ML, Ades AE, Peckham CS. Risk of human immunodeficiency virus type 1 transmission through breastfeeding. *Lancet* 1992;340:585–8.
 28. Connor EM, Sperling RS, Gelber R, Kiselev P, Scott G, O'Sullivan MJ, *et al.* Reduction of maternal–infant transmission of human immunodeficiency virus type 1 with zidovudine treatment. Pediatric AIDS Clinical Trials Group Protocol 076 Study Group. *N Engl J Med* 1994;331:1173–80.
 29. European Mode of Delivery Collaboration. Elective caesarean-section versus vaginal delivery in prevention of vertical HIV-1 transmission: a randomised clinical trial. *Lancet* 1999;353:1035–9.
 30. International Perinatal HIV Group. The mode of delivery and the risk of vertical transmission of human immunodeficiency virus type 1—a meta-analysis of 15 prospective cohort studies. *N Engl J Med* 1999;340:977–87.
 31. McMenamin MB, Jackson AD, Lambert J, Hall W, Butler K, Coulter-Smith S, *et al.* Obstetric management of hepatitis C-positive mothers: analysis of vertical transmission in 559 mother–infant pairs. *Am J Obstet Gynecol* 2008;199:315.e1–315.e5.
 32. European Paediatric HCV Network. A significant sex – but not elective cesarean section – effect on mother to child transmission of hepatitis C virus infection. *J Infect Dis* 2005;192:1872–9.
 33. Pappalardo BL. Influence of maternal human immunodeficiency virus (HIV) co-infection on vertical transmission of hepatitis C virus (HCV): a meta-analysis. *Int J Epidemiol* 2003;32:727–34.
 34. Hershow RC, Riestler KA, Lew J, Quinn TC, Mofenson LM, Davenny K, *et al.* Increased vertical transmission of human immunodeficiency virus from hepatitis C virus-coinfected mothers. Women and Infants Transmission Study. *J Infect Dis* 1997;176:414–20.
 35. Geretti AM, on behalf of the BHIVA Immunization Writing Committee. British HIV Association guidelines for immunization of HIV-infected adults 2008. *HIV Med* 2008;9:795–848. [http://www.bhiva.org/immunization2008.aspx].
 36. Leroy V, De CA, Ladner J, Bogaerts J, Van de PP, Dabis F. Should screening of genital infections be part of antenatal care in areas of high HIV prevalence? A prospective cohort study from Kigali, Rwanda, 1992–1993. The Pregnancy and HIV (EGE) Group. *Genitourin Med* 1995;71:207–11.
 37. Landesman SH, Kalish LA, Burns DN, Minkoff H, Fox HE, Zorrilla C, *et al.* Obstetrical factors and the transmission of human immunodeficiency virus type 1 from mother to child. The Women and Infants Transmission Study. *N Engl J Med* 1996;334:1617–23.
 38. Newell ML, Dunn DT, Peckham CS, Semprini AE, Pardi G. Vertical transmission of HIV-1: maternal immune status and obstetric factors. The European Collaborative Study. *AIDS* 1996;10:1675–81.
 39. Van Dyke RB, Korber BT, Popek E, Macken C, Widmayer SM, Bardeguez A, *et al.* The Ariel Project: A prospective cohort study of maternal–child transmission of human immunodeficiency virus type 1 in the era of maternal antiretroviral therapy. *J Infect Dis* 1999;179:319–28.
 40. Leitich H, Bodner-Adler B, Brunbauer M, Kaidler A, Egarter C, Husslein P. Bacterial vaginosis as a risk factor for preterm delivery: a meta-analysis. *Am J Obstet Gynecol* 2003;189:139–47.
 41. Hashemi FB, Ghassemi M, Roebuck KA, Spear GT. Activation of human immunodeficiency virus type 1 expression by *Gardnerella vaginalis*. *J Infect Dis* 1999;179:924–30.
 42. Hashemi FB, Ghassemi M, Faro S, Aroutcheva A, Spear GT. Induction of human immunodeficiency virus type 1 expression by anaerobes associated with bacterial vaginosis. *J Infect Dis* 2000;181:1574–80.

43. Townsend CL, Cortina-Borja M, Peckham CS, Tookey PA. Antiretroviral therapy and premature delivery in diagnosed HIV-infected women in the United Kingdom and Ireland. *AIDS* 2007;21:1019–26.
44. Beckerman KP, Morris AB, Stek A. Mode of delivery and the risk of vertical transmission of HIV-1. *N Engl J Med* 1999;341:205–6.
45. National Institute for Health and Clinical Excellence. *Antenatal Care: Routine Care for the Healthy Pregnant Woman*. Clinical Guidance No.62. London: NICE; 2008 [www.nice.org.uk/CG062].
46. Yudin MH, Prosen TL, Landers DV. Multiple-marker screening in human immunodeficiency virus-positive pregnant women: screen positivity rates with the triple and quad screens. *Am J Obstet Gynecol* 2003;189:973–6.
47. Gross S, Castillo W, Crane M, Espinosa B, Carter S, DeVaux R, et al. Maternal serum alpha-fetoprotein and human chorionic gonadotropin levels in women with human immunodeficiency virus. *Am J Obstet Gynecol* 2003;188:1052–6.
48. Einstein FH, Wright RL, Trentacoste S, Gross S, Merkatz IR, Bernstein PS. The impact of protease inhibitors on maternal serum screening analyte levels in pregnant women who are HIV positive. *Am J Obstet Gynecol* 2004;191:1004–8.
49. Brossard P, Bouvain M, Coll O, Barlow P, Aebi-Popp K, Bischof P, et al. Is screening for fetal anomalies reliable in HIV-infected pregnant women? A multicentre study. *AIDS* 2008;22:2013–7.
50. Tess BH, Rodrigues LC, Newell ML, Dunn DT, Lago TD. Breastfeeding, genetic, obstetric and other risk factors associated with mother-to-child transmission of HIV-1 in Sao Paulo State, Brazil. Sao Paulo Collaborative Study for Vertical Transmission of HIV-1. *AIDS* 1998;12:513–20.
51. Somigliana E, Bucceri AM, Tibaldi C, Alberico S, Ravizza M, Savasi V, et al. Early invasive diagnostic techniques in pregnant women who are infected with the HIV: a multicenter case series. *Am J Obstet Gynecol* 2005;193:437–42.
52. Mandelbrot L, Jasseron C, Ekoukou D, Batallan A, Bongain A, Pannier E, et al. Amniocentesis and mother-to-child human immunodeficiency virus transmission in the Agence Nationale de Recherches sur le SIDA et les Hépatites Virales French Perinatal Cohort. *Am J Obstet Gynecol* 2009;200:160.e1–9.
53. Coll O, Suy A, Hernandez S, Pisa S, Lonca M, Thorne C, et al. Prenatal diagnosis in human immunodeficiency virus-infected women: a new screening program for chromosomal anomalies. *Am J Obstet Gynecol* 2006;194:192–8.
54. Townsend CL, Willey BA, Cortina-Borja M, Peckham CS, Tookey PA. Antiretroviral therapy and congenital abnormalities in infants born to HIV-infected women in the UK and Ireland, 1990–2007. *AIDS* 2009;23:519–24.
55. Stratton P, Tuomala RE, Abboud R, Rodriguez E, Rich K, Pitt J, et al. Obstetric and newborn outcomes in a cohort of HIV-infected pregnant women: a report of the women and infants transmission study. *J Acquir Immune Defic Syndr Hum Retrovirol* 1999;20:179–86.
56. Suy A, Martinez E, Coll O, Lonca M, Palacio M, de LE, et al. Increased risk of pre-eclampsia and fetal death in HIV-infected pregnant women receiving highly active antiretroviral therapy. *AIDS* 2006;20:59–66.
57. European Collaborative Study, Swiss Mother and Child HIV Cohort Study. Combination antiretroviral therapy and duration of pregnancy. *AIDS* 2000;14:2913–30.
58. Grosch-Woerner I, Puch K, Maier RF, Niehues T, Notheis G, Patel D, et al. Increased rate of prematurity associated with antenatal antiretroviral therapy in a German/Austrian cohort of HIV-1-infected women. *HIV Med* 2008;9:6–13.
59. Boer K, Nellen JF, Patel D, Timmermans S, Tempelman C, Wibaut M, et al. The AmRo study: pregnancy outcome in HIV-1-infected women under effective highly active antiretroviral therapy and a policy of vaginal delivery. *BJOG* 2007;114:148–55.
60. International Perinatal HIV Group. Duration of ruptured membranes and vertical transmission of HIV-1: a meta-analysis from 15 prospective cohort studies. *AIDS* 2001;15:357–68.
61. Aagaard-Tillery KM, Lin MG, Lupo V, Buchbinder A, Ramsey PS. Preterm premature rupture of membranes in human immunodeficiency virus-infected women: a novel case series. *Infect Dis Obstet Gynecol* 2006;2006:532–34.
62. Alvarez JR, Bardeguéz A, Iffy L, Apuzzio JJ. Preterm premature rupture of membranes in pregnancies complicated by human immunodeficiency virus infection: a single center's five-year experience. *J Matern Fetal Neonat Med* 2007;20:853–7.
63. Cotter A, Duthely ML, Gonzalez-Quintero V, Sullivan MJO. Duration of membrane rupture and vertical transmission of HIV: Does the four hour rule still apply? *Am J Obstet Gynecol* 2004;191(6 Suppl 1):S56.
64. Garcia-Tejedor A, Maiques V, Perales A, Lopez-Aldeguer J. Influence of highly active antiretroviral treatment (HAART) on risk factors for vertical HIV transmission. *Acta Obstet Gynaecol Scand* 2009;88:882–7.
65. Lydon-Rochelle M, Holt VL, Easterling TR, et al. Risk of uterine rupture during labor among women with a prior cesarean delivery. *N Engl J Med* 2001;345:3–8.
66. Duarte G, Read JS, Gonin R, Freimanis L, Ivalo S, Melo VH, et al. Mode of delivery and postpartum morbidity in Latin American and Caribbean countries among women who are infected with human immunodeficiency virus-1: the NICHD International Site Development Initiative (NISDD) Perinatal Study. *Am J Obstet Gynecol* 2006;195:215–29.
67. Fiore S, Newell ML, Thorne C. Higher rates of post-partum complications in HIV-infected than in uninfected women irrespective of mode of delivery. *AIDS* 2004;18:933–8.
68. National Institute for Health and Clinical Excellence. *Intrapartum Care: Care of Healthy Women and their Babies during Childbirth*. Clinical Guidance No. 55. London: NICE; 2007 [http://guidance.nice.org.uk/CG55].
69. Fakoya A, Lamba H, Mackie N, Nandwani R, Brown A, Bernard E, et al. British HIV Association, BASHH and FSRH guidelines for the management of the sexual and reproductive health of people living with HIV infection 2008. *HIV Med* 2008;9:681–720.
70. Owens DK, Holodniy M, Garber AM, Scott J, Sonnad S, Moses L, et al. Polymerase chain reaction for the diagnosis of HIV infection in adults. A meta-analysis with recommendations for clinical practice and study design. *Ann Intern Med* 1996;124:803–15.
71. Lambert JS, Harris DR, Stiehm ER, Moye J Jr., Fowler MG, Meyer WA III, et al. Performance characteristics of HIV-1 culture and HIV-1 DNA and RNA amplification assays for early diagnosis of perinatal HIV-1 infection. *J Acquir Immune Defic Syndr* 2003;34:512–9.
72. Gilling-Smith C, Nicopoullos JD, Semprini AE, Frodsham LC. HIV and reproductive care: a review of current practice. *BJOG* 2006;113:869–78.
73. de Vicenzi LA. Longitudinal study of human immunodeficiency virus transmission by heterosexual partners. European Study Group on Heterosexual Transmission of HIV. *N Engl J Med* 1994;331:341–6.
74. Castilla J, Del RJ, Hernando V, Marincovich B, Garcia S, Rodriguez C. Effectiveness of highly active antiretroviral therapy in reducing heterosexual transmission of HIV. *J Acquir Immune Defic Syndr* 2005;40:96–101.
75. Semprini AE, Levi-Setti P, Bozzo M, Ravizza M, Taglioretta A, Sulpizio P, et al. Insemination of HIV-negative women with processed semen of HIV-positive partners. *Lancet* 1992;340:1317–19.
76. Gilling-Smith C. HIV prevention. Assisted reproduction in HIV-discordant couples. *AIDS Read* 2000;10:581–7.
77. Bujan L, Hollander L, Coudert M, Gilling-Smith C, Vucetich A, Guibert J, et al. Safety and efficacy of sperm washing in HIV-1-serodiscordant couples where the male is infected: results from the European CREAtH network. *AIDS* 2007;21:1909–14.
78. Wright TC, Jr, Ellerbrock TV, Chiasson MA, Van Devanter N, Sun XW. Cervical intraepithelial neoplasia in women infected with human immunodeficiency virus: prevalence, risk factors and validity of Papanicolaou smears. *Obstet Gynecol* 1994;84:591–7.

APPENDIX

Clinical guidelines are: 'systematically developed statements which assist clinicians and patients in making decisions about appropriate treatment for specific conditions'. Each guideline is systematically developed using a standardised methodology. Exact details of this process can be found in Clinical Governance Advice No. 1: *Development of RCOG Green-top Guidelines* (available on the RCOG website at www.rcog.org.uk/womens-health/clinical-guidance/development-rcog-green-top-guidelines-policies-and-processes). These recommendations are not intended to dictate an exclusive course of management or treatment. They must be evaluated with reference to individual patient needs, resources and limitations unique to the institution and variations in local populations. It is hoped that this process of local ownership will help to incorporate these guidelines into routine practice. Attention is drawn to areas of clinical uncertainty where further research may be indicated within the appropriate health services.

The evidence used in this guideline was graded using the scheme below and the recommendations formulated in a similar fashion with a standardised grading scheme. Once adapted for local use, these guidelines are no longer representative of the RCOG.

Classification of evidence levels	Grades of recommendations
1++ High-quality meta-analyses, systematic reviews of randomised controlled trials or randomised controlled trials with a very low risk of bias	A At least one meta-analysis, systematic reviews or randomised controlled trial rated as 1++ and directly applicable to the target population; or A systematic review of randomised controlled trials or a body of evidence consisting principally of studies rated as 1+, directly applicable to the target population and demonstrating overall consistency of results
1+ Well-conducted meta-analyses, systematic reviews of randomised controlled trials or randomised controlled trials with a low risk of bias	B A body of evidence including studies rated as 2++ directly applicable to the target population and demonstrating overall consistency of results; or Extrapolated evidence from studies rated as 1++ or 1+
1- Meta-analyses, systematic reviews of randomised controlled trials or randomised controlled trials with a high risk of bias	C A body of evidence including studies rated as 2+ directly applicable to the target population and demonstrating overall consistency of results; or Extrapolated evidence from studies rated as 2++
2++ High-quality systematic reviews of case-control or cohort studies or high-quality case-control or cohort studies with a very low risk of confounding, bias or chance and a high probability that the relationship is causal	D Evidence level 3 or 4; or Extrapolated evidence from studies rated as 2+
2+ Well-conducted case-control or cohort studies with a low risk of confounding, bias or chance and a moderate probability that the relationship is causal	Good practice point
2- Case-control or cohort studies with a high risk of confounding, bias or chance and a significant risk that the relationship is not causal	 Recommended best practice based on the clinical experience of the guideline development group
3 Non-analytical studies; e.g. case reports, case series	
4 Expert opinion	

This Guideline was produced on behalf of the Guidelines Committee of the Royal College of Obstetricians and Gynaecologists by: Dr NM Low-Beer MRCOG, London; Miss ZJ Penn FRCOG, London.

It was peer reviewed by: British HIV Association; Children's HIV Association; British Maternal and Fetal Medicine Society; Centre for Paediatric Epidemiology and Biostatistics Institute of Child Health; Dr Y Gileece, Brighton; Royal College of Midwives; Centre for Paediatric Epidemiology and Biostatistics Institute of Child Health; Royal College of Paediatrics and Child Health.

The final version is the responsibility of the Guidelines Committee of the RCOG.

The guideline review process will commence in 2013
unless otherwise indicated

DISCLAIMER

The Royal College of Obstetricians and Gynaecologists produces guidelines as an educational aid to good clinical practice. They present recognised methods and techniques of clinical practice, based on published evidence, for consideration by obstetricians and gynaecologists and other relevant health professionals. The ultimate judgement regarding a particular clinical procedure or treatment plan must be made by the doctor or other attendant in the light of clinical data presented by the patient and the diagnostic and treatment options available within the appropriate health services.

This means that RCOG Guidelines are unlike protocols or guidelines issued by employers, as they are not intended to be prescriptive directions defining a single course of management. Departure from the local prescriptive protocols or guidelines should be fully documented in the patient's case notes at the time the relevant decision is taken. Once adapted for local use, these guidelines no longer represent the views of the RCOG.