Royal College of Obstetricians and Gynaecologists

Setting standards to improve women's health

MANAGEMENT OF HIV IN PREGNANCY

1. Background

HIV infection is associated with high morbidity and mortality. Effective treatment with a combination of three or more anti-retroviral drugs, known as highly active anti-retroviral therapy (HAART), has the capacity to prolong greatly the quality and length of life. British HIV Association guidelines regarding the treatment of HIV infection and HAART regimens used are available from the website: www.aidsmap.com. In the UK, it is estimated that 49 500 adults are infected with HIV, of whom one-third are unaware of their diagnosis.[1] Among adults newly diagnosed with HIV in the UK, 58% are thought to have acquired their infection through heterosexual exposure, of whom the majority are of black African ethnicity and who were probably infected in sub-Saharan Africa.[1] The incidence of heterosexually acquired HIV infection in the UK is rising steadily. Life expectancy is increased as a result of HAART. These factors have led to an increase in the prevalence of pregnant women who are HIV positive in the UK.[1] The Unlinked Anonymous Prevalence Monitoring Programme was introduced in 1990 to assess the prevalence of HIV infection, both diagnosed and undiagnosed, in accessible groups of the adult population. Data from this programme showed that, in 2002, there were an estimated 686 births to HIV-positive women in the UK, with over 60% of these in London. The prevalence of HIV infection in women giving birth in London was 0.38%, compared with 0.06% in both the rest of England and in Scotland.[1]

The risk of mother-to-child transmission of HIV varies between 15% and 20% in non-breastfeeding women in Europe and between 25% and 40% in breastfeeding African populations.[2] Mother-to-child transmission of HIV is largely preventable where universal antenatal HIV screening is undertaken, exclusive artificial formula feeding is feasible and where there is the provision for anti-retroviral therapy and delivery by caesarean section. The principal risks of transmission are related to maternal plasma viral load, obstetric factors and infant feeding.

It is well established that advanced maternal HIV disease, low antenatal CD4 T-lymphocyte counts and high maternal plasma viral loads are associated with an increased risk of mother-to-child transmission.[3] The latter is now recognised as being the strongest predictor of transmission. Two large studies demonstrated that perinatal transmission was significantly associated with maternal plasma viral load.[4,5] These studies also showed that no transmission occurred where maternal plasma viral load was less than 1000 copies/ml (0/57)[4] and less than 500 copies/ml (0/84).[5] However, a meta-analysis of seven prospective studies demonstrated 44 cases of perinatal HIV transmission among 1202 women with plasma viral loads of less than 1000 copies/ml at or near the time of delivery.[6] These data suggest that, at present, there is insufficient evidence for a plasma viral load threshold below which transmission never occurs. Current plasma viral load assays have lower limits of detection than those used in the above studies (as low as 50 copies/ml).

In women who do not breastfeed, it is estimated that, in the absence of intervention, over 80% of HIV transmissions from mother to child occur late in the third trimester (from 36 weeks), during labour and at delivery, with fewer than 2% of transmissions occurring during the first and second trimesters.[7] The principal obstetric risk factors for mother-to-child HIV transmission are vaginal delivery, duration of membrane rupture, chorioamnionitis and preterm delivery.[8]

Breastfeeding is associated with a two-fold increase in the rate of HIV transmission. UK data obtained at a time when HAART was not yet available suggest that pregnant women who are HIV positive who breastfeed their baby increase the risk of mother-to-child transmission from approximately 14% to 28%.[9]

Observational studies from North America and Europe suggest that, in women without advanced HIV disease, there is no increased risk of accelerated immnosuppression in pregnancy, although CD4 T-lymphocyte counts fall during pregnancy and return to prepregnancy levels postpartum.

This guideline relates to the management of HIV in pregnancy in developed countries, as it was considered beyond the scope of a single guideline to address management in both developed and developing country settings.

2. Identification and assessment of evidence

A literature search was performed using Medline (1983–2002). The keywords used were 'HIV', 'pregnancy', 'mother-to-child transmission' and 'vertical transmission'. Reference lists of the articles identified were hand searched for additional articles. Articles relating to management of HIV in pregnancy in developing country settings were excluded (see above).

The definitions of the types of evidence used in this guideline originate from the US Agency for Health Care Research and Quality. 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 care

Pregnant women should be offered screening for HIV early in pregnancy because appropriate antenatal interventions can reduce maternal-to-child transmission of HIV infection.

| A |

Recognition of HIV infection in pregnant women is the key to the prevention of childhood HIV infection. Rates of diagnosis of HIV in pregnant women have increased since the introduction in 1999 of UK Department of Health guidelines stating that antenatal clinics should offer and recommend named voluntary HIV testing to all women across the country.[10-12]

Evidence level Ib

All midwives should have sufficient understanding of HIV and prevention of mother-to-child transmission to enable them to include HIV antibody testing among the routine booking investigations. However, a positive HIV antibody test result should be given to the woman in person by an appropriately trained health professional; this may be a specialist nurse, midwife, HIV physician or obstetrician.

Women diagnosed as HIV positive during pregnancy should be managed by a multidisciplinary team.

| C |

There should be a clear referral pathway for pregnant women who are HIV positive.[13] This should include an HIV physician, an obstetrician, a midwife, a paediatrician and may also include a psychiatric team and support groups.[14]

Evidence level IV

Women with particular social difficulties, such as those with housing or immigration problems, will require considerable input from social workers. Women who use drugs will require additional support from drug-dependency specialists. A carefully documented detailed plan of care and multidisciplinary meetings are important aspects of the antenatal care of the woman who is HIV positive, whether she is diagnosed before or during pregnancy, and training in giving this information. Counselling should encompass the full implications of an HIV-positive diagnosis during pregnancy, which must be addressed over several visits.

It is important that all health professionals involved in the antenatal and intrapartum care of a woman who is HIV positive are aware of her HIV diagnosis and plan of care, and this should be explained to the woman. However, she should be reassured that her confidentiality will be respected. The issue of disclosure of the HIV diagnosis to her partner should be handled with sensitivity. Detailed guidance has been published by the General Medical Council.[15] The woman's HIV diagnosis may be disclosed to a known sexual contact, in order to protect him from acquiring infection, where the woman has not informed him and cannot be persuaded to do so. The woman must be told of the disclosure and the clinician must be prepared to justify it. Information must not be disclosed to others, for example relatives, who are not at risk of infection. 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 such situations.

Women diagnosed HIV positive during pregnancy should be informed that interventions (such as anti-retroviral therapy, caesarean section and avoidance of breastfeeding) can reduce the risk of mother-to-child HIV transmission from 25–30% to less than 2%.

| **A** |

Interventions to reduce the risk of HIV transmission should be discussed:
- anti-retroviral therapy, given antenatally and intrapartum to the mother and to the neonate for the first 4–6 weeks of life
- delivery by elective caesarean section
- avoidance of breastfeeding.

Evidence level Ib

The implementation of these three interventions combined is associated with a vertical trans-mission rate of less than 2%.[16,17]

Plasma viral load and CD4 T-lymphocyte measurements should be reviewed by the HIV physicians at regular intervals during pregnancy. They will advise as to the choice and timing of anti-retroviral therapy and the need for prophylaxis of *Pneumocystis carinii* pneumonia (PCP). PCP prophylaxis is usually administered when the CD4 T-lymphocyte count is below 200×10^6/l. The first line treatment is co-trimoxazole (a folate antagonist). Women taking anti-retroviral drugs should be monitored for drug toxicities (full blood count, urea and electrolytes, liver function tests, lactate and blood glucose) and should have a detailed ultrasound scan to detect fetal anomalies potentially attributable to teratogenesis.

All women with HIV during pregnancy (whether diagnosed before or during pregnancy) should be reported to the National Study of HIV in Pregnancy and Childhood at the Royal College of Obstetricians and Gynaecologists.

| **C** |

Clinicians in the UK should report prospectively all women with HIV during pregnancy to the National Study of HIV in Pregnancy and Childhood (NSHPC), which complies with the Data Protection Act. An active quarterly reporting system is in place, with a nominated respondent who makes returns for each maternity unit in the UK and Ireland. On reporting a case to the NSHPC, the respondent is asked to complete a standard notification form and subsequently an outcome-of-pregnancy form. Completed forms should be sent to the NSHPC at the RCOG. Any clinician caring for HIV-infected pregnant women who is not aware of the name of the respondent for their unit should contact Dr Pat Tookey at the Institute of Child Health, London,

Evidence level IV

for further information (Tel 020 7829 8686). Data from this study are used in conjunction with the results of unlinked anonymous testing of pregnant women and newborns to estimate the proportion of pregnant women with HIV who are diagnosed by the time of delivery. Infants born to infected women are reported through a parallel paediatric reporting scheme run by the NSHPC in collaboration with the British Paediatric Surveillance Unit of the Royal College of Paediatrics and Child Health.[18]

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All pregnant women who are HIV positive should be screened for genital infections during pregnancy. This should be done as early as possible in pregnancy and repeated at around 28 weeks. Any infection detected should be treated according to UK national guidelines.

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The majority of pregnant women in the UK who are HIV positive come from sub-Saharan Africa, where the prevalence of genital infections is high. Usually, the genital tract viral load will mirror the plasma viral load,[19,20] but discordance may occur,[20] notably in the presence of inflammatory genital infections (*Chlamydia trachomatis* and *Neisseria gonorrhoeae*)[21] or ulceration.[22] Viral load in cervicovaginal secretions has been shown to correlate with mother-to-child HIV transmission.[23]

<div style="text-align: right">Evidence level IIb</div>

Organisms associated with bacterial vaginosis have been shown to stimulate HIV-1 *in vitro*.[24,25] There is a strong association between bacterial vaginosis and preterm birth,[26,27] and preliminary data suggest that bacterial vaginosis may be associated with an increased risk of mother-to-child HIV transmission.[28] Chorioamnionitis, prolonged rupture of membranes and preterm birth have been independently associated with mother-to-child HIV transmission and may be interlinked.[25–27,29]

<div style="text-align: right">Evidence level III</div>

In view of the biological plausibility that increased HIV replication in the genital tract secondary to local infection could increase the risk of mother-to-child HIV transmission, it is recommended that all pregnant women are screened for genital infections. This should include tests for *Chlamydia trachomatis*, *Neisseria gonorrhoeae* and bacterial vaginosis. Screening for syphilis, hepatitis B and hepatitis C should also be performed if this has not already been performed at booking.

Screening for Down syndrome and fetal anomalies should be offered. A detailed ultrasound scan for fetal anomalies is important after first-trimester exposure to HAART and folate antagonists used for prophylaxis against PCP.

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The risks of mother-to-child transmission with chorionic villus sampling or second-trimester amniocentesis are uncertain. Where invasive prenatal diagnosis is contemplated, the advice of the fetal medicine specialist and HIV physician should be sought and prophylaxis with HAART considered.

<div style="text-align: right">C</div>

An interim report of the International Anti-retroviral Pregnancy Registry, to which all women taking anti-retroviral therapy in pregnancy should be reported, has found no increase in the total number of fetal anomalies or any specific anomaly.[30] However, information regarding exposure to folate antagonists, such as co-trimoxazole, are not currently collected by this Registry. One multicentre retrospective study of 195 mother–infant pairs found that, compared with infants not exposed to anti-retroviral therapy or folate antagonists during the first trimester ($n = 148$), exposure to both anti-retroviral therapy and folate antagonists during the first trimester ($n = 13$) was associated with an increased risk of congenital abnormalities (4% versus 23.1%; OR 7.10, 95% CI 1.5–34.2), including one case of spina bifida. There was no evidence of teratogenicity associated with anti-retroviral therapy if given alone.[31] This study was limited by its small size and the absence of information on folic acid supplementation, exposure to other medications and illegal drug use. However, it highlights the need for vigilance with respect to the potential

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teratogenic risk of drugs used in the treatment of HIV infection. Whether periconceptual folate is effective in reducing the risk of neural tube defects in those taking folate antagonists such as co-trimoxazole is unknown.

<div style="text-align:right">Evidence level III</div>

There are few data on the risks of iatrogenic mother-to-child HIV transmission occurring as a result of chorionic villus sampling or amniocentesis. However, where such a procedure is performed and the pregnant woman is not already taking HAART, the HIV physician may advise that HAART be given prophylactically prior to the procedure to reduce transmission risk.[14]

<div style="text-align:right">Evidence level IV</div>

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

C

Preliminary data from a London cohort suggest that pre-eclampsia is more common among pregnant women treated with HAART compared with those not taking anti-retroviral therapy.[32] However, the clinical presentation of pre-eclampsia and toxic effects of anti-retroviral therapy may overlap: lactic acidosis is a recognised complication of certain HAART regimens and may mimic the symptoms and signs of pre-eclampsia. The deaths of three pregnant women who took the anti-retroviral drugs stavudine with didanosine have raised concern that pregnant women could be more susceptible to this complication.[33] Where this condition is suspected, liver function tests and blood lactate should be monitored. The presenting symptoms of lactic acidosis are often nonspecific but may include gastrointestinal disturbance, fatigue, fever and breathlessness.

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Other anti-retroviral drug toxicities include gastrointestinal disturbances, hepatotoxicity, rashes, glucose intolerance and diabetes. Significant toxicity relating to zidovudine given as single-agent therapy is rare, although a mild self-limiting anaemia is common.[14]

4. Recommendations for prescribing anti-retroviral therapy in pregnancy

Anti-retroviral therapy is given for two reasons during pregnancy; firstly for prevention of mother-to-child transmission (therapy usually discontinued at, or soon after, delivery) and secondly for treatment of the mother to prevent maternal disease progression (therapy continued indefinitely after delivery).

All women who are HIV positive should be advised to take anti-retroviral therapy during pregnancy and at delivery.

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The optimal regimen is determined by an HIV physician on a case-by-case basis. The decision to start, modify or stop anti-retroviral therapy should be undertaken by an HIV physician, in close liaison with other health professionals, notably the obstetrician and paediatrician.

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In 1994, the AIDS Clinical Trials Group (ACTG) protocol 076, which was conducted in the USA and France, demonstrated that zidovudine given as a single agent (zidovudine monotherapy), administered five times daily and initiated between 14 and 34 weeks of pregnancy, intravenously during delivery and to infants for six weeks, reduced the risk of HIV infection in non-breastfeeding populations by two-thirds, from 25.0% to 7.6%.[34] The benefit of this intervention, which was rapidly introduced with considerable success in developed countries, has been supported by many observational studies.

<div style="text-align:right">Evidence level Ib</div>

All pregnant women who are HIV positive should be offered anti-retroviral therapy to prevent mother-to-child transmission.[12,14] Maximising maternal benefit should guide anti-retroviral management. However, the decision to treat and the choice of treatment must take into account both maternal and fetal

considerations. In the UK, there are 17 anti-retroviral drugs currently licensed for the treatment of HIV infection. Zidovudine is the only anti-retroviral drug specifically indicated for use in pregnancy (excluding the first trimester) for prevention of mother-to-child transmission of HIV and is the only anti-retroviral drug available for intravenous administration. However, single-agent zidovudine therapy which does not suppress plasma viraemia to undetectable levels may allow the emergence of resistant virus, particularly in women with more advanced disease, as these women are more likely to have greater plasma viraemia and greater viral replication. Viral resistance may compromise the therapeutic options available to the mother when it becomes necessary for her to commence treatment for her own benefit.

Potent combinations of three or more anti-retroviral drugs, known as HAART, have now become the standard of care for all HIV-positive individuals requiring anti-retroviral therapy for their own health. HAART regimens may include zidovudine as one of their components. British HIV Association guidelines state that that pregnant women for whom HAART is indicated for treatment of their HIV infection (usually those with CD4 T-lymphocyte count of 200–350 $\times$ 10^6/l) should be treated with HAART in the same way as nonpregnant adults.[14] Optimum treatment of the mother will result in full suppression of plasma viraemia to undetectable levels (less than 50 copies/ml by current assays). Although robust data from epidemiological studies are lacking, it is biologically plausible that transmission at this level of plasma viraemia is very rare, except in the case of assay underestimation or discordance between plasma and genital tract viral loads.

Women who do NOT require HIV treatment for their own health require anti-retroviral therapy to prevent mother-to-child transmission. Anti-retroviral therapy is usually commenced between 28 and 32 weeks of gestation and should be continued intrapartum. A maternal sample for plasma viral load should be taken at delivery. Anti-retroviral therapy is usually discontinued soon after delivery but the precise time of discontinuation should be discussed with the HIV physician. Zidovudine is usually administered orally to the neonate for four to six weeks.

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These women usually have a low plasma viral load (less than 10 000–20 000 copies/ml) and a well-preserved CD4 T-lymphocyte count (greater than 350 $\times$ 10^6/l). Anti-retroviral therapy is usually initiated between 28 and 32 weeks of gestation but the timing will be influenced by the risk of preterm delivery. For instance, women with a multiple pregnancy or a history of previous preterm birth may start therapy earlier in order to achieve an undetectable plasma viral load by the time of delivery.

British HIV Association guidelines recommend one of two therapeutic options for women who do not yet require HIV treatment for their own health.[14]

One option is the use of a simplified single-agent zidovudine regimen, given orally twice daily antenatally, intravenously intrapartum and discontinued immediately after delivery. This is in accordance with the data from the aforementioned ACTG 076 study.[34] It is recommended that all women receiving a single-agent zidovudine regimen should be delivered by elective caesarean section.

Evidence level Ib

An alternative option is a short-term anti-retroviral therapy (START) regimen, where HAART is taken for the duration of the pregnancy and discontinued shortly after delivery, provided that the maternal viral load is undetectable. For this reason it is important that a maternal blood sample for viral load is taken at the time of delivery. The precise time at which START is discontinued should be discussed with the HIV physician.

Evidence level IV

For women not requiring HIV treatment for their own health, there is debate about the relative value of START compared with single-agent zidovudine therapy. The advantage of START is that maternal plasma viraemia is more likely to be suppressed to undetectable levels; it may therefore

Evidence level IV

be expected that fewer transmissions will occur with START and that the risk of the mother developing resistant virus may be lower. However, these factors must be balanced against exposure of the mother and fetus to larger numbers of potentially toxic drugs.

Women with advanced HIV should be treated with a HAART regimen. The start of treatment should be deferred until after the first trimester, if possible, and should be continued after delivery.

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These women are likely to have symptomatic HIV infection, a falling or low CD4 T-lymphocyte count (less than 350×10^6/l) and/or a high viral load (greater than 10 000–20 000 copies/ml).

By suppression of plasma viraemia, treatment with HAART is indicated both to improve maternal morbidity and mortality and to prevent mother-to-child transmission.

Initiation of HAART should be deferred until after the first trimester if possible. Resistance-testing may be performed. Many HIV physicians advise that unless zidovudine resistance is detected, this drug should be incorporated into the HAART regimen, as it is the anti-retroviral drug for which the most extensive safety data are available regarding use in pregnancy. The maternal regimen should be continued after delivery and care should be taken to ensure that doses are not missed around the time of delivery.[14]

Women who conceive while taking HAART should continue their HAART regimen if it is effectively suppressing plasma viraemia. For women whose regimen is not suppressing viraemia, a change in therapy after the first trimester may be indicated.

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If the HAART regimen being used is effectively suppressing viraemia, this should be continued, both to improve maternal morbidity and mortality and to reduce transmission.[4,5]

For women whose HAART regimen is not suppressing their viraemia, resistance-testing should be undertaken, and a change in therapy after the first trimester may be indicated.[14]

Women who present with HIV late in pregnancy or during labour, such that a formal immunological and virological assessment is not possible, should be treated with HAART, to include zidovudine. Zidovudine should be administered intravenously intrapartum and the HAART regimen should be continued intrapartum and postpartum until the results of the CD4 T-lymphocyte count and plasma viral load are known.

For these women, a HAART regimen including zidovudine, should be used. Zidovudine should be administered intravenously intrapartum and the HAART regimen should be continued intrapartum and postpartum until the results of the CD4 count and viral load are available.[14] These women should be delivered by caesarean section. Consideration should be given to the timing of caesarean section to allow peak concentrations in the fetal circulation.

All women who receive anti-retroviral therapy in pregnancy should be registered prospectively with the Anti-retroviral Pregnancy Registry, which in Europe is managed by GlaxoSmithKline (http://uk.gsk.com).[15]

5.   Mode of delivery

For women who are HIV positive not taking HAART during pregnancy 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 HIV transmission.[12] However, whether elective caesarean section is of benefit in women taking HAART who have an undetectable plasma viral load at the time of delivery is uncertain.

Women who are HIV positive who have a detectable plasma viral load and/or who are NOT taking HAART should be offered a planned caesarean section as it reduces the risk of mother-to-child transmission of HIV.

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A zidovudine infusion should be started four hours before beginning the caesarean section and should continue until the umbilical cord has been clamped. A maternal sample for plasma viral load should be taken at delivery. The cord should be clamped as early as possible after delivery and the baby should be bathed immediately after the birth.

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Further research is needed to evaluate the effect on mother-to-child transmission and maternal health of planned caesarean section for women who are taking HAART or who have very low viral loads.

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A systematic review of interventions to reduce mother-to-child transmission of HIV included an international multicentre randomised controlled trial of planned caesarean section at 38 weeks compared with planned vaginal birth. This showed a significant reduction in the mother-to-child transmission of HIV with planned caesarean section (RR 0.17, 95% CI 0.05–0.55).[12,14] Similar proportions of women were on anti-retroviral treatment groups between the groups and none of the women breastfed their infants. Secondary non-intention-to-treat analysis by actual mode of birth revealed a 70% reduction in infection of the infant with HIV with elective caesarean section (OR 0.3, 95% CI 0.1–0.8) but no reduction with emergency caesarean section (OR 1.0, 95% CI 0.3–3.7)[17].

Evidence level Ib

A subgroup-analysis of this study showed that, where women received single-agent zidovudine and were delivered by elective caesarean section, the risk of transmission was less than 1%.

These findings are supported by a meta-analysis of 15 prospective cohort studies which included 8533 mother–child pairs. It reported a 50% reduction in the transmission rate in women who underwent an elective caesarean section before the onset of labour or rupture of the membranes.[35] This protective effect persisted when anti-retroviral therapy was used.

Evidence level IIb

It is recommended that delivery by elective caesarean section should be timed to take place after 38 weeks of gestation. This timing reflects the need to balance the risk of respiratory complications in the neonate with the risk of perinatal HIV transmission associated with labour.[14]

Delivery by caesarean section is associated with anaesthetic, intraoperative and postoperative complications. The morbidity related to caesarean section in women who are HIV-positive is not consistent. Some studies have suggested that postoperative complications, particularly sepsis, are increased in women who are HIV-infected compared with those who are uninfected, with complication rates related to the level of maternal immunocompromise.[36-38] However, other studies have found no difference. In the European randomised mode of delivery trial, elective caesarean section was not associated with increased morbidity or mortality compared with vaginal delivery.[17] All women who are HIV-positive undergoing caesarean section should receive prophylactic antibiotics.

Evidence level III

It is biologically plausible that, where women who are HIV positive are delivered by elective caesarean section, the use of a technique of 'bloodless' caesarean section may further reduce the risk of mother-to-child transmission. This involves opening the uterus with a staple gun, which simultaneously cuts and gives haemostasis, thus allowing delivery of the baby through a relatively dry field and contact with maternal blood is avoided.[39]

The randomised controlled study of mode of delivery in Europe was undertaken before widespread use

of HAART. Participants were taking either single-agent zidovudine or no anti-retroviral therapy and viral load data were not available.[17] In a subsequent meta-analysis of seven prospective studies from the USA and Europe of those with plasma viral loads of less than 1000 at or around delivery, the transmission rate for mothers taking anti-retroviral therapy was 1% compared with 9.8% for those not taking anti-retroviral therapy.[6] In a multivariate analysis, transmission was lower with: anti-retroviral therapy, caesarean section, greater birth weight and higher CD4 count. These data suggest that caesarean section reduces transmission risk even where plasma viral load is less than 1000 copies/ml. However, the impact on maternal and child health of caesarean delivery in women with viral loads less than 50 copies/ml is uncertain.

Observational studies have reported very low rates of transmission among women taking HAART with no protective effect of elective caesarean section on mother-to-child transmission risk.[40,41] However, published data are limited.

Some women will prefer to avoid caesarean section and the views of the mother and her obstetric history are important factors. Long labours, particularly those with prolonged ruptured membranes and those ending in emergency caesarean section, should be avoided. Multiparous women who have delivered vaginally before may be particularly favourable candidates for vaginal delivery. Women who are planning to return to a country where subsequent caesarean section deliveries may not be possible or safe may have a particularly strong preference for vaginal delivery.[14]	Evidence level IIb
Women who opt for a planned vaginal delivery should have their membranes left intact for as long as possible. Use of fetal scalp electrodes and fetal blood sampling should be avoided. Women should continue their HAART regimen throughout labour and if an intravenous infusion of zidovudine is required it should be commenced at the onset of labour and continued until the umbilical cord has been clamped. A maternal sample for plasma viral load should be taken at delivery. The cord should be clamped as early as possible after delivery and the baby should be bathed immediately after the birth.	**C** Evidence level III/IV
Women taking HAART, who have an undetectable plasma viral load, should continue their usual oral HAART regimen throughout labour. In addition, intravenous zidovudine infusion during labour may be recommended by the HIV physician in certain circumstances; for example, for a woman who chooses to deliver vaginally despite a detectable plasma viral load. If a zidovudine infusion is required, it should be started at the onset of labour and should be continued until the umbilical cord has been clamped.	Evidence level Ib
Electronic fetal monitoring should be performed according to guidelines from the National Institute for Clinical Excellence (NICE).[42] HIV infection *per se* is not an indication for continuous electronic fetal monitoring. The membranes should be left intact for as long as possible. Fetal scalp electrodes and fetal blood sampling should be avoided. An emergency caesarean section should be performed for the usual obstetric reasons and to avoid a prolonged labour and prolonged rupture of membranes.	Evidence level IV
Studies conducted before the advent of HAART found that ruptured membranes for more than four hours were associated with double 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.[43] The relevance of these studies for women taking HAART who have undetectable viral loads is uncertain.	Evidence level IIa
If there is preterm rupture of membranes, with or without labour, the risk of HIV transmission should be set against the risk of preterm delivery. Preterm infants are more likely to be infected with HIV. This may be attributable to underlying chorioamnionitis[29] or to increased susceptibility	Evidence level IIa

of preterm infants to HIV transmission, because of immature immune function, incompetent mucosal barriers or reduced levels of acquired maternal antibody.

<div align="right">Evidence level IIa</div>

There is no known contraindication to the use of short-term steroids to promote fetal lung maturation.

<div align="right">Evidence level IV</div>

6. Postpartum management for the mother

In the UK all women who are HIV positive should be advised not to breastfeed their babies.

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In the UK, where safe infant feeding alternatives are available, women who are HIV positive are advised not to breastfeed. It is estimated that breastfeeding increases the overall mother-to-child HIV transmission rate by 14% for women infected with HIV before birth and by 30% in mothers infected postnatally.[9]

<div align="right">Evidence level Ib</div>

7. Management of the neonate

All infants born to women who are HIV positive should be treated with anti-retroviral therapy from birth.

<div align="right">**A**</div>

In UK centres, all infants born to women who are HIV positive are currently treated with anti-retroviral therapy from birth. Unless the mother started anti-retroviral therapy late in pregnancy (within four weeks of delivery) treatment of the infant may be discontinued after four to six weeks.[14]

<div align="right">Evidence level Ib</div>

Infants of mothers who received zidovudine antenatally and intrapartum, either as single-agent therapy or as part of a HAART regimen, should be given single-agent oral zidovudine.

HAART for neonates may be considered in the case of mothers who started anti-retroviral therapy late in pregnancy. Preterm or sick infants may not tolerate oral therapy and zidovudine is the only anti-retroviral drug available as an intravenous preparation.[14]

<div align="right">Evidence level IV</div>

Maternal antibodies crossing the placenta are detectable in most neonates of mother who are HIV-positive. For this reason, direct viral amplification by polymerase chain reaction (PCR) is used for the diagnosis of infant infections. Typically, tests are carried out at birth, then at three weeks, six weeks and six months. For non-breastfed babies, over 99% of those testing HIV-negative by PCR at six months will be uninfected. The definitive test is the HIV antibody test: a negative result at 18 months of age confirms that the child is uninfected.

<div align="right">Evidence level IV</div>

8. Prepregnancy management

For couples discordant for HIV infection who wish to conceive, appropriate advice should be given to optimise the chance of conception while minimising the risk of sexual transmission. *In vitro* fertilisation (IVF) is now considered to be ethically acceptable for couples with subfertility.

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For couples wishing to conceive where one or both partners is HIV positive, prepregnancy counselling should be undertaken by an appropriately trained health professional. For HIV discordant couples where the woman is HIV positive, the couple should be advised on how to perform artificial insemination at the time of ovulation, and quills, syringes and Gallipots may be provided.[44] Where a woman who is HIV negative has an HIV-positive partner, the risk of transmission to the woman, estimated as approximately 1:500 per sexual act, can be reduced by limiting sexual intercourse to around the time of ovulation.[45] 'Sperm washing,' whereby

<div align="right">Evidence level III</div>

spermatozoa are separated from surrounding HIV-infected seminal plasma by a sperm swim-up technique,[46] is available in a number of centres across the UK. NHS funding may be available. To date, there have been no seroconversions in women inseminated with washed sperm.[47] HIV-positive men with low sperm counts may be offered intracytoplasmic sperm injection following sperm washing.[48]

Evidence level III

IVF is now considered ethically acceptable in view of vertical transmission rates of less than 2% and increased life expectancy for parents taking HAART.[49]

Evidence level IV

References

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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: *Guidance for the Development of RCOG Green-top Guidelines* (available on the RCOG website at www.rcog.org.uk/clingov1). 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.

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.

Classification of evidence levels	Grades of recommendations
Ia Evidence obtained from meta-analysis of randomised controlled trials.	**A** Requires at least one randomised controlled trial as part of a body of literature of overall good quality and consistency addressing the specific recommendation. (Evidence levels Ia, Ib)
Ib Evidence obtained from at least one randomised controlled trial.	
IIa Evidence obtained from at least one well-designed controlled study without randomisation.	**B** Requires the availability of well controlled clinical studies but no randomised clinical trials on the topic of recommendations. (Evidence levels IIa, IIb, III)
IIb Evidence obtained from at least one other type of well-designed quasi-experimental study.	
III Evidence obtained from well-designed non-experimental descriptive studies, such as comparative studies, correlation studies and case studies.	**C** Requires evidence obtained from expert committee reports or opinions and/or clinical experiences of respected authorities. Indicates an absence of directly applicable clinical studies of good quality. (Evidence level IV)
IV Evidence obtained from expert committee reports or opinions and/or clinical experience of respected authorities.	**Good practice point**
	✓ Recommended best practice based on the clinical experience of the guideline development group.

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

Valid until April 2007
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