Reducing Mother to Child Transmission of HIV Infection in the United Kingdom

Update Report of an Intercollegiate Working Party
July 2006

Royal College of Paediatrics and Child Health

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Preface

At the time of publication of the first intercollegiate report in 1998, the proportion of pregnant women with HIV in the UK whose diagnosis was known before delivery was very low. This meant that an opportunity for reducing mother to child transmission of the virus was being missed. Since that time, enormous strides have been made in improving the uptake of testing in antenatal clinics, achieving the Department of Health target of 80% uptake by the end of 2002 and since surpassing it. The agencies and health professionals involved can feel justifiably proud of this outstanding achievement.

This updated brief report details the progress made to date and then goes on to address some of the challenges in clinical management that health professionals are still facing. It is not meant to be a comprehensive treatise on the management of HIV in pregnancy as such publications are available elsewhere. Rather, this publication is meant to document the success that has been achieved, to act as a reminder that there is no room for complacency and to provide recommendations for addressing ongoing and future challenges in the field.

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Working Party Chairman

On behalf of:
Royal College of Paediatrics and Child Health
Royal College of Pathologists
Royal College of Obstetricians and Gynaecologists
Royal College of Physicians
Royal College of Midwives
Royal College of General Practitioners
Royal College of Nursing
Health Protection Agency
Faculty of Public Health
Background

Prior to 1998 the UK was lagging behind comparable countries in making HIV testing available for pregnant women. A national Intercollegiate Working Party issued recommendations for action designed to reduce mother to child transmission in the UK by making an offer and recommendation of voluntary confidential HIV testing a routine part of all antenatal care\textsuperscript{1}. The Working Party included members of the UK medical, nursing and midwifery royal colleges and faculties, the Public Health Laboratory Service and other public health bodies, and was also advised by members of groups representing the interests of clients and ethnic minority groups. In 2002 the Working Party reconvened to review progress against its recommendations and against the instructions in a Health Service Circular issued by the Department of Health (DH) in 1999 \textsuperscript{2}. The offer and recommendation of HIV testing to all pregnant women as a routine part of antenatal care has been established nationwide, and there is good evidence that most women are offered testing and accept it. Diagnosed pregnant women will generally opt for the interventions that reduce the likelihood that infection will be passed on to their child and there has been a substantial reduction in the proportion of exposed\textsuperscript{*} infants born with HIV infection. New challenges are emerging because of the increasing complexity of the issues involved in HIV therapy. For example, although antiretroviral therapy substantially reduces mother to child transmission of infection, there are also concerns that fetal exposure to powerful antiretroviral drugs may have unwanted side effects. This update summarises the progress to date in epidemiological terms, highlights future challenges, and makes recommendations for addressing them.

\* Exposed infants – i.e. those born to mothers who are HIV positive
Progress made to date

HIV amongst women in the UK continues to be a significant public health problem. Overall, about 3000 women were newly diagnosed in 2004 compared to about 640 in 1997. At least 90% of women reported in 2004 probably acquired infection through sexual transmission and about three-quarters of these women were probably infected in African countries, Zimbabwe being the single largest contributor.

The prevalence of HIV infection amongst women giving birth has increased markedly since 1997 in London and elsewhere (Figure 1). In 2004 the prevalence in London, the region with the greatest number of births to HIV infected women, was 0.45% (0.19% in 1997). Elsewhere in England the prevalence rose to 0.11% in 2004 (0.016% in 1997). The prevalence among women born in sub-Saharan Africa increased from 1.5% in 1997 to 2.2% in 2004, whereas for those born in the UK prevalence remained low at about 0.03% from 1997 to 2003, although there was a significant increase in 2004 to 0.07%.

![Overall prevalence of HIV infection in pregnant women by area of residence, England and Scotland, 1995-2004](image)

1Unlinked anonymous testing of newborn infant dried blood spots
2Includes previously diagnosed, those diagnosed through antenatal screening and those remaining undiagnosed

Figure 1
Since the introduction in 2000 of the universal offer and recommendation of an HIV test to pregnant women in England as a routine part of antenatal care, and the subsequent implementation of similar policies elsewhere in the UK, uptake of testing has improved substantially. This has led to a considerable improvement in the proportion of previously undiagnosed women being diagnosed during the antenatal period. In England about 30 women were reported as diagnosed in pregnancy in 1997, and this rose to over 560 in 2004; at the same time, an increasing number of women having babies were aware of their diagnosis before becoming pregnant, the number rising from about 70 in 1997 to over 470 in 2004 (unpublished data from the National Study of HIV in Pregnancy and Childhood [NSHPC]).

In 1997 almost 300 HIV infected women gave birth in the UK, of whom only around one third were diagnosed prior to delivery. In 2004 about 1000 HIV infected women gave birth in the UK and detection rate estimates indicate that over 90% of these women were diagnosed prior to delivery (Figure 2).
Improved HIV detection rates have resulted in a reduction in the proportion of exposed children who acquire the infection vertically. In 2004 about 4% of UK-born infants who were exposed to maternal HIV are likely to have been infected (Figure 3); this is in contrast to around 20% in 1997 when the majority of infected women were not diagnosed prior to delivery*. However, the number of HIV infected women giving birth each year in the UK is increasing (and has more than tripled between 1997 and 2004) and this means that there has not been a great reduction in the actual number of infected infants born each year.

Figure 3

*These estimates are based on transmission rates of 26.5% for infants born to undiagnosed women and 2.2% for infants born to diagnosed mothers*.
Future challenges and recommendations

Despite these improvements in antenatal detection rates, and the reduction in the proportion of infected infants, a number of challenges remain, including: development of networks for sharing of expertise and facilities; improvement of case management; evolution in the management of HIV disease; and long term follow-up of infants exposed to antiretroviral drugs.

1. Development of networks

   a) Local multi-disciplinary working

   There are now few parts of the UK where maternity units have not managed cases of HIV infection in pregnancy. However, unit workload is extremely variable with some centres dealing with 40-50 cases per year while others see only an occasional case. Although the management of most cases is straightforward, some require considerable input from the multi-disciplinary team. Early discussions about treatment and delivery options enable the woman to make her own choices in consultation with the professionals. Regular perinatal meetings are necessary to facilitate this, and may include: HIV physicians; midwives; obstetricians; pharmacists; neonatal paediatricians; neonatal nurses; social workers; primary care teams; infectious disease paediatricians and nurses. There are advantages to including a patient representative for generic discussions around policies and practice. Every possible measure needs to be taken to reassure women that disclosure of their diagnosis to the primary care team will not compromise confidentiality in the local community. Failure to disclose the diagnosis to the GP and Health Visitor can result in conflicting advice being given by the primary care team and the hospital and midwifery teams with regard to issues such as breast feeding and infant immunisation.

   **Recommendation:** Every maternity unit should have a regular multi-disciplinary forum for managing HIV in pregnancy with a recognised process for the development of individual birth plans. Such plans should be available at a designated secure site at all times for ready access by labour ward staff. All professionals in the multi-disciplinary team require appropriate training in HIV management. Women should be encouraged to allow disclosure of their diagnosis to the primary care team.
b) Strengthening the national network

The national guidelines produced by the British HIV Association (BHIVA) and the Children’s HIV Association (CHIVA) for the management of HIV in pregnancy and prevention of infant transmission (see websites\textsuperscript{6,7}) have been used as a template by most units for the development of their services and local protocols. A national BHIVA audit (BHIVA Clinical Audit Report 2003-4) was undertaken to assess the use of the guidelines in pregnancy\textsuperscript{6}. This demonstrated that the majority of centres were undertaking appropriate care for pregnant HIV positive women. Nationwide, there is an informal network of HIV specialists who give advice to colleagues on more complex case management. This network needs to be strengthened as do links between services to facilitate the smooth transfer of care for women who move to a different area during pregnancy. UK paediatric HIV services were reviewed in 2004 by the DH, Royal College of Paediatrics and Child Health, Royal College of General Practitioners, BHIVA and CHIVA (Children’s HIV National Network, CHINN, review). The report (to be published) recommends the setting up of Regional Centres for family-based management with a lead paediatrician co-ordinating the post-natal component of care including the follow-up of uninfected infants born to positive mothers.

**Recommendation:** The current informal networks for the management of HIV in pregnancy should be strengthened and formalised on a regional basis. Units with larger and more complex workloads should be recognised and resourced appropriately. The CHINN review recommendations on developing a paediatric HIV network should be implemented to include the follow-up of all children, infected and uninfected, who have been exposed to antiretroviral treatment pre- or post-natally.

2. Case management

There are a number of relatively infrequent situations in which there is an increased risk of vertical transmission of HIV. The management of these scenarios may require different approaches to the routine. They include:

a) Refusal to be tested/denial of an HIV diagnosis

Women who decline an HIV test may do so out of fear of the consequences. After detailed counselling, some may change their minds and a second offer of testing should be made. A similar situation arises for women who accept the offered HIV test but subsequently do not accept the positive result. Considerable effort is required by the multi-disciplinary team to work with these women to make sure that they fully
understand the issues. However, if they choose not to accept treatment before delivery, then avoidance of breast feeding and post-exposure prophylactic treatment for the child may still reduce the risk of transmission. This needs careful planning through a case conference involving social services, ideally held before the birth.

**Recommendation:** Units should have a policy on how to revisit the offer of HIV testing sympathetically at a later stage in pregnancy. For those women who are positive but refuse interventions in pregnancy, a pre-birth case conference should be held to plan post-natal interventions to reduce the risk of transmission.

b) **Emergency treatment in pregnancy to prevent transmission**

HIV and its treatment can have effects on the outcome of pregnancy, with an increased risk of premature delivery\(^8\). Premature infants are also at increased risk of HIV transmission\(^9\). Women who deliver early may not have had time to be tested or, if they have been, to start antiretroviral treatment. Maternity units looking after women with HIV should have emergency protocols for the management of these circumstances. Some women with HIV present late or un-booked at term and only an emergency package of interventions can be applied in this situation. Similarly there are cases where diagnosis is only made in the mother after delivery of the infant, but post-exposure prophylaxis, and avoidance of breast feeding, can still be recommended to reduce the risk of transmission.

**Recommendation:** Labour ward staff should be familiar with the emergency management of deliveries where pre-planning of interventions has not been possible through premature delivery or late/non-booking of the mother in order to reduce the risk of infant infection as far as possible.

c) **Multi-drug resistant virus**

As women with HIV are enjoying better health and survival, some who have been infected for many years are now choosing to become pregnant. Such women may have been exposed to a number of different antiretroviral drugs and are at risk of having multi-drug resistant virus, which is likely to pose a challenge in terms of prevention of transmission. Very close monitoring in pregnancy is required to develop the most appropriate maternal treatment and delivery plan as well as treatment for the infant. In these circumstances it is possible that antiretroviral drugs for which there is relatively little experience of usage in pregnancy will be required, which could have unforeseen side effects in both mother and infant. Such complex cases may increase over the next 5–10 years.
**Recommendation:** The existing National Database for HIV Drug Resistance should be developed to monitor resistance patterns in pregnant women.

d) Maintaining standards

There are a number of reasons why mother to child transmission of HIV may still occur in the UK. In a small proportion of mother-infant pairs, viral transmission occurs despite standard recommended measures. Avoidable transmission may occur when there is failure to offer and recommend HIV testing in pregnancy. The Department of Health has published standards on screening for infectious diseases in pregnancy\(^\text{10}\) to support the UK Antenatal Screening Programme. An increasing number of HIV positive women are giving birth in the UK, and in order to continue to reduce the number of infants with vertically acquired infection it will be important to continue to maintain and improve the uptake of antenatal testing and thus the use of preventive measures in HIV positive women. A confidential enquiry programme into cases where mother to child transmission is known to have occurred would serve to identify systems failures and would inform future strategies for achieving further improvements in outcomes. An audit of cases of vertical transmission in England, 2002-2005, is being undertaken in 2006 by the NSHPC, the London HIV Consortium and the Audit, Information and Analysis Unit (AIAU) for Specialised Services; this project has the backing of CHIVA. The aim is to investigate the circumstances surrounding recent cases of vertical transmission and to make proposals which will contribute to more timely diagnosis, better management and a further reduction in transmission rates.

**Recommendation:** All maternity units should have policies in place adhering to the agreed national standards for Antenatal Screening for Infectious Diseases. A national confidential enquiry programme for investigating cases in which mother to child transmission of HIV occurs should be established in the UK.

3. **Evolution of the management of HIV disease**

The development of new drugs and drug combinations for HIV has been one of the most rapidly evolving treatment areas in the history of medicine. HIV is now considered a chronic infection, requiring long-term management, rather than a rapidly fatal condition. The mainstay of management for preventing HIV transmission since the early 1990s has been zidovudine monotherapy, elective Caesarean section and avoidance of breast feeding for all women regardless of whether they had early or more advanced disease\(^\text{11,12}\) (see table on page 18). A number of aspects of standard care are being reviewed in the
light of HIV treatment developments, but as yet a firm evidence base for a general alteration of policy is lacking. Specific issues are:

a) **Choice of antiretroviral treatment (ART)**
   The management of HIV in general has evolved with the use of highly active antiretroviral therapy (HAART), which has the ability to suppress viral replication. The role of such combination treatments in pregnancy is, as yet, unclear and their use does carry a potential risk of side effects for both mother and fetus. In women already receiving HAART there is little dispute that this should be continued through pregnancy, but in early HIV disease in the mother, whether to commence combination therapy specifically because of the pregnancy or to use standard zidovudine monotherapy and Caesarean section remains an area of uncertainty. As more new classes of antiretroviral treatments become available, this will continue to be an evolving field.

b) **Caesarean section**
   Pre-labour Caesarean section delivery further reduces the risk of transmission in women receiving zidovudine monotherapy and avoiding breast feeding from 6-8% to less than 2% (see table on page 18). In women on HAART with viral loads <50 copies/ml, the rate of transmission is already very low but there is insufficient evidence to know whether there will be a further reduction through performing Caesarean section. Some authorities have suggested that Caesarean section might be unnecessary in selected women with undetectable viral loads on HAART and in whom the likelihood of the need for emergency Caesarean section is low6. Currently in the USA, Caesarean section is only recommended for women with a viral load of >1000 copies/ml13,14.

c) **Breast feeding**
   For women not infected with HIV, breast feeding is the ideal way to feed infants and should be promoted15. However in HIV infected women, breast feeding will contribute significantly to mother to child transmission (see table on page 18). In the UK, nutritionally adequate formula milk alternatives are available and can be obtained on prescription for infants of HIV positive mothers. However, for some women, avoidance of breast feeding is culturally difficult and may be considered a sign to others that the mother is HIV positive. The possibility that some women receiving HAART with undetectable viral load could breast feed safely has been raised. However, although studies are under way, to date there is insufficient evidence to change the current recommendation of universal avoidance of breast feeding. In particular, there is poor knowledge concerning viral loads in breast milk and concerns over the safety of breast feeding while the mother is on HAART16.
**Recommendation:** Surveillance and analysis of the results of different interventions for preventing HIV transmission should be continued so as to enable mothers to receive the best evidence-based management.

4. **Long-term follow-up of antiretroviral exposure in utero**

Animal experiments have demonstrated teratogenic side effects of the different classes of antiretroviral therapy when fetal animals are exposed in utero. The international Antiretroviral Pregnancy Registry (APR) is a voluntary prospective registry of outcome of pregnancy in women treated with ART. Unfortunately, only a small proportion of women treated worldwide are reported to the registry. However, to date (data received by mid-July 2005), no overall increase in congenital abnormalities nor any increase in any particular type of congenital abnormality in relation to any of the classes of antiretroviral drugs has been seen. Similarly, analysis of over 3000 births reported in the UK and Ireland between 1990 and 2003 revealed no significant association between the prevalence of congenital abnormalities and exposure to ART, nor according to whether or not there was first trimester exposure, nor between type of abnormality and class of drug. From 2006, aggregated UK data from the NSHPC has been supplied to the APR and will appear in future reports.

Nucleoside analogues affect mitochondrial DNA in patients on treatment for HIV. Evidence of mitochondrial damage/disease has been demonstrated in a small number of infants in the French cohort of children exposed to antiretroviral therapy in utero, although this has not been confirmed in other cohorts. This is an area requiring continued investigation and surveillance.

Nucleoside analogues intercalate within host DNA and could, potentially, be involved in subsequent processes of carcinogenesis. To date, no increase in malignancies has been reported in infants exposed to antiretrovirals but this may not become apparent for two or three decades. CHART (children exposed to antiretroviral therapy), a Medical Research Council funded 5-year follow-up study of uninfected children exposed to ART in early or fetal life in the UK, based on the NSHPC, was concluded in 2005. One of the study aims was to explore the logistics and feasibility of longer term follow-up of such children and recommendations based on the study findings should be available later in 2006. In addition, although technically complicated because of the need to maintain anonymity, a method of flagging infants born to HIV infected women has been developed by the NSHPC, with the Office for National Statistics, so that deaths or malignancies in ART-exposed children can be identified over the long term.

**Recommendation:** All pregnancies in HIV infected women and their infants should be reported prospectively to the NSHPC and the APR (for addresses see page 17). Robust
mechanisms for very long term follow-up of antiretroviral exposed infants should be continued and enhanced. The CHINN network (see above) should be involved in collecting these data. Currently, funding arrangements for paediatric HIV services are dependent on the reporting of outcomes for infected and uninfected infants and this requirement should be continued. Families will need to be kept fully informed with up-to-date evidence.

References


7. www.bhiva.org/chiva


17. www.apregistry.com


**Useful Addresses**

**National Study of HIV in Pregnancy and Childhood (NSHPC)**
This is the UK surveillance system for obstetric and paediatric HIV for the UK and Ireland, based at the Institute of Child Health, London. HIV infected children and children born to HIV infected women are mainly reported through the British Paediatric Surveillance Unit of the Royal College of Paediatrics and Child Health. Diagnosed pregnant women are mainly reported through a parallel reporting scheme run under the auspices of the Royal College of Obstetricians and Gynaecologists. For further information, contact the principal investigator for the NSHPC: Dr Pat Tookey 0207 829 8686, email: nshpc@ich.ucl.ac.uk

**Antiretroviral Pregnancy Registry (in Europe managed by GlaxoSmithKline)**
GlaxoSmithKline Ltd, Greenford Rd, Greenford, UB6 0HE
Tel no: 020 8966 4500;
Fax 0208 966 2338
www.apregistry.com
## Table of historical interventions to reduce transmission of HIV from mother to child

<table>
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<tr>
<th>Intervention</th>
<th>Approximate Transmission Rate</th>
<th>References</th>
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<tr>
<td>None</td>
<td>25 – 30%</td>
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<tr>
<td>Avoidance of breast feeding</td>
<td>12 – 15%</td>
<td>b</td>
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<tr>
<td>Zidovudine (ZDV) monotherapy</td>
<td>6 – 8%</td>
<td>c,d,e,f,g</td>
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<tr>
<td>Pre-labour Caesarean Section (CS) (+/- ART)</td>
<td>2%</td>
<td>h,i</td>
</tr>
<tr>
<td>Pre-labour CS + ZDV monotherapy</td>
<td>&lt;2%</td>
<td>h</td>
</tr>
<tr>
<td>Combination antiretroviral therapy +/- CS</td>
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<td>j</td>
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<td>(delivery viral load &lt; 400 copies/ml)</td>
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### References

Appendix 1

Lay summary

Infection with HIV continues to be an increasing public health problem in the UK. In 2004 there were around 3000 new diagnoses of HIV in women in the UK and the number of pregnant women infected with HIV continues to rise. The first Intercollegiate Working Party Report, published in 1998, proposed that HIV testing should be offered and recommended to all pregnant women. Since that time there has been a very dramatic increase in the proportion of HIV positive women in the UK who are diagnosed before or during pregnancy, rising from around only one in three in 1997 to about 9 out of 10 in 2004. This has passed the target, set in 1999 by the Department of Health for the end of 2002, of at least 8 out of every 10 affected mothers having their infection diagnosed before delivery. As a result, it has been possible to offer treatment in most affected pregnancies to prevent mother to child transmission of the virus. Consequently, there has been a dramatic fall in the proportion of infants born to HIV positive mothers who have become infected. The health professionals involved in the care of women and their infants can feel justifiably pleased with this achievement. However, since the number of HIV positive women having babies has trebled during this time, the actual overall number of infants becoming infected with HIV has not fallen significantly and there is no room for complacency.

A number of challenges remain to be tackled in order to continue the progress that has been made so far. This follow-up Intercollegiate Report addresses some of these. The remaining challenges include establishing and maintaining standards and ensuring equality of access to specialist expertise and advice, through multi-disciplinary networks of care. Such networks are needed to cater for the fact that HIV positive women are having their babies in maternity units throughout the UK (outside the specialist centres). Continued and improved monitoring of the uptake of HIV testing and the outcomes for mothers and babies remains very important for providing evidence for the effectiveness and safety of different interventions for preventing mother to child transmission of the virus. This will help ensure that mothers are offered the best possible treatment based on up-to-date evidence.
Appendix 2

Members of the Intercollegiate Working Party

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