HIV in pregnant women and prevention of perinatal transmission

Women with HIV who have access to treatment can expect to have a normal life expectancy. With effective antiretroviral therapy, an undetectable viral load, and avoidance of breastfeeding, the rate of perinatal transmission is extremely low (<1%). A Caesarean section is no longer routinely recommended nor is intrapartum zidovudine. Women living with HIV should be supported in their decision regarding parenthood given their excellent prognosis, low risk of perinatal transmission and reproductive rights. If interventions to reduce perinatal HIV transmission during pregnancy and post-partum are embraced, women can expect to have an uninfected infant.

This article provides a succinct review of women, HIV and pregnancy and is focused on the resource rich setting. Differences exist in management and access to interventions in the resource-poor setting but this will not be discussed in this manuscript.

Women with HIV who have access to lifelong combination antiretroviral therapy can expect to have a normal life expectancy. This combined with extremely low rates of perinatal transmission has resulted in many women now contemplating plans for parenthood. One important step in this decision-making is the optimal and safest method of conception. Options for conception need to take into account the HIV status of the partner and fertility issues. Women who are infected with HIV have the option of condomless sex with their partner, self-insemination or assisted reproduction depending on availability and any existing fertility issues. The most important intervention to reduce transmission of HIV to the uninfected partner is treatment with antiretroviral therapy, either as treatment for prevention to the HIV infected partner or as pre-exposure prophylaxis (PrEP) in the HIV-uninfected partner. Data regarding the use of PrEP for conception are limited to observational studies.

Conception

The prognosis of adults living with HIV has continued to improve in the past two decades with the use of combination antiretroviral therapy. Mathematical modelling now suggests that for an adult newly diagnosed with HIV in a resource rich setting, with access to lifelong medication, life expectancy approaches that of HIV uninfected adults. This combined with the extremely low rates of perinatal transmission reported many women living with HIV are contemplating their options for parenthood. One important step in this decision-making is the optimal and safest method of conception. Options for conception need to take into account the HIV status of the partner and fertility issues. Women who are infected with HIV have the option of condomless sex with their partner, self-insemination or assisted reproduction depending on availability and any existing fertility issues. The most important intervention to reduce transmission of HIV to the uninfected partner is treatment with antiretroviral therapy, either as treatment for prevention to the HIV infected partner or as pre-exposure prophylaxis (PrEP) in the HIV-uninfected partner. Data regarding the use of PrEP for conception are limited to observational studies.

Management during pregnancy

The most important intervention to reduce perinatal HIV transmission is antiretroviral therapy for the mother. It has been well established that combination therapy (rather than monotherapy) is the most effective method for reducing maternal viral load, the most important predictor of perinatal transmission. Recent data suggest that the earlier treatment is started, the lower the transmission rate and if women enter pregnancy already on antiretrovirals then these should be continued. Although safety data are still lacking on some of the newer antiretrovirals, the antiretroviral pregnancy registry provides reassuring data excluding teratogenicity for the majority of prescribed first line antiretrovirals.
Historically, elective Caesarean section was recommended as an intervention to reduce perinatal transmission, although the data to support this were primarily before the advent of combination therapy with more recent analyses suggesting the risk of perinatal HIV transmission is comparable in women with an undetectable viral load\textsuperscript{10,11}. Today, vaginal birth is the recommended mode of delivery in women with an undetectable viral load (defined as either <50 copies/mL in guidelines from the United Kingdom to <1000 copies/mL in guidelines from the United States)\textsuperscript{12,13} unless there is an obstetric indication for a Caesarean section. Similarly, intrapartum zidovudine was previously prescribed routinely but is now reserved for women with a viral load at the time of delivery of >1000 copies/mL\textsuperscript{12,13}. In addition to antiretrovirals for the mother, it is recommended that exposed neonates receive four weeks of monotherapy to further reduce the risk of HIV transmission.

### Breastfeeding

When considering breastfeeding, the individual setting needs to be taken into account as guidelines regarding breastfeeding differ significantly between resource rich and resource poor settings. HIV has been found in breast milk and the only way to guarantee that HIV will not be transmitted after birth is for complete avoidance of breastfeeding. However when this is not possible or safe, recent studies have confirmed that with the use of antiretroviral therapy to either the mother or the infant for the duration of breastfeeding, rates of transmission can be reduced\textsuperscript{14–16}. This has re-ignited debate regarding the support of women especially in resource rich settings who desire to breastfeed despite the availability of safe, affordable, culturally appropriate alternatives. In this setting, although the recommendation remains avoidance of breastfeeding, it is becoming increasingly recognised that if a well informed woman elects to breastfeed, knowing the potential risk associated with this, that she should be supported in this decision making process to maximize the likelihood of adherence to antiretroviral therapy rather than it be seen as a child protection issue\textsuperscript{17}.

### Management of the neonate

It is essential that infants born to HIV infected mothers are appropriately followed up and tested after birth. The options for testing include a p24 antigen, HIV RNA, and/or an HIV proviral DNA. The choice of test depends on local availability. For diagnosis of HIV in the neonate, all these tests are suitable and appropriate. The most important issue is that the infant has follow up testing, rather than which test is available, given the equivalent performance of these tests in experienced hands. The recommended timing of testing also varies depending on the individual setting but commonly accepted protocols for follow up testing includes testing in the first week of life, at six weeks, and then three months provided no ongoing exposure via breastfeeding occurs.

### Conclusion

Women living with HIV should be supported in their decision regarding parenthood given their excellent prognosis, low risk of perinatal transmission and reproductive rights. Importantly however, these women need to be well informed regarding the interventions available to reduce risk of HIV transmission to their partners (if they are HIV negative) and to their infant. If these are embraced women can have normal vaginal births and expect to have an uninfected infant.

### References


Diagnosis of congenital syphilis and toxoplasmosis

Syphilis, toxoplasmosis, and cytomegalovirus represent disparate entities. The bacterial spirochaete Treponema pallidum ssp. pallidum causes syphilis, the ‘The Great Imitator’; the organism’s sole natural host is humans and it remains exquisitely sensitive to penicillin. By contrast, the zoonotic parasite Toxoplasma gondii causes toxoplasmosis. Infection is usually self-limited, although serious disease can occur in the immunocompromised. Meanwhile, the human cytomegalovirus (CMV; human herpesvirus 5) is a relatively prevalent enveloped DNA betaherpesvirus with infection specific to humans. Despite nomenclatural, ecological and therapeutic disparities, however, these agents exhibit several concordances, including various, and at times, cryptic syndromes in child and often mother; congenital infections with potentially devastating outcomes; diagnostic dilemmas. This article primarily discusses the latter of these issues in relationship to congenital syphilis and toxoplasmosis in the Australian context.

Syphilis

The number of cases of congenital syphilis has fallen in Australia over the past two decades (1995–2004: 146 cases; 2005–2014: 64 cases)\(^1\). However, there has been a recent resurgence of syphilis particularly amongst men who have sex with men\(^2\), with the overall incidence of infectious syphilis of less than 2 years duration more than doubling (2004–2006: mean 3.5/100 000; 2012–2014: mean 7.7/100 000)\(^3\). Additionally, the burden of disease in indigenous populations is well recognised, and it is possible that fly-in fly-out workers could transmit infections\(^3\). In the United States and United Kingdom re-emergence is also underway, and congenital infections have been linked particularly to primary and secondary syphilis in females\(^4\)–\(^6\). Given the potential for further spread in Australia, ongoing vigilance is required.

Vertical transmission is highest in primary and secondary syphilis, continuing throughout pregnancy while the severity of outcomes decreases\(^7\). Adverse outcomes can include stillbirth or miscarriage, perinatal death, prematurity, low birthweight, and a series of early congenital manifestations (e.g. snuffles, hepatosplenomegaly, generalised lymphadenopathy, bony lesions) and late congenital manifestations (typically due to chronic granulomatous inflammation)\(^4\)–\(^9\).

In Australia, universal screening for syphilis is recommended in pregnancy, with a treponemal-specific serological assay performed at the first antenatal visit, and repeat screening in high-risk populations should be considered at 28 weeks\(^8\),\(^9\). Modalities available for diagnosing congenital syphilis in Australia include both treponemal-specific and non-treponemal specific serology, nucleic acid detection, direct fluorescent antibody testing, and histochemical staining (e.g. Warthin-Starry silver stain) (Table 1); methods of historical