As lifelong maternal cART is now the WHO recommendation, these infant PrEP regimens are less likely to be used on a large scale. There are no clinical trials of maternal cART plus infant PrEP in the context of breastfeeding, although it has been suggested that this could be a feasible approach in resource-poor settings where women may not have fully suppressed viral load and may be more likely to give medication to the infant than take it themselves [77].

Given the health benefits of cART for the woman herself, and the equivalent efficacy of maternal cART and infant PrEP in reducing risk of vertical transmission of HIV through breastfeeding, we recommend that maternal cART (rather than infant PrEP) be used in cases where a woman chooses to breastfeed. There is no need to extend infant PEP beyond 2 weeks simply because of breastfeeding if all of the criteria for VERY LOW RISK are met.

Healthcare providers requiring advice on use of medicines during the breastfeeding period can contact the UK Drugs in Lactation Advisory Service (www.sps.nhs.uk/ukdilas).

When a woman decides to breastfeed, she and her infant should be reviewed monthly in clinic for HIV RNA viral load testing during and for 2 months after stopping breastfeeding (see section 9.5.1.2).

The NSHPC is now collecting enhanced surveillance data on women with HIV who breastfeed and their infants. This will contribute to epidemiological data for the future (www.ucl.ac.uk/nshpc).

9.4.5 Communication with health professionals

With sensitivity to concerns about confidentiality, women should be strongly encouraged to inform partners/families and healthcare providers (including midwives, health visitors and GPs) and anyone else involved in their care (such as lactation consultants) about their HIV status. This will enable the family and local team to give appropriate support and advice, especially regarding feeding, vaccinations and medical assessment of the infant.

9.5 Diagnosis of infant HIV status

9.5.1 Non-breastfed infants

9.5.1.1	Molecular diagnostics for HIV infection should be performed on the following occasions:	1C
	• During the first 48 hours and prior to hospital discharge; • At 6 weeks (or at least 2 weeks after cessation of infant prophylaxis*); • At 12 weeks (or at least 8 weeks after cessation of infant prophylaxis*); • On other occasions if additional risk including at 2 weeks of age if HIGH RISK at delivery. *BHIVA guidelines on duration of PEP have changed for VERY LOW-RISK infants (see section 8.1).	
9.5.1.2	Antibody testing • If the mother's antibody status is not documented, an HIV antibody test should be performed on the first sample from the infant. • HIV antibody testing for seroreversion should be checked at age 22–24 months. • Although an HIV antibody test may be negative before this time, engagement in care should continue until at least 18 months of age.	

9.5.2 Breastfed infants

9.5.2.1	Molecular diagnostics for HIV infection should be performed on the following occasions:	
	• During the first 48 hours and prior to hospital discharge;	1C
	• At 2 weeks of age;	1D

	• Monthly for the duration of breastfeeding;	1D
	• At 4 and 8 weeks after cessation of breastfeeding.	1D
9.5.2.2.	Antibody testing • If the mother's HIV status is not documented, an HIV antibody test should be performed on the first sample from the infant. • HIV antibody testing for seroreversion should be checked at age 22–24 months, or at a minimum of 8 weeks after cessation of breastfeeding, if this is later.	1C

9.5.3 Management of infants diagnosed with HIV

	• Infants with a positive test for HIV should be started on cotrimoxazole prophylaxis from 4 weeks of age.	
	• Infants with a positive test for HIV should be referred urgently to a specialist centre for management of HIV according to Children's HIV Association (CHIVA) and Paediatric European Network for Treatment of AIDS (Penta) guidelines.	
	• A positive HIV diagnosis in an infant should be fed back to the obstetric unit where the infant was born to allow investigation of any avoidable factors in transmission.	

The gold standard test for HIV infection in infancy was HIV DNA PCR on peripheral blood lymphocytes. In a number of studies, including the large French perinatal cohort, equal or increased early sensitivity with amplification of viral RNA with no false-positive results has been reported [78,79].

Infants acquiring HIV intrapartum may have low peripheral blood HIV levels, so HIV DNA/RNA may not be amplified from all infected infants at birth. Indeed, a positive HIV DNA/RNA result within 72 hours of birth is taken as presumptive evidence of intrauterine transmission. Within the first few weeks of life the sensitivity of the viral diagnostic tests increases dramatically and by 3 months of age 100% of non-breastfed infants with HIV are likely to be detected [78].

Although HIV RNA and DNA assays have similar sensitivity, RNA assays commonly require 1 mL plasma, whereas DNA can be performed on smaller samples. If the sample requires dilution due to a low volume, which is often the case with paediatric samples, the lower limit of detection will be increased (with a corresponding decrease in assay sensitivity). In addition, where transmission may have occurred *in utero*, subsequent maternal ART with agents that cross the placenta could lead to a false-negative RNA result in an infected infant. In this situation, the infant should be tested using DNA PCR. As HIV DNA PCR is not widely available, a faster result may be obtained with a local RNA test. However, if HIV RNA is detected, HIV DNA PCR is recommended as a confirmatory test.

The same considerations regarding using primers known to amplify maternal virus apply to both RNA and DNA assays. In view of the genomic diversity of HIV, a maternal sample should always be obtained for HIV DNA or RNA amplification with, or prior to, the first infant sample to confirm that the primers used detect the maternal virus. If the maternal virus cannot be detected, a different primer set and/or test should be used. There has been an increase in the number of cases, usually in women established on ART with undetectable HIV viral load, where it has not been possible to amplify maternal DNA using four different primer sets. An HIV antibody test at 18 months is of particular importance in this scenario.

Evidence from the French perinatal cohort demonstrated that neonatal ART, especially if more than one drug, can delay the detection of both HIV DNA and RNA in the infant [79]. For this reason, the second and third HIV molecular tests are performed at 2 weeks and 2 months after stopping PEP, i.e. usually at 4–6 weeks and 10–12 weeks of age depending on PEP duration. If all tests are negative and the baby is not being/has not been breastfed, parents can be informed that the child does not have HIV. For infants at HIGH RISK of infection, an additional early HIV test may be undertaken at 2–3 weeks of age. For infants breastfeeding from women on cART

(see section 9.4), HIV viral diagnostic tests should be undertaken at least monthly for the woman and infant while breastfeeding, and then additionally for the infant, at 4 and 8 weeks after complete cessation of breastfeeding.

Loss of maternal HIV antibodies should be confirmed at 22–24 months of age [80]. Ideally an HIV antibody test should be used to confirm loss of maternal antibodies rather than a combined HIV antibody–antigen test, and this will almost always be negative by 18 months of age in an uninfected infant. However, combined tests (fourth generation and above) are commonly used and may still give a positive HIV result until up to 2 years of age [81]. Testing for loss of maternal HIV antibody remains important as, rarely, late postnatal infection may occur, even when all early HIV viral genome diagnostic tests were negative (French Perinatal cohort: 5/4539 cases) [82]. This may be due to breastfeeding, premastication of infant food or unknown intrafamilial exposure.

9.5.3 Management of infants diagnosed with HIV

If any of the infant HIV tests are found to be positive, an immediate repeat test on a new sample should be requested to confirm infection. When an infant is diagnosed with HIV, PCP prophylaxis should be started as soon as the baby reaches age 4 weeks, or immediately of the infants is already aged more than 4 weeks. An urgent referral should be made to the local specialist HIV clinic to initiate infant cART. Maternal and infant HIV resistance testing should be undertaken to help delineate reasons for PEP failure and guide treatment. The infant's HIV diagnosis should be fed back to the obstetric unit where the infant was delivered to allow investigation of the circumstances of the transmission.

HIV services for children in the UK are organised in managed networks; details of the Children's HIV National Network (CHINN) and contacts for local paediatricians can be found on the CHIVA website (www.chiva.org.uk).

9.6. Neonatal management in maternal hepatitis co-infection

9.6.1	Follow national guidance for management of maternal HBV in pregnancy and for prevention of transmission of HIV to the infant (see also section 7.1).	1D

Immunoprophylaxis with HBV vaccine with or without HBIG given to the neonate has been shown in separate meta-analyses of randomised controlled trials to significantly reduce vertical transmission from women with HBV alone.

HBIG should be given to the neonate if:

- Maternal HBV DNA concentration is $>10^6$ IU/mL;
- And/or a woman is HBeAg positive;
- Or anti-HBe negative;
- Or anti-HBe is unknown [83].

In the absence of neonatal immunisation with HBV vaccine with or without HBIG, the rate of vertical transmission from a pregnant woman with HBV alone who is both HBsAg and HBeAg positive is 70–90% and for a woman who is HBsAg positive but HBeAg negative is 10–40%. By co-administering vaccination (effectiveness of vaccine *vs* placebo: RR 0.28; 95% CI 0.2–0.4) and HBIG (effectiveness of HBIG/vaccine *vs* vaccine alone: RR 0.54; 95% CI 0.41–0.73), transmission rates can be reduced to between 0% and 14%. The most important determinant of prophylaxis failure has been shown to be maternal serum HBV DNA levels.

Failure of birth-dose vaccine and HBIG in up to 9% of infants despite appropriate post-delivery immunoprophylaxis occurs mainly because of infection *in utero* [84]. Therefore, maternal cART together with prompt post-delivery neonatal immunoprophylaxis is the ideal approach for preventing vertical transmission of HBV.

9.6.2	Follow usual practice for investigation and management of maternal HCV in pregnancy (see also section 7.2).	1D

No postnatal interventions are currently available for reducing risk of transmission of HCV to infants of women with HCV and HIV. Testing and follow-up of these infants should follow usual practice recommended for infants

born to women with HCV alone, with consideration of combining HIV and HCV follow-up assessments in the first 18 months to 2 years.

9.7 HIV exposed but uninfected (HEU)

9.7.1	In light of evidence for possible increased infectious morbidity in HIV exposed but uninfected (HEU) children, timely routine vaccination should be ensured and general practitioners (GPs), health visitors and secondary care physicians should be made aware of possible increased risk in order to inform decisions when assessing risk in primary care.	1D

With increasingly successful rollout of prevention of vertical transmission of HIV interventions across the globe, the number of HEU children is increasing in parallel. A growing body of evidence, mainly from observational studies in low- and middle-income countries, suggests that these children may be at increased risk of morbidity (mainly infection related) in early life (reviewed in [85] and [86]). Multiple potential confounding factors make interpretation and conclusions from such studies challenging. *In utero* exposure to an altered maternal immune system and ART have both been proposed as potential factors contributing to an impairment in HEU neonatal immunity [86]. Much less information is available from high-income settings and findings are inconsistent [87-90].

In view of these concerns, although it remains to be demonstrated that HEU children in the UK are at increased risk of morbidity, the writing group recommends that all healthcare professionals involved in the care of HEU children in early life are made aware of this potential additional risk factor. The need for timely and complete routine immunisations should also be emphasised.

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