LRI Children's Hospital

Human Immunodeficiency Virus (HIV) Infection in Children

Staff relevant to:	Medical & Nursing staff working within UHL Children's Hospital
Team approval date:	July 2022
Version:	6
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Reviewed by:	S Bandi
Trust Ref:	C84/2006

1. Introduction and Who Guideline applies to

This outlines the appropriate management of babies born to HIV positive mothers and children who are known to have HIV infection. It is not fully comprehensive but is intended to give guidance for the management of common clinical presentations.

Given that paediatric HIV care is a rapidly evolving field, up-to-date guidance can be obtained from the Children's HIV Association (CHIVA) at www.chiva.org.uk and from the Paediatric European Network of Treatment in AIDS (PENTA) at www.pentatrials.org.

The management of HIV in pregnancy guidance is available at https://www.bhiva.org/guidelines

This guideline is intended for use by the Medical & Nursing staff working within UHL Children's Hospital

Related documents:

UHL C63/2004 - HIV Screening and Management in Pregnancy UHL Obstetric Guideline

UHL B42/2007 - Blood Borne Viruses (HBV, HCV and HIV) Occupational Exposure UHL Policy

UHL B28/2017 - Needlestick Injuries UHL Childrens Hospital Guideline

2. Guideline Standards and Procedures

Overview:
Globally 36.9 million people are living with HIV/AIDS at the end of 2017(WHO 2018). The number of people receiving HIV related care in the UK was 93,385 in 2017. (PHE 2018).

Children acquire HIV through:

1. Vertical Transmission – this accounts for around 90% of all infections in children (see below for prevention of vertical transmission guidelines)
2. Infected Blood Products – this is rare in the UK
3. Sexual Exposure – including sexual abuse and assault, is extremely rare

2.1 Signs and Symptoms of HIV Infection in Children

Perinatally infected infants and children have accelerated disease progression due to a higher viral set-point and an active thymus (with a larger pool of cells permissive to HIV infection). In addition, naïve T cells have an impaired functional phenotype and are unable to process pathogens effectively. Infants and children may therefore present with diverse, non-specific signs, and a detailed history (including country of origin, mode of delivery, infant feeding, immunisations and prior episodes) is vital in establishing risk of HIV infection.

Some of the more common signs and symptoms include:

1. Failure to Thrive. Many children do not gain weight or grow properly and may fail to reach important milestones.
2. Opportunistic Infections. Risks are generally related to CD4%, but may be seen in young infants with apparently healthy CD4%. Pneumocystis Jiroveci (Carinii)
3. Pneumonia (PJP) is the leading cause of death in children with AIDS worldwide. May be primary presentation; especially in infants under 6 months of age.
4. Recurrent bacterial infections. Sinusitis, otitis media, pneumonia, meningitis and skin infections are commonly seen
5. Candidiasis, may be oral and/or oesophageal. May also cause failure to thrive in HIV infected infants
6. Chronic diarrhoea. May be caused by infectious agents but may also be a direct consequence of HIV in the gut.
7. Lymphoid Interstitial Pneumonitis. Whilst rare in adults, is seen frequently in children and often resolves after the introduction of Anti-Retroviral Therapy (ART)
8. Persistent Generalised Lymphadenopathy. This is a common pulmonary manifestation, which often resolves once ART is effectively introduced.
9. Neuro-developmental delay. This is a frequent manifestation of HIV in children and may be caused by opportunistic infections or neoplasms, but is most commonly due to HIV crossing the blood-brain barrier directly. Children may present with developmental delay, spastic diplegia or regression of milestones in young children, impairment of expressive language in 2-4year olds, and behavioral abnormalities with loss of concentration and memory, cognitive impairment in older children.

2.2 Testing for HIV Infection in Children

Who to consider for HIV testing:

- infants and children whatever their age where the mother has HIV, or may have died of an HIV- associated condition
- infants born to mothers known to have HIV in pregnancy
- infants born to mothers who have refused an HIV test in pregnancy
- infants and children who are presented for fostering/adoption where there is any risk of blood-borne infections
- infants and children newly arrived in the UK from high-prevalence areas (they may be unaccompanied minors)
- infants and children with signs and symptoms suspicious of an HIV infection
- infants and children being screened for immunodeficiency
- infants and children in circumstances of post-exposure prophylaxis
- Infants and children in cases where there has been sexual abuse

If a child is suspected to be HIV positive, the parents/ carers and child (where appropriate) must be counselled before the testing takes place. The Children's HIV specialist nurse is available to undertake the pre and post- test counselling (contact via Hospital Switchboard).
Further guidance on testing is available from the CHIVA website at:
https://chiva.org.uk/guidelines/testing/

Which tests should be undertaken?

1. If the child is under 18 months of age and vertical transmission is suspected HIV PCR should be performed. Send on a virology form (2ml EDTA Sample). Use biohazard bag/stickers on the form/ bottle(s)

2. If the child is over 18 months of age an HIV 1+ 2 antibody test should be performed. Send on a virology form (2ml Clotted sample). Use biohazard bag/ stickers of form/bottle(s).

2.3 Admission to hospital:

Any child requiring hospital admission should be treated on the designated 'on take' ward as their condition dictates. Their HIV care will continue to be provided by the paediatric HIV team as appropriate. Please notify the children's HIV specialist nurse. Decisions on the need to isolate the child should consider the child's current immune function, their presenting problem, and any potential infection risks to the child of being in the open ward.

Infection Control:

Care should be taken to minimise both the risks of HIV transmission to health care workers, family and other contacts, and expose of HIV infected children to other infections. All specimens must be labelled with 'Danger of Infection' stickers and placed in 'Biohazard' bags. Please contact the Infection Control department or the Children's HIV specialist nurse if you have any questions.

2.4 Follow Up For HIV Positive Children:

Children will be seen in the quarterly clinic, held on the second friday of the month in the children's outpatient department. Contact children's HIV specialist nurse to book a clinic appointment.

Confidentiality:

Confidentiality of the child and family must be maintained at all times, and disclosure of diagnosis must only occur on a 'need to know' basis. Do not assume that partners, extended family, friends or the child are aware of the diagnosis. Clear rationale for disclosing the diagnosis should be given, and parental consent should be sought. Do not include HIV diagnosis on hospital discharge letters, as this summary is circulated to other organisations, including schools. Medical and nursing notes must not be marked in a way that discloses the diagnosis. Families will be encouraged to inform their GP and Health Visitor (where appropriate) of their child's HIV status, but information must not be shared until consent is obtained. If in doubt, do not include the diagnosis. Contact children's HIV specialist nurse for advice and further information.

2.5 Highly Active Anti-Retroviral Therapy (HAART) in Children

Principles of HAART

The primary aims of HAART are to:

1. Reduce the amount of HIV circulating in the child's bloodstream (viral load)
2. Increase the child's CD4 cell count or percentage
3. Prevent selection of drug resistant strains of HIV
4. Promote normal growth and development in the child
5. Prevent immune system damage and disease progression by minimising viral replication

Treatment is currently recommended for all children with HIV infection irrespective of the CD4 count (%) and/or viral load.

Medications are available in suspensions, tablets or capsules (only Zidovudine is currently available as an intravenous preparation). They must be given consistently to prevent the risks of viral replication at different stages of its life cycle. Please check for drug interactions as many common medications interact with HAART. (https://www.hiv-druginteractions.org/checker)

HIV therapy must be continued during any hospital admission. Parents/ carers are encouraged to bring medications with them, but when this does not happen, it is possible to obtain them from the hospital pharmacy.

HAART should be prescribed to coincide with existing times given by parents/carers.

2.6 Neonatal Guidelines for the Management of HIV-Exposed Infants

This protocol has been re-written following updated guidelines from the British HIV Association (BHIVA) 2018 (interim update 2020). More detailed information can be found at:
https://www.bhiva.org/file/5f1aab1ab9aba/BHIVA-Pregnancy-guidelines-2020-3rd-interim-update.pdf

2.6.1 Neonatal management: (Post Exposure Prophylaxis (PEP)

- Neonatal PEP should be commenced as soon as possible after birth, and at least within 4 hours.
- In the context of known maternal resistance to zidovudine with VERY LOW or LOW RISK, zidovudine monotherapy is still recommended for infant PEP.
- If HIGH RISK (combination PEP indicated) and there is a history of documented maternal zidovudine and/or nevirapine resistance, seek expert advice. If advice is not immediately available, commence standard three-drug PEP (zidovudine, lamivudine and nevirapine) until guidance is provided.

2.6.2 Very low risk:

Two weeks of zidovudine monotherapy is recommended if all the following criteria are met:
• The woman has been on cART (**c**ombined **A**nti**R**etroviral **T**herapy) for longer than 10 weeks;
AND
• Two documented maternal HIV viral loads <50 HIV RNA copies/mL during pregnancy at least 4 weeks apart;
AND
• Maternal HIV viral load <50 HIV RNA copies/mL at or after 36 weeks.

2.6.3 Low risk:

Extend to 4 weeks of zidovudine monotherapy:
• If the criteria in 2.6.1 are not all fulfilled but maternal HIV viral load is <50 HIV RNA copies/mL at or after 36 weeks;
• If the infant is born prematurely (<34 weeks) but most recent maternal HIV viral load is <50 HIV RNA copies/mL.

2.6.4 High risk:

Use combination PEP if maternal birth HIV viral load is known to be or likely to be >50 HIV RNA copies/mL on day of birth, if uncertainty about recent maternal adherence or if viral load is not known.

2.6.5 PEP and HIV-2

If a woman is known to have HIV-2 infection, follow the above advice as for HIV infant PEP but if HIGH RISK (combination PEP indicated) nevirapine will not be effective. Seek expert advice. If advice is not immediately available, commence zidovudine, lamivudine and raltegravir until guidance is available (see Appendix 3).

2.7 Pneumocystis jiroveci prophylaxis:

Co-trimoxazole prophylaxis is recommended from 1 month of age if HIV PCR screening is positive at any stage or if the infant is confirmed to be diagnosed with HIV. This should only be stopped if HIV infection is subsequently excluded.

2.8 Immunisation:

- Immunisations should be given as per the national schedule outlined in the Green Book.
- Rotavirus vaccine is not contraindicated (unless HIV diagnosis has been confirmed and infant is severely immunosuppressed)

- If there is VERY LOW or LOW RISK of HIV transmission and BCG at birth is indicated as per UK guidelines, this should not be delayed.

2.9 Infant feeding:

- In the UK and other high-income settings, the safest way to feed infants born to women with HIV is with formula milk, to avoid HIV exposure through breast feeding Hence the recommendation is that women living with HIV feed their babies with formula milk.

- Women who are virologically suppressed on cART with good adherence and who choose to breastfeed should be supported to do so, but should be informed about the low risk of transmission of HIV through breastfeeding in this situation and the requirement for extra maternal and infant clinical monitoring.

- 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.

- Maternal cART (rather than infant pre-exposure prophylaxis [PrEP]) is advised to minimise HIV transmission through breastfeeding and safeguard the woman's health.

3. Diagnosis (testing) of infant HIV status:

3.1 Non-breastfed infants: (pro viral DNA along with maternal sample)

- During the first 48 hours and prior to hospital discharge;
- If HIGH RISK, at 2 weeks of age;
- 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
-

HIV antibody testing:

If the mother's antibody status is not documented, an HIV antibody test should be performed on the first sample received 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 with follow-up of the infant should continue until at least 18 months of age.

3.2 Breastfed infants:

- During the first 48 hours and prior to hospital discharge
- At 2 weeks of age
- Monthly for the duration of breastfeeding
- At 4 and 8 weeks after cessation of breastfeeding HIV antibody testing

If the mother's antibody status is not documented, an HIV antibody test should be performed on the first sample received from the infant.
HIV antibody testing for seroversion should be checked at age 22-24 months or at a minimum of 8 week after cessation of breastfeeding, if this is later. Engagement in care should continue until this time.

3.3 Drug Doses for infants

<table>
<tr><th>Drug</th><th>Dose</th><th>Comments/side effects</th></tr>
<tr><td colspan="3">NRTIs: nucleoside reverse transcriptase inhibitors</td></tr>
<tr><td>Zidovudine
(AZT/ZDV)

Liquid – 10 mg/mL</td><td>Oral
≥ 34/40 gestation at birth and > 2kg – see dose banding table

≥34/40 gestation at birth and < 2 kg – 4 mg/kg bd (round upto the nearest 0.5 mg to assist administration)

30-34/40 gestation at birth –
2 mg/kg bd for two weeks then
2 mg/kg three times daily

<30/40 gestation at birth –
2 mg/kg bd
Duration oral dosing:
VERY LOW RISK monotherapy – 2 weeks
LOW RISK monotherapy – 4 weeks
Combination therapy – 4 weeks

Intravenous:
≥34/40 gestation – 1.5 mg/kg four times a day
<34/40 gestation – 1.5 mg/kg bd, change to four times a day at 34/40</td><td>Anaemia, neutropaenia
<table><tr><th>Weight range (kg)</th><th>Oral dose (equivalent to 4 mg/kg)

<u>TWICE A DAY</u></th><th>Volume to be given Orally <u>TWICE A DAY</u></th></tr><tr><td>2.01-2.12</td><td>8.5 mg</td><td>0.85 ml</td></tr><tr><td>2.13-2.25</td><td>9 mg</td><td>0.9 ml</td></tr><tr><td>2.26-2.37</td><td>9.5 mg</td><td>0.95ml</td></tr><tr><td>2.38-2.50</td><td>10 mg</td><td>1 ml</td></tr><tr><td>2.51-2.75</td><td>11 mg</td><td>1.1 ml</td></tr><tr><td>2.76-3.00</td><td>12 mg</td><td>1.2 ml</td></tr><tr><td>3.01-3.25</td><td>13 mg</td><td>1.3 ml</td></tr><tr><td>3.26-3.50</td><td>14 mg</td><td>1.4 ml</td></tr><tr><td>3.51-3.75</td><td>15 mg</td><td>1.5 ml</td></tr><tr><td>3.76-4.00</td><td>16 mg</td><td>1.6 ml</td></tr><tr><td>4.01-4.25</td><td>17 mg</td><td>1.7 ml</td></tr><tr><td>4.26-4.50</td><td>18 mg</td><td>1.8 ml</td></tr><tr><td>4.51-4.75</td><td>19 mg</td><td>1.9 ml</td></tr><tr><td>4.76-5.00</td><td>20 mg</td><td>2 ml</td></tr></table></td></tr>
<tr><td>Lamivudine (10 mg/ml)
(3TC)</td><td>2mg/kg BD – round dose up to 0.5 mg to assist administration</td><td>Anaemia, neutropaenia</td></tr>
<tr><td>Abacavir
(ABC)
Liquid 20 mg/ml</td><td>2mg/kg BD – round dose up to nearest 1mg to assist administration</td><td>Hypersensitivity reaction have not noted in neonates</td></tr>
<tr><td>Tenofovir (TDF)

245 mg tenofovir disoproxil = 300 mg TDF</td><td>Oral: usually as part of combination therapy
All doses now based on tenofovir disoproxil salt (TD)
(*245 mg TD tablet dissolved in 24.5 mL water gives 10 mg/mL)
4.9 mg/kg (0.49 mL/kg*) once a day (round dose up to the nearest 0.5 mg (<10 mg) or 1 mg (≥10 mg) to assist administration)</td><td>Renal dysfunction: consider monitoring renal function weekly</td></tr>
<tr><td colspan="3">NNRTI: non-nucleoside reverse transcriptase inhibitor</td></tr>
<tr><td>Nevirapine
(NVP)</td><td>2mg/kg once a day for 1st week then 4 mg/kg once a day for 1 week and then stop.
(Use 4 mg/kg once a day for 2 weeks if mother has received more than 3 days NVP).</td><td>Rash and liver dysfunction – rare in neonates.
Stop at 2 weeks in view of long half- life. Continue other ART for full 4 weeks</td></tr>
</table>

<table>
<tr><td colspan="3">INSTI: integrase strand transfer inhibitor</td></tr>
<tr><td>Raltegravir
(RAL) (Isentress®)
100 mg sachets for oral suspension (10 mg/mL)</td><td>Oral: usually as part of combination therapy
1.5 mg/kg once a day from birth to day 7, then 3 mg/kg twice a day until 4 weeks of age. See dose banding:
<table><tr><th>Body weight</th><th>Dose</th></tr><tr><td colspan="2">In full term neonates > 37 weeks</td></tr><tr><td colspan="2">Birth to 1 week - once a day dosing</td></tr><tr><td>2 to < 3 kg</td><td>4 mg once a day</td></tr><tr><td>3 to < 4 kg</td><td>5 mg once a day</td></tr><tr><td>4 to < 5 kg</td><td>7 mg once a day</td></tr><tr><td colspan="2">1 to 4 weeks – twice a day dosing</td></tr><tr><td>2 to < 3 kg</td><td>8 mg twice a day</td></tr><tr><td>3 to < 4 kg</td><td>10 mg twice a day</td></tr><tr><td>4 to < 5 kg</td><td>15 mg twice a day</td></tr></table></td><td>Rash and liver dysfunction: monitor liver function tests at 5–7 days of age</td></tr>
<tr><td colspan="3">PI - protease inhibitor</td></tr>
<tr><td>Lopinavir/ritonavir
(Kaletra®)
Liquid:
5 mL = (Lopinavir 400 mg + ritonavir 100 mg)</td><td>Oral: usually as part of combination therapy
300 mg/m2 (of lopinavir) twice a day – use dose banding table below:
<table><tr><th>Weight range (kg)</th><th>Surface area range</th><th>Kaletra volume to be given orally TWICE A DAY</th></tr><tr><td>1 – 1.5</td><td>0.1 – 0.13</td><td>0.5 ml</td></tr><tr><td>1.51 – 2</td><td>0.14 – 0.16</td><td>0.6 ml</td></tr><tr><td>2.01 – 2.5</td><td>0.17 – 0.19</td><td>0.75 ml</td></tr><tr><td>2.51 – 3</td><td>0.2 – 0.21</td><td>0.8 ml</td></tr><tr><td>3.01 – 3.5</td><td>0.22 – 0.24</td><td>0.9 ml</td></tr><tr><td>3.51 – 4</td><td>0.25 – 0.26</td><td>1 ml</td></tr><tr><td>4.01 – 4.5</td><td>0.27 – 0.28</td><td>1.1 ml</td></tr><tr><td>4.51 - 5</td><td>0.29 – 0.30</td><td>1.2 ml</td></tr></table></td><td>Severe adrenal dysfunction, electrolyte imbalance and cardiogenic shock in neonates, especially premature infants.

Avoid in premature infants, only use, as per birth plan, when benefit of giving outweighs the potential risks.

Monitor for signs of toxicity, check U+E, pH, glucose, lactate, LFT, daily for first 5 days</td></tr>
<tr><td colspan="3">FI: fusion inhibitor</td></tr>
<tr><td>Enfuvirtide
(Fuzeon®)
(T-20)</td><td>Intravenous: usually as part of combination therapy
2 mg/kg IV twice a day (as infusion over 30 minutes)
Method: To reconstitute the 108 mg vial slowly add 1.1 mL of water for injections from the vial of diluent provided to the vial of enfuvirtide powder, do not shake or invert the vial. The powder will take up to 45 minutes to dissolve. The resulting solution contains 90 mg in 1 mL. Add 1 mL (90 mg) of the solution to 10 mL of water for injections, then further dilute to 45 mL with water for injections, do not shake or invert the syringe. The final solution contains 90 mg in 45 mL (2 mg in 1 mL) from which to administer the required dose</td><td>Experimental IV dosing regime.
Use only, as per birth plan, when benefit of giving outweighs the potential risks</td></tr>
<tr><td colspan="3">PCP prophylaxis</td></tr>
<tr><td>Co-trimoxazole
(Septrin®)
240 mg in 5 mL liquid</td><td>BW ≥2 kg 120 mg = 2.5 mL BW <2 kg 60 mg = 1.25 mL
ONCE a day on 3 days per week</td><td>Only HIV-infected infants, start at 4 weeks of age. May rarely cause rash and bone marrow suppression</td></tr>
</table>

4. Education and Training

None

5. Monitoring Compliance

What will be measured to monitor compliance	How will compliance be monitored	Monitoring Lead	Frequency	Reporting arrangements
Management of babies born to HIV positive mothers	Audit	S Bandi	4 yearly	Departmental presentation

6. Supporting References

1. http://www.who.int/gho/hiv/en/
2. BHIVA (2018). Guidelines for the Management of HIV infection in Pregnant Women and the Prevention of Mother-to-Child Transmission of HIV. Available at www.bhiva.org/

7. Key Words

Abacavir, AIDS, ART, AntiRetroviral Therapy, Human Immunodeficiency Virus (HIV), Lamivudine, Nevirapine, Raltegravir, Tenofovir, Zidovudine

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The Trust recognises the diversity of the local community it serves. Our aim therefore is to provide a safe environment free from discrimination and treat all individuals fairly with dignity and appropriately according to their needs.
As part of its development, this policy and its impact on equality have been reviewed and no detriment was identified.

CONTACT AND REVIEW DETAILS	
Guideline Lead (Name and Title) Srini Bandi – Consultant Paediatrician	**Executive Lead** Chief Nurse
Details of Changes made during review: **2022** **Follow-up arrangements updated** **Updated testing of breastfed and non-breastfed infants whose mothers' HIV status is not documented**	