The Child with HIV and Acute Illness

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Contents

Summary

- Assess degree of immune suppression (see table 1)
- Take history including previous infections, travel, animals, unwell contacts
- Take: FBC, blood culture, CRP, biochemistry (other cultures as appropriate + malaria films if travel in last 12 months)
- If unwell/ septic, start IV ceftriaxone. NB: Before starting treatment, check for allergies and refer to local antibiotic guidance
- Contact the allocated paediatric HIV team who normally see the child or regional centre if new presentation in UK. (https://www.chiva.org.uk/ourworkprof/regional-networks/)
- Check which antiretroviral drugs the child takes; prescribe these if being admitted, or ensure the family has sufficient supply if being treated as outpatient. Ensure that you check drug interactions: http://www.hiv-druginteractions.org/checker

1. Introduction

Children with HIV infection are told to come to hospital if they become unwell. This is usually either because they have a fever, vomiting and diarrhoea, or a chest infection. These guidelines describe the acute management of these presentations. It is important to notify and/or discuss cases of intercurrent illness in HIV infected children with their allocated paediatric HIV team.

Although viruses are likely to be the most common causes of fever especially in children on effective combination antiretroviral therapy (cART) and good CD4 count/percentage, children with HIV have an increased risk of bacterial infections. General principles are: think about bacterial infection, investigate accordingly, treat with antibiotics earlier, with higher recommended dosing options and discuss the optimal duration with a clinician experienced in the care of HIV infected children (usually the allocated centre for that child).

The commonest *bacterial* causes of fever in HIV infected children are bacteraemia, urinary tract infection (UTI) or pneumonia.[1]

2. HIV disease staging

Severe immunosuppression secondary to HIV infection results in susceptibility to serious infection and can associated with a lack of clinical signs to aid diagnosis or to indicate a clear focus.

- Note the stage of the child's HIV disease.
- Look in medical notes/electronic records or on results system for recent letters and CD4 count. A recent undetectable viral load likely indicates that adherence to antiretroviral therapy has been good.

The CD4 count or percentage indicating severe immune suppression is age dependent.

Table 1: WHO classification of HIV-associated immunodeficiency in infants and children[2]

Classification of HIV-associated immunodeficiency	Age-related CD4 Values			
	< 12 months (% CD4)	12–35 Months (% CD4)	36–59 Months (% CD4)	> 5 years(absolute number/µl or % CD4)
None or not significant	> 35%	> 30%	> 25%	> 500
Mild	30–35%	25–30%	20–25%	350-499
Advanced	25–29%	20–24%	15-19%	200-349
Severe	< 25%	< 20%	< 15%	< 200 or < 15%

3. Medical history and clinical examination

- **BE AWARE THAT YOUNGER CHILDREN AND SOMETIMES OLDER CHILDREN MAY NOT BE AWARE OF THEIR HIV DIAGNOSIS AND THIS SHOULD BE CLARIFIED BEFORE DISCUSSING HIV IN FRONT OF THEM**
- Accompanying adults may not be aware of the HIV diagnosis and this should be clarified with the parent before discussing HIV openly
- Take a detailed history of the acute illness in order to identify a focus of infection and guide treatment.
- Check past medical history from parents and refer to medical notes and letters as parents often find it difficult to reiterate history because of stigma and complexity.
- Note if the child has previously had a severe or opportunistic infection as this increases the likelihood of significant infection
- Check if the child receives antimicrobial prophylaxis
- Record immunisation history (including travel vaccinations)
- Ask about travel history including malaria prophylaxis
- Ask about known TB contact
- Examine the child thoroughly. Signs of other pathology may be masked

4. Antiretroviral drugs

It is important to ensure that antiretroviral drugs have been given and tolerated while the child is unwell, including during admission to hospital for acute illness. HIV viral load may increase and resistance to drugs will develop if antiretroviral drugs are not given as prescribed.

4.1. What medication is the child taking?

- Has the child missed any doses? Record the time they usually take their medications and when the last dose was given
- Has the child vomited their medications? If vomited within 1 hour of a dose, repeat dose. If unable to take, or keep down medication, admit to hospital and give via nasogastric tube (NGT) if possible. Consider ondansetron (anti-emetic) to give the best chance of tolerating medication.

Liquid medication is often large in volume – if not tolerating liquids with antiemetic, consider the use

of crushed tablets (ask pharmacist or check the Summary of Product characteristics (https://www.medicines.org.uk/emc/) if tablets can be crushed; some tablets cannot be cut or crushed (E.g. Kaletra tablets).

5. Initial Investigations – no focus of infection

All children with fever should be tested for COVID-19, if found to be COVID-19 positive discuss with the allocated paediatric HIV team for the child. Initial investigations should be guided by medical history and clinical examination findings. However, if no focus is identified:

5.1. Request the following investigations

- Full blood count and differential (and malaria films if in malaria endemic region within last 12 months)
- CRP
- Blood cultures
- Urea and electrolytes and lactate
- Liver function tests and amylase
- Save serum
- Urine dipstick and M,S+C
- NPA/throat swabs for virology/microbiology

5.2. Other investigations

For children with respiratory symptoms consider:

- Chest x-ray
- Oxygen saturations
- If coryzal, send nasopharyngeal aspirate (NPA) or a throat swab for viral PCR. Immunocompromised children with influenza are eligible for treatment with oseltamivir/ zanamavir[3] and in times of active flu circulation empiric cover should be started.

For children with diarrhoea consider:

- Stool culture for *Salmonella*, *Shigella*, *Campylobacter*, *E Coli*
- Stool microscopy for ova, cysts and parasites
- Stool virology (PCR, ELISA, culture depending on local lab)
- Blood and urine cultures (if febrile)
- Consideration of stool *C difficile* toxin, stool reducing substances (as appropriate)

Other investigations to consider:

- Bacterial throat swabs

- Lumbar puncture if signs of meningitis (measure opening pressure, glucose, protein and send microscopy and culture, microscopy for AFB, India Ink stain and cryptococcal antigen, viral PCR)
- Note: CD4 count & HIV viral load are likely to be unreliable in acutely unwell child. Discuss with the allocated paediatric HIV team for the child and consider ordering these tests if not done within the last four months.

6. Treatment

ALL NEW MEDICATIONS SHOULD BE CHECKED FOR INTERACTIONS WITH CURRENT ANTIRETROVIRAL REGIMEN. http://www.hiv-druginteractions.org/

Check for allergies and use appropriate alternative antibiotics if known drug allergies. If unsure, discuss with the local consultant or Paediatric ID/Microbiology team. Below is the suggested guide for the initial antibiotic choice.

6.1. Antibiotics

If the child is unwell or septic: Treatment with antibiotics should not be delayed pending investigation results. Start intravenous Ceftriaxone or Cefotaxime. Use cBNF dosing options for severe infection.

If the child is well: It may be acceptable to observe, pending investigations to identify cause of illness and target therapy.

6.2. Treatment of specific causes of illness

6.2.1. Influenza

- Immunocompromised children with influenza should be prescribed treatment with oseltamivir (or zanamavir)

6.2.2. Septicaemia

- Mainly pneumococcal (or in children recently arrived from sub-Saharan Africa, non-typhoid salmonella) – symptoms/signs may be masked.
- Admit with investigations as outlined above
- Treat with IV Ceftriaxone or Cefotaxime, use cBNF dosing for severe infection

6.2.3. ENT infections

- Sinusitis: Take throat swabs – viral and bacterial. Treat with oral co-amoxiclav for 10 days and chase results.
- Cervical lymphadenitis. If mild treat with oral co-amoxiclav. If severe may need IV antibiotics (e.g. start with IV ceftriaxone and change to narrow spectrum antibiotics when microbiology

results are back). If fluctuant request an urgent surgical opinion.

6.2.4. Skin infections and abscesses

- Pus (if available) should be sent directly to the laboratory for culture.
    - Take viral, bacterial and fungal swabs.
    - Treat with co-amoxiclav (or follow local antimicrobial guidelines).

6.2.5. Oral infections

- Look for Candida and/ or herpes simplex.
- Take swabs – viral and bacterial.
- Treat with oral fluconazole and/or oral acyclovir (see cBNF for doses).
- If child is having difficulty swallowing, consider endoscopy and biopsy for oesophagitis.

6.2.6. Urinary tract infection (UTI)

- Collect urine sample (method of collection depends on age of child – clean catch, catheter specimen, Supra-Pubic Aspiration)
- Urinalysis, including leucocytes and nitrites
- Send urine culture
- Treat with co-amoxiclav (or follow local antimicrobial guidelines).

6.2.7. Meningitis

- Cross reference NICE meningitis guidelines[4]. Standard first line therapy is cefotaxime/ceftriaxone (use cBNF meningitis doses) +/- clarithromycin +/- acyclovir if signs of encephalitis.
- Consider TB meningitis, cryptococcal meningitis and discuss with allocated HIV lead team.

6.2.8. Pneumonia

- Treat with IV Ceftriaxone or Cefotaxime (use cBNF doses for severe infection). If the child does not improve quickly (24 hours) consider adding a macrolide antibiotics (see cBNF doses).
- If there is a good clinical response, continue the antibiotics for at least 10 days. Co-amoxiclav, or azithromycin are suitable oral options.
- If there is hypoxia or no clinical improvement in 48 hours then a bronchoscopy should be organised to look for Pneumocystis jirovecii pneumonia (PCP) and other atypical respiratory pathogens.

  If bronchoalveolar lavage (BAL) cannot be performed straight away, discuss with allocated paediatric HIV team and start empiric treatment for PCP; intravenous cotrimoxazole (see cBNF doses for PCP). Arrange BAL as soon as possible - can obtain positive results for PCP for several days after starting treatment, PCP PCR can stay positive for some time in spite of

successful treatment. Positive results should be discussed with allocated paediatric HIV team and interpreted in context of clinical symptoms. False positive results may occur. Pneumocystis pneumonitis is a category C defining diagnosis, it is very important to make a definitive diagnosis even after commencing treatment. Steroids should be considered for moderate or severe PCP cases, starting within 72 hours of diagnosis (dosing regimens are outlined in the AIDS*info* NIH guidelines: https://clinicalinfo.hiv.gov/sites/default/files/inline-files/oi_guidelines_pediatrics.pdf

6.2.9. Acute Diarrhoea

- If child is febrile/septic, start IV ceftriaxone/cefotaxime (use cBNF doses for severe infection)
- If stool cultures positive give treatment, guided by lab sensitivities; if not available, consider:
    - *Salmonella*: ceftriaxone or ciprofloxacin
    - *Shigella*: ceftriaxone or ciprofloxacin
    - *Campylobacter*: oral azithromycin or ciprofloxacin
    - *Cryptosporidium:* No agent has proven efficacy in immunocompromised patients. Effective ART and supportive care with attention to fluid balance, electrolyte levels and nutrition constitute the main treatment. Discuss use of Nitazoxanide with allocated paediatric HIV team and local ID/Microbiology team.
    - Microsporidiosis: Albendazole (7.5mg/kg/dose, max 400mg, orally BD) effective against many species except *Enterocytozoon bieneusi*. Nitazoxanide may have activity against *Enterocytozoon bieneusi*.

6.2.10. Concealed sites of infection:

- Consider other occult sites of infection: bone/joints/abdomen/disseminated systemic infection (Mycobacteria/CMV/EBV / measles with no rash, etc).
- Further investigations may be required.
- Ensure that the allocated paediatric HIV team is aware of the child. Re-discuss if fever does not respond to initial treatment.

6.2.11. Oral Candidiasis:

- If prescribing oral/IV antibiotics, warn child/carers to look out for oral candidiasis. If this develops, treat with Miconazole Oral gel or Nystatin.
- If treatment to control candidiasis fails or severe candidiasis develops, give Fluconazole (see cBNF for doses), whilst onantibiotics).

7. Other important points

- Ensure the allocated paediatric HIV team know that you are assessing the child/young person, as soon as possible. Unless very minor illness, the child should be managed jointly with them.
- If being admitted, check if the child is on cART and has their medications with them.
- Ensure child or young person and parent understands the information they have been given.

Further information on management of opportunistic infections can be found in the updated DHHS US Guidelines for Prevention and Treatment of Opportunistic Infections in HIV-Exposed and HIV-Infected Children

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