The Child with HIV and Gastroenteritis

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1. Introduction

HIV-infected children may be severely immunosuppressed (for example, at first presentation) and develop severe or persistent gastroenteritis due to unusual opportunistic organisms, or they may be stable on HAART and develop gastroenteritis with the same pathogens that cause gastroenteritis in HIV-uninfected children.

2. HIV disease staging
Note the stage of the child’s illness.

- The more severely immunosuppressed, the more likely to have minimal signs and serious pathology. Note the stage of the child’s HIV disease.
- Look in notes or on results system for recent letters and CD4 count. A recent undetectable viral load 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

<table>
<thead>
<tr>
<th>Classification of HIV-associated immunodeficiency</th>
<th>Age-related CD4 Values</th>
<th>&lt; 12 months (%) CD4</th>
<th>12–35 months (%) CD4</th>
<th>36–59 months (%) CD4</th>
<th>&gt; 5 years (absolute number/µl or % CD4)</th>
</tr>
</thead>
<tbody>
<tr>
<td>None or not significant</td>
<td>&gt; 35%</td>
<td>&gt; 30%</td>
<td>&gt; 25%</td>
<td>&gt; 500</td>
<td></td>
</tr>
<tr>
<td>Advanced</td>
<td>25–29%</td>
<td>20–24%</td>
<td>15–19%</td>
<td>200–349</td>
<td></td>
</tr>
<tr>
<td>Severe</td>
<td>&lt; 25%</td>
<td>&lt; 20%</td>
<td>&lt; 15%</td>
<td>&lt; 200 or &lt; 15%</td>
<td></td>
</tr>
</tbody>
</table>

### 3. Causes of gastroenteritis

Most children with diarrhoea/vomiting will have an infectious cause:

**Table 2. Causes of Diarrhoea and Vomiting in children with HIV**

<table>
<thead>
<tr>
<th>Minimal immunosuppression</th>
<th>Severe immunosuppression</th>
</tr>
</thead>
<tbody>
<tr>
<td>Viral:</td>
<td>As for minimal immunosuppression group <strong>plus:</strong></td>
</tr>
<tr>
<td>• Rotavirus</td>
<td>Viral:</td>
</tr>
<tr>
<td>• Adenovirus</td>
<td>• CMV</td>
</tr>
<tr>
<td>• Norovirus</td>
<td>• HSV</td>
</tr>
<tr>
<td>• Calcivirus</td>
<td>• HIV enteropathy</td>
</tr>
<tr>
<td>• Astrovirus</td>
<td>Bacterial:</td>
</tr>
<tr>
<td></td>
<td>• <em>Mycobacterium avium</em> complex</td>
</tr>
<tr>
<td><strong>Bacterial:</strong></td>
<td>Protozoal:</td>
</tr>
<tr>
<td>• <em>Campylobacter</em></td>
<td>• <em>Cryptosporidium</em></td>
</tr>
<tr>
<td>• <em>Shigella</em></td>
<td></td>
</tr>
<tr>
<td>• <em>Salmonella</em></td>
<td></td>
</tr>
<tr>
<td>• <em>E Coli</em></td>
<td></td>
</tr>
</tbody>
</table>
• *Yersinia enterocolitica*
• *Clostridium difficile*<sup>a</sup>

**Protozoal:**
• *Giardia*
• *Cryptosporidium*
• *Ameobiasis*

**Helminths:**
• *Ascaris*
• Hookworm
• *Trichiuris*

• *Microsporidia*<sup>b</sup>
• *Isospora belli*
• *Cyclospora*

**Fungi:**
• *Candida*

**Malignancy:**
• Kaposi sarcoma
• Small bowel lymphoma
• Leiomyosarcoma

<sup>a</sup>If recent antibiotic treatment

<sup>b</sup>Most cases due to *Enterocytozoon bieneusi* or *Encephalitozoon intestinalis*

Certain conditions are **WHO Stage IV (AIDS-defining) illnesses:**
• Disseminated mycobacteriosis (e.g. MAC)
• Chronic cryptosporidiosis
• Chronic *Isospora* infection
• Histological diagnosis of CMV infection.

4. **Differential diagnosis**

Not all children with diarrhoea and vomiting have gastroenteritis!

4.1. **Other infections**
• UTI, meningitis, pneumonia, septicaemia
• *Helicobacter pylori* infection
• Children with *Candida* oesophagitis may present with vomiting in addition to dysphagia and retrosternal pain
• Children returning from abroad may present with malaria, typhoid or hepatitis A (all can present with gastroenteritis-like illness)

4.2. **Surgical conditions**
• As for HIV-uninfected children
Consider pancreatitis (secondary to HIV, CMV, Cryptosporidium, ddI, d4T) – check lipase as amylase may be raised due to parotid enlargement

4.3. Medical conditions

- Lactose intolerance is more common in HIV-infected children

4.4. Medication

- Children recently started on HAART may develop gastrointestinal side-effects
  - Abacavir, lamivudine, zidovudine, stavudine most frequently associated with nausea and vomiting
  - Protease inhibitors associated with diarrhoea
- Side effects usually improve over time
- Sometimes short-term loperamide can be helpful.

5. History

- Past history from parents or clinic letters (parents may find it difficult to reiterate history due to stigma)
- Take a good history of the current illness
- Is this acute diarrhoea or persistent (>14 days) diarrhoea?
- Description of diarrhoea
  - Watery stool suggests small intestinal cause
  - Fresh blood suggests colitis
  - Melaena suggests lesions of mouth, nasopharynx, oesophagus or stomach
- Medication history (recently started HAART?)
- Immunisation history
- Travel history (including malaria prophylaxis)
- Note any acute or chronic weight loss

6. Examination

- ABC, signs of shock and acidosis
- Assessment of dehydration
- Signs of toxicity/sepsis
- Signs of other pathology mimicking/masking gastroenteritis

7. Investigations

CHIVA guidelines 2012
• All HIV-infected children with diarrhoea should have the following investigations undertaken:
  o Stool culture for *Salmonella, Shigella, Campylobacter, E Coli*
  o Stool microscopy for ova, cysts and parasites
  o Stool virology (PCR, ELISA, culture depending on local lab)
  o Blood and urine cultures (if febrile)
  o Consideration of stool *C difficile* toxin, stool reducing substances (as appropriate)

• Other investigations should be conducted depending on the clinical situation (see Management below).

8. Management

8.1. Acute diarrhoea

- Children with gastroenteritis and minimal immunosuppression should be managed according to NICE guidelines\(^2\) (Diarrhoea and Vomiting in Children)
- Consider invasive bacterial infection if febrile/toxic and start IV ceftriaxone
- If bacterial stool cultures positive start antibiotics, guided by lab sensitivities; if not available, consider:
  - *Salmonella*: ciprofloxacin or ceftriaxone
  - *Shigella*: ciprofloxacin
  - *Campylobacter*: oral erythromycin or ciprofloxacin
- If an HIV-infected child with acute diarrhoea is not improving on standard treatment, discuss with an HIV paediatrician
- It is important to ensure that antiretroviral drugs have been given and tolerated while the child is unwell.
  - What medication is the child taking?
  - Has the child missed any doses?
  - If vomited within 1 hour of dose – should be given again.
    If unable to take, or keep down medication need to admit and give via NGT. Ondansetron can be given prior to dose in order to give best chance of tolerating dose.
  - Liquid medication is often large in volume – if not tolerating liquids with ondansetron consider use of
crushed tablets.

- Viral load will increase and resistance to drugs will develop if antiretroviral drugs are not given regularly.

### 8.2. Persistent diarrhoea

- Persistent diarrhoea is common in HIV-infected children and repeated investigations may be required to identify a cause.
- Unexplained persistent diarrhoea (>14 days), not responding to standard treatment, is a WHO Stage III disease.
- Pay particular attention to weight and nutrition.
- Send daily stools for culture/OCP/virology for 3 days.
- Check stool reducing substances.
- Include a dietician and consider use of a hydrolysed formula.
- Discuss with HIV paediatrician regarding empirical course of treatment with metronidazole (7 days) and/or ciprofloxacin.
- Consider endoscopy/jejunal biopsy ± colonoscopy if persistent culture-negative diarrhoea:
  - Send biopsy to histopathology (ask for CMV, Cryptosporidium, fungal and AFB stains).
  - Send biopsy for culture (including mycobacteria) and virology.

### 8.3. Severe immunosuppression

- Children with advanced HIV disease may have overlapping and interacting problems of immunodeficiency, enteric infection, malabsorption and malnutrition.
- Involve an HIV paediatrician early in their care.
- Children with advanced disease and diarrhoea may be very sick at presentation:
  - Undertake fluid resuscitation.
  - Check blood gas, electrolytes, chloride, glucose.
  - Correct metabolic acidosis if severe.
  - If toxic/febrile, consider broad-spectrum antibiotics (eg ceftriaxone ± metronidazole).
  - If severe wasting, involve dietician regarding choice of feeds, investigation of micronutrient deficiency and risk of
Re-feeding syndrome

- Repeated investigations should be undertaken to look for all of the conditions listed below
- In cases of severe immunosuppression and culture-negative diarrhoea, the cause may be HIV enteropathy and HAART is needed for improvement
- In cases of severe malabsorption, may need therapeutic drug monitoring to assess levels of antiretroviral drugs.

8.4. **Cryptosporidium**

- Highly contagious, spread through childcare centres, recreational facilities such as swimming pools, water supply (despite chlorination – only boiling kills oocysts)
- Usually frequent, persistent, non-bloody watery diarrhoea
- Abdominal cramps, vomiting, anorexia
- In severely immunosuppressed (CD4<50) can present as cholera-like illness
- Diagnosis: modified ZN stain or Auramine (ask lab specifically)
- No agent has proven efficacy in immunocompromised patients
- Oral nitazoxanide may have some efficacy:
  - 100mg BD (1-3 years)
  - 200mg BD (4-11 years)
  - 500mg BD (>12 years)
- Most children need HAART to enable immune reconstitution and clearance of organisms
- Unproven efficacy for paromomycin and azithromycin, but trial of treatment may be warranted.

8.5. **Microsporidiosis**

- Obligate, intracellular, spore-forming protozoa related to fungi
- Similar presentation to *Cryptosporidium*
- Need to request lab specifically to look for microspora (eg modified trichrome stain) – may be sent away
- Albendazole (7.5mg/kg/dose, max 400mg, orally BD) effective against many species except *Enterocytozoon bieneusi*
- Nitazoxanide may have activity against *Enterocytozoon bieneusi*.
8.6.  *Isospora / cyclospora*
- Ask lab specifically to look for spores in stool
- Prolonged treatment course of cotrimoxazole required.

8.7.  *CMV*[^3]
- Can affect any part of the GI tract, typically causing ulceration
- May present with toxic dilatation of colon and bloody diarrhoea
- Gut biopsy needed to confirm inclusion bodies on histology
- Treat with IV ganciclovir (foscarnet is an alternative).

8.8.  *Mycobacterium avium complex*[^3]
- Environmental organisms
- Typical presentation with persistent diarrhoea, weight loss, fever, abdominal pain
- May have anaemia, leucopenia, thrombocytopenia
- Mycobacterial blood cultures required for diagnosis
- Treat with clarithromycin and ethambutol (± rifabutin) up to 8-12 weeks plus HAART.

9.  References