

25. PAEDIATRIC HIV INFECTION

25.1 Introduction

30-40% of pregnant women in Zimbabwe carry HIV and 30-40% of them will pass on the infection to their child during pregnancy or breastfeeding. 50-60% of childhood admissions to Hospital are HIV related.

25.2 Diagnosis of HIV infection in children

- Under the age of 18 months it is difficult to distinguish the child who is actually infected with the virus from the one who is just carrying maternal antibody using the HIV tests available in Zimbabwe. No totally satisfactory clinical diagnostic criteria have been established except in the presence of recognizable AIDS defining illnesses.
- It is important to take a good history and carry out a thorough examination.
- If HIV is suspected then precounseling is important before an HIV test is done.
- After 18 months of age a positive HIV test is diagnostic of HIV disease in a child. Clinical suspicion of HIV disease should always be confirmed by an HIV anti body test at or after 18 months of age.
- Many conditions in a developing country context are common in both the HIV infected and the non infected :- malnutrition, Tuberculosis, persistent diarrhoea, generalised lymphadenopathy.
- The presence of any 2 of the conditions listed below and positive HIV serology should lead to a suspicion of HIV infection till proved otherwise at 18 months till proved otherwise.

In children HIV infection may be suspected if:

- The child's mother is known to be HIV positive,
- One or both parents have had tuberculosis or are known to be chronically ill
- One or both parents are dead
- One or more siblings are known to be chronically ill or have died
- Child has one or more of the symptoms listed below:

25.2.1 General clinical features

The following symptoms and signs are suggestive of HIV if they occur in the absence any known concurrent illness:

- Growth failure in a child less than six months who is fully breastfed.
- Growth failure lasting three months or more.
- Severe stunting in a child less than 12 years.
- Child falls below the 5th percentile on the weight for height chart on 2 consecutive measurements taken 30 days or more apart
- Fever lasting more than one month, recurrent or continuous.
- Serious recurrent bacterial conditions, septicaemia, pneumonia, bone or joint infection, abscess of an internal organ or body cavity.
- Generalised lymphadenopathy - lymph nodes at two or more sites measuring at least 0.5cm and present for more than 1 month
- Parotid enlargement lasting more than one month
- Severe dental caries in an African child
- Oral and oral pharyngeal candidiasis in a breastfed child older than one month
- Oesophageal candidiasis.
- Finger clubbing in the absence of congenital heart disease

25.2.2 Respiratory system

- Severe /very severe pneumonia in a child 2-12 months of age.
- LIP/PLH as diagnosed on chest x-ray - persistent generalised miliary like nodular pattern in a well child
- Chronic suppurative lung disease

25.2.3 Cardiovascular system

- Cor pulmonale
- Cardiomyopathy

25.2.4 Gastrointestinal system

- Persistent or recurrent diarrhoea: at least two loose stools a day for >30 days
- Persistent hepatomegaly/splenomegaly in the absence of any other condition other than HIV
- Acquired rectovaginal fistula

25.2.5 Central nervous system

- Failure to attain, or loss of, developmental milestones or loss of intellectual ability
- Acquired microcephaly demonstrated by head circumference measurements or brain atrophy as seen on CT scan
- Acquired symmetric motor deficit manifested by two or more of the following, paresis, pathological reflexes, ataxia, or gait disturbance, increased muscle tone
- Recurrent bacterial meningitis in the absence of a predisposing factor
- Cryptococcal meningitis,

25.2.6 Dermatologic manifestations

- Severe seborrhoeic dermatitis
- Zoster
- Generalised fungal dermatitis
- Kaposi's Sarcoma
- Extensive perineal or skin warts

25.2.7 General Infections

- Children with HIV have a tendency to recurrent bacterial infections which may need treatment with antibacterials for longer period than for non-HIV children.
- Daily Cotrimoxazole prophylaxis in symptomatic HIV children may reduce morbidity and hospital admissions and prolong life.

25.3 The respiratory system in children with HIV

In the first year of life respiratory infections are the commonest cause of morbidity and mortality. PCP and CMV dominate the picture in the first 6 months while bacterial infections and PCP in that order dominate the picture from the second 6 months of life. After the first year of life recurrent bacterial infections are the common causes of morbidity and mortality. Both acute and chronic tuberculosis are found in children of all age groups. Mixed infections occur commonly.

25.3.1 Management of severe and very severe pneumonia in high (10% or more) HIV prevalence areas

- Admit the child.
- Treat with crystalline penicillin/ ampicillin and gentamycin given IV and high dose cotrimoxazole given orally.
- Give steroids 2mg/kg/day once daily
- If there is no improvement after 5 days think of other conditions, do a lumbar puncture, arrange for a chest x-ray (if not done

previously) and consider changing the crystalline penicillin/ampicillin to chloramphenicol or cephalosporin,

- If the child is still not better and is spiking temperatures after 10 days, consider the addition of anti-tuberculous treatment
- Always give supportive therapy described in the box below: Supportive therapy is always critical

Supportive therapy

- Oxygen by headbox, nasal prongs, mask.
- If very cyanosed and able to monitor IV fluids give 75mls per kg per 24 hours of 1/2 dextrose darrows, Maintelyte or neonatolyte.
- If unable to monitor fluids pass a nasogastric tube and give Expressed breast milk at 80-100ml per kilogram per day 3 hourly.
- Feed by cup once improvement has occurred after 48 hours.
- If frothing with acute pulmonary oedema give stat dose of frusemide 0.5mg/kg IV or IM followed by 1mg/kg PO.

- If the child is improving continue to treat with high-dose cotrimoxazole for a minimum of 21 days and send home on cotrimoxazole prophylaxis for PCP in those whose HIV status is positive or unknown. Start tapering off steroid dose after 7 days.

25.3.2 Children 12-24 months with severe pneumonia

- Treat with crystalline penicillin/ampicillin and gentamycin
- Review after 48 hours
- If the child is improving, continue treatment for a total of 10 days
- If the child is not improving, add steroids as above and high-dose cotrimoxazole to the regimen and look for other causes of problems,

such as, missed meningitis and empyema and investigate for tuberculosis.

- If not totally better by 10 days consider commencing antituberculous treatment and refer the child for specialist opinion
- Check the HIV status and if positive send home on PCP prophylaxis.

25.3.3 Children 2-16 years of age with severe pneumonia

- Treat with crystalline penicillin or ampicillin or amoxycillin
- If not responding add gentamicin and high dose cotrimoxazole
- Look for TB and other infections
- If not improving after 10 days refer the child for specialist opinion

Steroid use

The use of steroids in children with pneumonia remains a controversial topic as it is possible that CMV infection and TB may be disseminated and worsened in children with these infections. Studies are currently underway to determine whether steroids have a beneficial effect and until such a time that the results of such studies are known it is recommended that steroids in the form of hydrocortisone or prednisolone be used only in desperately ill children:

Prednisolone 2mg/kg/day in two divided doses orally.

25.3.4 Pulmonary lymphoid hyperplasia

This is a slowly progressive lung disease whose aetiology is unknown. It is an AIDS-defining illness and is usually seen after the first year of life. It is often associated with parotid enlargement, generalised lymphadenopathy, hepatosplenomegally and digital clubbing. Children are usually well though in severe cases they may have chronic cough, progressive breathlessness and getting fatigue with exercise. Chest X-ray may look like miliary tuberculosis and the X-ray features do not change with TB treated. Cor pulmonale may complicate its course. Such children should be referred for specialist opinion.

25.3.5 Suppurative lung disease and bronchiectasis in children aged 2 to 16 years

This may be suspected clinically in children with a productive cough that is worse in the mornings and on going to bed. There may be persistent rales in one or more lobes of the lung, and there may be lung fibrosis with tracheal traction to one side of the chest. Chest x-ray may show the lesions but it is best diagnosed on CT scan of the chest with or without contrast. Sputum examination and culture may reveal organisms such as *Pseudomonas*, *Klebsiella* or *Staphylococcus*.

Treatment is with chest physiotherapy for drainage and crystalline penicillin, ampicillin, chloramphenicol or gentamicin are given for 10 days or more. The child should be referred for specialist opinion and management.

25.3.6 Tuberculosis

Both acute and chronic tuberculosis occur commonly in children with HIV infection. Tuberculosis has always been a difficult diagnosis to make in children and the problem is more complex in children with HIV infection as a number of conditions that occur in HIV infected children mimic TB. These include HIV related failure to thrive, unexplained fever and chronic cough. In addition immunosuppressed persons may have an unreactive Mantoux test. Tuberculosis accelerates the progress to AIDS and HIV makes Tuberculosis worse. *A high index of suspicion for TB needs to be maintained at all times*. The diagnosis and case finding would be greatly facilitated if contact tracing for TB was efficient.

In children under 5 years treatment for latent tuberculosis is recommended as the risk of progression of the primary complex is higher than in adults.

Suspect TB in the presence of the following:

- Persistent pyrexia despite treatment with antibiotics and cotrimoxazole
- Persistent cough of more than three weeks,
- Unexplained loss of appetite and weight
- Abnormal episodes of sweating,

- Recurrent chest pains that are often poorly defined.
- Contact with a tuberculous adult
- Unresponsive failure to thrive
- Isolated or generalised lymphadenopathy
- Recurrent subacute intestinal obstruction
- Persistent lobar consolidation/collapse shadows on chest x-ray
- Straw coloured high protein non-purulent pleural, pericardial or ascitic fluid
- Monoarthritis
- Erythema nodosum

Diagnosis

Every effort must be made to get microbiological or pathological confirmation. Acid fast bacilli (AFB) should be looked for in induced sputum, and gastric aspirates may also show AFBs. A reactive Mantoux test greater than 5mm is suggestive of TB. Histologic examination of lymph node and liver biopsies and pleural, pericardial, synovial and peritoneal biopsies may be diagnostic. Lymph node aspirates should be examined for AFBs. Bone marrow aspirates should also be examined for AFBs.

All material should be sent for microscopy, culture and sensitivity in order to monitor for multi-drug resistant TB.

If TB is strongly suspected and laboratory tests do not confirm the diagnosis there is room for a trial of TB therapy provided this is carried out in controlled circumstances and for a period not exceeding two months and after consultation with a specialist.

Treatment

Follow the National TB Guidelines.
Identify and treat the adult from whom the child got TB and other family members who are at risk.

25.4 ENT conditions

Recurrent, chronic suppurative otitis media is common in HIV infected children and may contribute to social isolation in the older child because of the foul smelling ear. *It is difficult to treat.*

Microscopy and culture of the discharge may grow pseudomonas, s.aureus, anaerobic organisms, or multiple drug resistant organisms.

It may be complicated by mastoiditis and facial nerve palsy, brain abscess, partial deafness.

For acute episodes of less than 2 weeks duration should be treated with Amoxycillin. Acute on chronic episodes should also be treated with Amoxycillin.

Mainstay of treatment for chronic otitis media is dry mopping of the ear as often as is necessary to keep the ear dry. If still discharging for more than 2 months refer.

Mothers must be discouraged from plugging ears or instilling any form of eardrops into the ears.

Acute Sinusitis:

Acute sinusitis is a common cause of headache in the older HIV positive child. It usually occurs 3 to 5 days after a bout of an acute cold. The cold may be more severe than usual often associated with a high fever of $>39^{\circ}\text{C}$, periorbital oedema and facial pain and tenderness. Nasal blockage may be present or there may be an upper respiratory tract infection that is not getting better after 10 days. Postnasal discharge is often present. The diagnosis is by examining x-rays of the facial sinuses. It is important to exclude other causes of headache. Children should be treated with Amoxycillin, for 14-21 days.

25.5 Gastrointestinal system

25.5.1 Mouth

Several conditions affect the mouth of the child with HIV and are critical to the nutrition of the child.

SEE CHAPTER ON ORAL MANIFESTATIONS OF HIV INFECTION.

Oral candidiasis

This is a major cause of morbidity and malnutrition in children. Children may present with the following symptoms:

- Refusal to eat or to suck
- Alteration in taste
- Burning taste in mouth
- Odynophagia, painful swallowing
- Dysphagia
- Sores in the mouth
- Often discovered on routine exam

The diagnosis is usually made on clinical examination. The child may have white plaques on an erythematous base. Other presentations of oral candidiasis include erythematous and pseudomembranous candidiasis and angular cheilitis.

Refer to Oral chapter for treatment

Herpetic gingival stomatitis

This condition usually appears as small painful white ulcers on the tongue, tonsils or gingival margin associated with erythema and bleeding from the gums with or without some herpetic vesicles around the mouth area. If the condition is severe, persistent, extensive or recurrent, the child should be referred for specialist opinion.

REFER TO ORAL CHAPTER FOR MANAGEMENT

25.5.2 Oesophagus**Oesophageal Candidiasis**

The diagnosis of candidial oesophagitis should always be considered in severely immunosuppressed children and in children with oral candidiasis. The child may be unable to suck or to eat or swallow and may cry on

feeding, swallowing and vomiting. The older child may complain of retrosternal pain and heartburn.

REFER TO CHAPTER ON FUNGAL OPPORTUNISTIC INFECTIONS

25.5.3 Gastroenteritis

It is important to note that acute, recurrent, and especially persistent diarrhoea is more common, and up to 10 times more deadly in HIV positive infants compared to HIV negative infants. Risk factors for gastroenteritis include:

- Early introduction of other foods other than breastmilk,
- Mother is ill or has died
- Malnutrition

The importance of exclusive breastfeeding in the first six months of life for those mothers who are HIV negative or whose status is unknown or who are HIV positive but have not got the capacity to use breast milk substitutes cannot be over-emphasised.

Hand washing with soap or ash is the most effective proven method of prevention.

The most important considerations in managing children with diarrhoea are the prevention and management of dehydration and the prevention and management of malnutrition. All children should be managed according to the Guidelines set out in EDLIZ and in the IMCI manuals.

Persistent diarrhoea

Persistent diarrhoea is defined as diarrhoea lasting more than 2 weeks. This is much more frequent in HIV infected children and is often the cause of malnutrition and death. The more frequent the episodes of recurrent diarrhoea are in an infant, the greater the risk for development of persistent diarrhoea and malnutrition. ***Rehydration and the maintenance of nutritional status of the HIV child thus becomes the most important strategy for survival in diarrhoeal episodes.*** Always consider the possibility of lactose intolerance and hence test the stool for reducing

substances if possible. The possibility of systemic illness like urinary tract infection should always be considered.

Pathogens associated with persistent diarrhoea

Children with HIV infection and immunosuppression are prone to infection with a number of enteric pathogens. Whenever such an infection is suspected attempts should be made to identify these through laboratory tests. Table 25.1 summarises the features associated with some of these pathogens.

Organism	Clinical signs	Diagnosis	Treatment
Cryptosporidiosis	Frequent non-bloody diarrhoea, abdominal cramps, fever, vomiting, anorexia, weight loss	Stool microscopy, for <i>C. parvum</i> . 3 stool samples on separate days	None consistently effective. Paramomycin, Spiramicin Azithromycin and Bovine colostrum has been tried
Campylobacter	Fever, abdominal pain, malaise, visible or occult blood in stool	Darkfield microscopy or culture with special isolation techniques	Erythromycin 40-60mg /kg /day in 3-4 doses Tetracycline for children >8 years Aminoglycosides for septicaemia
Isospora belli	Protracted, foul smelling watery diarrhoea, abdominal pain, anorexia, weight loss, fever, vomiting, headache	Oocysts in stool and duodenal aspirates	Cotrimoxazole for 2 to 4 weeks, or if allergic, Pyrimethamine 50-75mg/kg per day for 1 month, then 25mg / kg / day plus folic acid 5mg daily
Microsporidium	Watery, non-bloody diarrhoea, weight loss	Formalin fixed specimen of stool for spores or duodenal aspirates	Albendazole for 3 weeks, or Metronidazole, or Ataovoquone, and Nutritional supplements Diarrhoea may recur after therapy

NOTE:

- Milk feeds should be mixed with porridge to reduce lactose concentration,
- Sour milk or yoghurt are better tolerated
- Foods rich in vitamin A, folic acid and Zinc include liver, kidney, green vegetables, fish, beans should be encouraged
- Vitamin supplements should be given

Bloody diarrhoea

If a child presents with diarrhoea with blood and mucus in stools he/she should be managed as for dysentery. It is important to try and identify the cause of the dysentery by sending fresh stool specimens to the laboratory for microscopy culture and sensitivity.

Children are usually managed initially with Nalidixic acid and rehydration together with nutritional advice. If the patient fails to respond to initial treatment consider other organisms, such as, *Salmonella spp.*, *Campylobacter*, *Escherichia coli* as causes. Alternative treatments are Ciprofloxacin 7.5 - 15mg/kg/day or Ceftriaxone 20 to 80mg/kg/day for 3 to 5 days.

25.6 Central nervous system

80% of HIV-infected children develop nervous system involvement. Direct effects of HIV infection in children are seen on the brain, spinal cord and the peripheral nerves. In addition the nervous system may be affected by the development of opportunistic infections and cancers. Children also suffer from illnesses of the nervous system not related to HIV infection and immunosuppression and need to be treated for these if they occur.

25.6.1 AIDS dementia complex

AIDS dementia complex results from HIV infection of the brain resulting in progressive cerebral atrophy with decline in cognitive, behavioural and motor function. It carries a poor prognosis and invariably has a fatal outcome.

Clinical manifestations

Affected children usually fail to attain expected milestones, have evidence of regression of milestones already acquired. Microcephaly may be evident and there may be symmetrically increased or decreased muscle tone and pathological reflexes. The onset may be abrupt or insidious and progression is relentless, with chronic or relapsing features. Nervous deficits may however remain static for some time. Seizures do not usually occur and

when they do occur other causes should be sought. Older children may have features similar to those seen in adults.

SEE CHAPTER ON NEUROLOGIC MANIFESTATIONS

25.6.2 Focal encephalitis

Focal encephalitis may occur in HIV infected children and is usually the result of opportunistic infection such as toxoplasmosis, herpes simplex virus infection and cytomegalovirus infection.

Diagnosis

The diagnosis of focal encephalitis is made on clinical suspicion confirmed by brain imaging and serology.

The treatment of toxoplasma encephalitis is with:

- Cotrimoxazole 60mg/kg 12 hourly for 2 weeks, Or
- Pyrimethamine 2mg/kg/day for 3 days then 1mg/kg /day (maximum 25mg) given for 4weeks, Plus
- Sulfadiazine 100-200mg/kg/day for 3 to 4 weeks, Plus
- Folinic acid 5mg PO OD, Plus
- Lifelong prophylaxis with Pyrimethamine 1mg/kg /day (maximum 25mg) PLUS Sulfadiazine 85 to 120mg/kg/day given with Folinic acid 5mg given every 3 days.

SEE CHAPTER ON NEUROLOGIC MANIFESTATIONS

25.6.3 Diffuse encephalitis

Diffuse encephalitis may be caused by meningitis or malaria.

SEE CHAPTER ON NEUROLOGIC MANIFESTATIONS

25.6.4 Spinal cord

HIV infection can lead to vacuolar myelopathy. This causes gait dysfunction. The lower extremities are affected more than the upper extremities. There may also be mild sensory loss and cognitive decline.

Diagnosis

Spinal cord imaging may reveal atrophy of the cord with vacuolation. Cerebrospinal fluid examination should be carried out to exclude tuberculous and cryptococcal meningitis.

SEE CHAPTER ON NEUROLOGIC MANIFESTATIONS

25.7 Nutrition

HIV infection itself leads to weight loss in the advanced stages. The problem is compounded by the lack of macro- and micro-nutrient supplementation. Malnutrition alone can lead to immunosuppression, and is a major determinant of outcome of common afflictions in the HIV infected child.

It is important to carry out nutritional assessments in all children and simple measures may be used for this. Children who are malnourished may require admission and hospitalized care. The following criteria may be used for admitting children:

- Weight for height less than 70%
- Presence of bilateral pedal pitting oedema
- Mid upper arm circumference less than 12cm in a child in child more than 6 months old
- Marasmus (Weight less than 60% of expected weight for age with no oedema) if no height available.
- Visible severe wasting - if no measurements are available

25.6.1 Treatment of malnutrition

All children aged less than 6 months who have not gained weight for more than two months should be referred.

For the management of severe acute malnutrition therapeutic feeding is usually carried out with two formulae F75 which has 100 Kcals per 130 mls and F100 which is equivalent to 100 Kcals per 100mls. These formulae are easily prepared from local ingredients (see appendix 3). In severe malnutrition, the oral rehydration solution (Resomal) is different (see appendix 3).

In children aged 6 months or more malnutrition is treated in 3 phases:

Phase 1: Return to normal homeostasis and treatment of complications.

- Treat immediate complications like infections, heart failure, anaemia, hypoglycaemia, hypothermia, septic shock, dehydration.
- Severe infections are difficult to detect in children with severe malnutrition. It is therefore advisable to treat all treat with crystalline penicillin and gentamycin for 7 days.
- Give F75 at 130 ml/kg/day in 8 meals - (F75 - 130mls =100 calories). If very severe oedema or child very sick reduce this by 20% till child can better tolerate full dose.

Continue F75 until child has a good appetite and has evidence of loosing oedema and has no diarrhoea or other severe illness.

Transition phase give F100 at the same dose for at least 2 days or until the oedema has completely subsided.

Phase 2: Promote rapid weight gain.

- Give 160-220 calories/kg/day - (F100 - 160-220 mls /kg/day) - To be started when child has good appetite, all oedema has gone, and no more complications.
- Can be given in 6-8 meals
- Can be given as outpatient in day care units
- Start introducing normal diet slowly making sure child takes all prescribed F100

- Any time complications arise go back to phase 1.
- Vitamins and minerals should be given as well as folate 5 mg once then 5mg twice weekly, vitamin A on days 1, 2, and 14, and ferrous sulphate after 2days in phase 2.

Vitamin A dose: 0-6 months 50,000 IU 7-11months 100,000 IU,
12 months and above 200,000 IU

- Mebendazole 200 mg on discharge where indicated.

NOTE:

- If not possible to carry out this feeding programme as prescribed treat as in EDLIZ. Only non-complicated cases of severe malnutrition should be treated in District.
- If very severe oedema present or no response to F75 in 7 days, refer
- Malnutrition in HIV child not qualifying for therapeutic feeding manage as in EDLIZ

25.8 Haematological disorders

Anaemia

Anaemia is common in children with HIV infection and can independently worsen the outcome of infection. Anaemia is defined as a haemoglobin or haematocrit level of less than that shown for the age groups below:

6 months to 4 years -	Haemoglobin: 11g/dl	Haematocrit: 33%
5 to 11 years -	Haemoglobin: 11.5g/dl	Haematocrit: 34%
12 to 14 years -	Haemoglobin: 12g/dl	Haematocrit: 36%

Symptoms of anaemia do not usually develop until the haemoglobin level drops to less than 8g/dl.

Causes of anaemia in HIV-infected children include:

- Anaemia of chronic infections or infiltrations
- Malabsorption of folate
- Iron deficiency from chronic bleeding, low birth weight, dietary deficiency and causes such as malaria and hookworm infestations.

Iron deficiency is very common in non-breastfed infants and should be looked for.

Diagnosis

The diagnosis of anaemia is usually made on clinical findings and confirmed by laboratory tests. In all children with anaemia blood should be sent to the laboratory for a full blood count (FBC), peripheral blood film examination and comment, reticulocyte count, malaria parasites, and unconjugated bilirubin levels, and stool should be examined for parasites.

Treatment

- Treat the underlying cause, such as, underlying infection, TB, worm infestation and malaria
- Give Iron and Folate as in EDLIZ.
- If not responding after one month refer.

Transfusion may be indicated if,

- Anaemia is severe, i.e., haemoglobin level less than 4g/dl
- There is overt or impending congestive cardiac failure and the haemoglobin level is less than 6g/dl
- There is malaria and a haemoglobin level of less than 6g/dl
- There is respiratory distress in a child with malaria

Thrombocytopenia

Usually cause by auto-immune reactions.

Need to rule out other serious underlying conditions such as sepsis.

Treat with steroids is level below 10,000 or actively bleeding.

Pancytopenia

Need to rule out other serious underlying conditions such as sepsis.
Treat with steroids.

25.9 Skin conditions

REFER TO SECTION ON SKIN CONDITIONS