

Clinical Tract

Module on

The management of HIV- exposed and HIV- infected children

LEARNING OUTCOMES FOR DOCTORS AND NURSES

After completion of this module the learner should:

- Describe the importance of growth monitoring and nutritional support in HIV-exposed and HIV-infected children
- Prescribe the correct prophylactic and routine medications for HIV-exposed and HIV-positive children
- Describe the role and importance of immunizations of all children
- Know when to refer a child for further management
- Describe common respiratory diseases in HIV-infected children
- Recognise the importance of the correct management of acute and persistent diarrhoea
- Know the important bacterial, fungal and viral infections that HIV-infected children are prone to get

LEARNING OUTCOMES FOR COUNSELLORS, SOCIAL WORKERS, DIETICIANS, PHARMACISTS, LABORATORY TECHNICIANS AND DATA TYPISTS

After completion of this module the learner should:

- Know why growth monitoring and nutrition are important in HIV-exposed and HIV-infected children
- Know which prophylactic and routine medications HIV-exposed and HIV-positive children should receive
- Describe why immunizations are important in all children
- Know when a child should be referred for further management
- Have a basic knowledge regarding common infectious diseases in HIV-infected children

1. AN APPROACH TO HIV-EXPOSED AND HIV-INFECTED CHILDREN

A. Introduction

Adequate care of HIV-exposed and HIV-infected children starts long before the initiation of antiretroviral therapy. The first goal in the management of these children is to maintain their health, growth and development. In the initial stages of the disease, this can be facilitated by care at the primary health care level (clinics or family practitioners). This is done mainly through the routine well-baby- and immunization visits. According to the IMCI / WHO guidelines, all children, regardless of HIV-exposure, should be followed up monthly in the first year of life, and 3 monthly thereafter until the age of 5 years. Health education, counselling and support are provided at these visits. Referral to social and community services, as well as help with the application for social grants, e.g. child support grants, care dependency grants, foster care grants, etc. can be facilitated at this level of care.

B. Growth monitoring

Growth monitoring and dietary advice are important in the care of HIV-exposed and HIV-infected children. Mothers should be counselled regarding the choices of infant feeding. A mother, who is known to be HIV-infected, should be informed that breast-feeding is an additional risk for HIV infection in her baby. However, it should be remembered that formula feeding is not always an acceptable or feasible alternative, and the options should be discussed with the mother. If no program to supply formula feeds free of charge is available, the financial implications of buying formula feeds need to be discussed. The need to access clean water for the mixing of the feeds is also of great importance. It should be remembered that babies on formula feeds are at greater risk of other diseases, especially Rotavirus diarrhoea, which can be a fatal disease in infants.

Guidelines regarding infant feeding in HIV-exposed infants state that breast-feeding should be avoided if formula feeding is available, affordable, acceptable, safe and sustainable. The other option is exclusive breastfeeding, meaning that only breast milk and medication is given, with abrupt weaning as soon as this is feasible. Mixed feeding (which means either mixing breast milk and formula milk, or breast milk and solid foods) should be avoided, since the transmission rate of HIV is increased in these children.

Growth monitoring of HIV-exposed and HIV-infected children is an important function of primary health care. The Road-to-Health Chart is an important tool in this regard, and the weight of the child should be plotted at each contact that the child has with the health services. The IMCI guidelines on the follow-up of children with growth failure should be used in conjunction with the Road-to-Health Chart (Refer to the IMCI guidelines, Jan 2003: p 17-20). Common causes of growth failure include tuberculosis, chronic diarrhoea, HIV disease itself, as well as poor intake due to feeding difficulties, local lesions in the mouth or the unavailability of food. If a child does not gain weight adequately, dietary advice regarding a high calorie diet and nutritional support should be given. If possible, a dietician should be involved in this process. If the child does not respond to the intervention, he/she should be referred to the next level of care to ensure that the cause for the growth failure is diagnosed.

C. Prophylaxis and treatment

The provision of prophylactic treatment is also a function of the primary health care system. Prophylaxis with co-trimoxazole (Bactrim®) is given to prevent *Pneumocystis jiroveci* pneumonia (PCP). Although there is a strong association between CD4+ percentage and the risk of opportunistic diseases, PCP may occur in the first year of life despite CD4+ counts that are within the normal limits for age.

Co-trimoxazole prophylaxis is indicated in the following children:

- All HIV-infected and HIV-exposed children from the age of 6 weeks onwards until 1 year of age. The prophylaxis can be stopped in these children under the following conditions:
 - At 1 year of age if the CD4+% is >15%, or
 - When HIV infection has been reasonably excluded (i.e. the HIV Elisa is negative or the HIV DNA PCR is negative 3 months after cessation of breastfeeding).
- Previous PCP
- Children with AIDS-defining diseases
- CD4+ percentages under 15%

The dose of co-trimoxazole is 8mg of trimethoprim/kg/day (which translates into 0.625ml/kg/day) once daily. (Co-trimoxazole syrup contains 40mg trimethoprim and 200mg sulphamethoxazole per 5 ml.)

Appropriate dosages for co-trimoxazole prophylaxis (according to the IMCI guidelines):

Weight	Cotrimoxazole daily dose
2.5 – 5 kg	4 ml
5.1 – 10 kg	7.5 ml
10.1 – 14 kg	10 ml
14.1 – 20 kg	10 ml or 1 tablet

Counselling a mother regarding the general principles of hygiene is also important, as infectious diseases should be prevented as far as possible. Dental hygiene is also important, since dental caries is a very common problem amongst HIV-infected children.

It is important to remember that HIV-infected children often suffer from common diseases of childhood, and early and adequate treatment for these should be provided, using the IMCI guidelines as for all other children.

Maintaining adequate hydration in children during diarrhoeal episodes is extremely important. Mothers should be counselled on how to administer the oral rehydration solution. In cases of severe diarrhoea, intravenous rehydration may become necessary.

Other routine medication that is administered to HIV-infected children consists of:

- A daily supplement of vitamins, in the form of a multivitamin syrup (5ml daily).
- Folic acid (2.5mg – 5mg daily) can also be considered, especially in children on long-term co-trimoxazole prophylaxis, as this drug is a folic acid antagonist.

- Vitamin A supplementation should be given to all children according to the IMCI guidelines (refer to p16 of the IMCI guidelines, Jan 2003). One dose of 50 000 IU is given to non-breastfed infants under six months of age. Thereafter all infants receive a dose of 100 000 IU between the ages of 6 and 11 months. A dose of 200 000 IU is given at 12 months, and this is then repeated every 6 months until the age of 60 months.
- Routine antihelmintic treatment (albenazole or mebendazole) should also be given every 6 months to children over one year of age, to treat possible worm infestation.
- Iron-deficiency anaemia should always be actively excluded in the children, as they often have a poor dietary intake of iron, and this should then be treated by dietary advice and the administration of supplemental oral iron.

Pain relief is often overlooked in children with HIV-disease. It should always be offered to a child if needed. There are many conditions in HIV-disease which are potentially painful. These include:

- Medical procedures
- Severe and/or chronic bacterial, viral, fungal and parasitic infections
- Dental disease, oral lesions
- Encephalopathy with spasticity, neuropathy
- Malignancies, etc.

The cause of the pain should always be established, if possible, and the underlying condition then treated. The assessment of the severity of the pain by the parent/caregiver is an important criterion when deciding on the intervention needed for the pain. Pain scales are also available – see below. The level of pain should be assessed regularly, and adequate regular doses of analgesics should be administered, and not only when the pain is evident (medication not to be given p.r.n.) Pain caused by medical procedures should be anticipated, and managed appropriately.

FLACC Scale for Determining the Intensity of Pain of a Child who Cannot Speak
(under 3 years or very ill)

Score	0	1	2
<u>F</u>ace	No particular expression or smile	Occasional grimace or frown, withdrawn, disinterested	Frequent to constant quivering chin, clenched jaw
<u>L</u>egs	Normal position or relaxed	Uneasy, restless, tense	Kicking, or legs drawn up
<u>A</u>ctivity	Lying quietly, normal position, moves easily	Squirming, shifting back and forth, tense	Arched, rigid or jerking
<u>C</u>ry	No cry (awake or asleep)	Moans or whimpers; occasional complaint	Crying steadily, screams or sobs, frequent complaints
<u>C</u>onsolability	Content, relaxed	Reassured by occasional touching, hugging or being talked to, distractible	Difficult to console or comfort

Each of the five categories (F) Face; (L) Legs; (A) Activity; (C) Cry; (C) Consolability is scored from 0-2, which results in a total score between zero and ten.

From *The FLACC: A behavioral scale for scoring postoperative pain in young children*, by S Merkel and others, 1997, *Pediatr Nurse* 23(3), p. 293-297. Copyright 1997 by Jannetti Co. University of Michigan Medical Center. Reprinted with permission. <http://www.childcancerpain.org/content.cfm?content=assess13>

Pain management should follow a stepwise approach - titrating the medication according to the need of the patient – see the analgesic ladder below. If possible, the medication should be given orally. When using opioid drugs, it is important to remember that addiction normally does not occur at dosages needed for analgesia. It is however recommended not to stop the treatment abruptly, but to reduce the doses gradually over a period of time. Side effects of drugs, for example constipation with the use of opioid drugs, should be anticipated and managed appropriately.

The analgesic ladder

Step 1: Mild pain

- Oral paracetamol 10 mg/kg/dose, every 4 to 6 hours, with a maximum of four doses daily.

Paracetamol				
Weight kg	Dose mg	Syrup 120 mg/5 ml	Tab 500 mg	Approximate Age years
6 to 10 kg	60	2.5 ml	—	3 to 12 months
10 to 18 kg	120	5 ml	—	1 to 5 years
18 to 25 kg	240	10 ml	½ tab	5 to 8 years
25 to 50 kg	500	—	1 tab	8 to 14 years
> 50 kg; adults	1000	—	2 tabs	>14 years

- Oral ibuprofen 4–20 mg/kg/day in divided doses. Safety in children under 2 years has not yet been established. (Syrup 100mg/5ml, tablets 200 mg / 400 mg / 600 mg)

Step 2: Moderate pain

- Add oral codeine phosphate syrup to Step 1.
Dose: 0,5 mg/kg, 4 – 6 hourly as needed. (Syrup 25mg/5ml, tablets 30 mg)
- Tilidine (Valoron drops): 1 drop for each year of age, given 3 – 4 times daily.
Not recommended for infants under 1 year of age

Step 3: Severe pain

- Morphine should be added to the previously given analgesia. Oral morphine is given 4 hourly, starting with a dose of 0.1-0.3 mg/kg/dose. There is no maximum dose for morphine – the dose is adjusted according to the effect on the pain.

Important points to remember when using morphine:

- Use lower starting doses for younger children (within the age range)
- Allow 24 hours before considering a dose increase; and then increase the dose by 30-50%
- There is no maximum dose - titrate the dose to the analgesic response
- If patient has pain within dosing interval, additional 'break-through' doses must be prescribed
- Intravenous morphine should only be used in a hospital or hospice setting
- Opioids can alleviate other problems like cough and intractable diarrhoea

D. Immunizations

Immunizations play an important role in the care of HIV-infected children, as the prevention of infectious diseases is important in these children. All routine immunizations in the South African National immunization schedule are given. BCG, however, should not be given to children with AIDS, due to the risk of causing disseminated disease.

It is important to ensure that HIV-uninfected siblings are also fully immunized, in order to minimize the risk of the HIV-infected child contracting potentially preventable diseases through a household contact. Other immunizations, which are not on the routine RSA immunization schedule, that are beneficial to HIV-infected patients include vaccines against varicella, pneumococcus and influenza. These can be considered if the financial means are available.

E. Referrals

Clinical staging of the HIV-disease and CD4+ counts should ideally be done at primary health care level, with subsequent referral of children to antiretroviral treatment facilities. Other indications for referral include children who do not respond to conventional treatment offered at clinic level (IMCI guidelines).

Severely ill children and those with unusual complications should also be referred. It is the aim to keep hospital admissions as short-term as possible. The child is then referred back to the clinic for further care. Another indication for the referral of a patient would be to obtain expert opinion, for instance on whether or not palliative or terminal care should be instituted. Once this decision has been taken, the provision of palliative and terminal care should be through the channels of the primary health care system.

2. MANAGEMENT OF COMMON DISEASES AND OPPORTUNISTIC INFECTIONS IN HIV-INFECTED CHILDREN

A. Introduction

HIV-positive children present with common diseases of childhood and opportunistic infections, and this picture can be varied and mixed. Common problems that are encountered will now be described in more detail. Please also refer back to the module on opportunistic infections in adults.

B. Respiratory disorders

1) *Pneumocystis jiroveci* pneumonia (PCP)

Pneumocystis jiroveci pneumonia, previously known as *pneumocystis carinii* pneumonia is a common opportunistic infection in HIV-infected infants, which is preventable by administering co-trimoxazole (Bactrim®) prophylaxis. The disease is especially seen in HIV-infected children below one year of age. The prevalence in children with severe pneumonia is estimated at 10%. A high index of suspicion is therefore needed in children, especially in the age group 3 to 6 months, who present with an acute onset of severe pneumonia. These children present with fever, a non-productive cough, severe tachypnoea and dyspnoea, as well as with severe cyanosis. Only a few, if any crepitations are heard on auscultation of the lungs. The chest X-ray shows a diffuse alveolar or interstitial infiltrate, and the serum LDH-level is often > 500 IU/l. Furthermore the child shows no improvement on conventional antibiotic therapy.

The treatment consists of oxygen, high-dose co-trimoxazole (20mg/kg/day of the trimethoprim component, given six-hourly, intravenously or orally for 3 weeks), steroids (prednisone 1-2 mg/kg/day orally for 2 weeks) and supportive care. Other first-line antibiotics (e.g. ampicillin, ceftriaxone) should also be administered to cover the child for a possible bacterial pneumonia. The mortality of PCP, even with treatment, remains high, and therefore the need for effective prophylaxis of this disease must be emphasized again, as the prophylaxis decreases the risk by over 80%.

2) Tuberculosis (TB):

Tuberculosis (TB) is a common disease in HIV-infected children, and it can present as a respiratory illness, or with disseminated disease. The diagnosis of TB in any child is difficult, and this problem is compounded in children with HIV-disease. A full TB work-up, consisting of a TB skin test, chest X-ray and gastric aspirates or sputa for TB-microscopy and culture, should be done if any suspicion of TB arises. TB skin tests are seldom positive, even with the lower cut-off of >5mm for positivity of the Mantoux reaction. This is due to the underlying T-cell defect in children with HIV-disease. Therefore it is of utmost importance to obtain samples for microscopy and culture of *Mycobacterium tuberculosis*, although the low positive yield of about 30% for three sputum or gastric aspirate samples is a major problem. Chest X-ray changes can also be difficult to interpret, especially in children with recurrent viral and bacterial respiratory infections, as well as in children with other respiratory diseases like lymphoid interstitial pneumonia (LIP).

TB treatment is therefore often started on clinical grounds alone. The response to treatment is then seen as a therapeutic trial. The problem with this approach is, that both the mortality and the response to TB-treatment are known to be worse in HIV-infected children with tuberculosis. But the option of empirical TB-treatment should be followed if deemed necessary by the treating clinician. This is due to the high prevalence of TB in our communities, with its associated morbidity and mortality.

Standard TB-treatment, consisting of three drugs (rifampicin, isoniazid and pyrazinamide) that are given for six months under the DOTS program, is currently given to children with suspected and proven tuberculosis. This treatment should be modified, when the tuberculosis recurs after previous full treatment, when a poor response to treatment is seen, or if disseminated tuberculosis is being treated. Modifications to the treatment can consist of adding additional drugs (like ethambutol, streptomycin or ethionamide), as well as by extending the duration of treatment. Expert opinion should be sought in these cases.

3) Atypical mycobacterial disease

Atypical mycobacterial disease is not as common as tuberculosis, and it is mainly seen in children in the advanced stages of HIV-disease/ AIDS. Cervical lymphadenitis, as well as disseminated disease is seen. The most important organism is *Mycobacterium avium-intracellulare* (also known as the *Mycobacterium avium* complex, MAC), although other mycobacteria can also cause opportunistic infections in children with AIDS.

The clinical presentation of disseminated atypical mycobacterial disease is a slowly progressive disease with fever, weight loss, abdominal pain and anaemia. Night sweats, diarrhoea, malaise, neutropenia and hepatomegaly have also been described. Without effective treatment the survival time of these patients is short. Therapy of the disease is associated with a decrease in the bacterial burden, improved symptoms and increase in the time of survival. The initial treatment for a disseminated MAC infection should include clarithromycin (or azithromycin), with ethambutol and/or rifabutin. Expert opinion should be sought.

4) Lymphoid Interstitial Pneumonia (LIP)

LIP is a slowly progressive interstitial lung disease, which usually presents after the first year of life. The clinical picture of the children includes a chronic cough, fatigue when exercising and progressive hypoxia. Generalized lymphadenopathy and parotid and other salivary gland enlargement is usually present, as well as clubbing of the fingers. Auscultation of the lungs is normal. On chest X-ray a diffuse, bilateral reticulo-nodular pattern, with or without hilar or paratracheal lymph node enlargement is seen. The treatment is symptomatic, using steroids in hypoxic children. Severe LIP is also an indication to start antiretroviral therapy.

C. Gastrointestinal disorders

Gastro-intestinal symptoms, which include anorexia, vomiting and diarrhoea, are extremely common in children with HIV-disease, and should be managed appropriately. The management of acute and persistent diarrhoea will now be discussed in greater detail.

1) Acute diarrhoea

Acute diarrhoea in HIV-infected children is treated like in their HIV-negative counterparts, using the IMCI guidelines, with the focus on the management of dehydration, the continuation of feeding as well as on counselling the mother about the danger signs of dehydration. (Please refer to the IMCI guidelines, Jan 2003: p3, 14, 15) The mother should be counselled on how to prepare and administer sugar-salt solution (SSS) and/or oral rehydration solution (ORS). To make SSS 1 litre of boiled and then cooled water is mixed with 8 teaspoons of sugar and ½ a teaspoon of salt. To make ORS the contents of one sachet of ORS is mixed with clean water. The mother is counselled to give frequent small sips from a cup. This can still be continued, although at a slower rate, if a child is vomiting. Giving extra fluid is continued until the diarrhoea has stopped. If this treatment is unsuccessful, intravenous rehydration may become necessary. Antidiarrhoeal agents are not beneficial in children and may have severe adverse effects, and should therefore be avoided.

Most episodes of acute diarrhoea are viral in origin (mostly rota- or astrovirus) and do not require any antibiotic treatment. Antibiotic therapy may be required in neonates, severely malnourished children, systemically ill children, and children with bloody diarrhoea (dysentery). Acute infectious diarrhoea can persist to become chronic diarrhoea, with devastating effects on the nutritional state of the child.

2) Persistent diarrhoea

Persistent diarrhoea is initially indistinguishable from other episodes of acute gastroenteritis, but then the diarrhoea does not resolve due to factors like mucosal damage of the gut, bacterial overgrowth and/or persistent or new infections of the gut. Malabsorption of sugars (lactose or monosaccharides) and fats may occur, with a vicious cycle of malnutrition and persisting diarrhoea.

Other causes for chronic diarrhoea in children are infectious causes like *Campylobacter jejuni*, *Shigella flexnerii*, *Salmonella* species, tuberculosis and *Entamoeba histolytica*. Cryptosporidium, microsporidia, cytomegalovirus and MAC infection are other etiological factors in chronic diarrhoea. AIDS enteropathy with atrophy of the intestinal villi can also be the cause for the problem, as can infections in other parts of the body, like urinary tract infections.

The management consists of:

- Oral rehydration solution to prevent dehydration
- Nutritional advice: Breastfeeding should not be stopped. Other milk feeds can be substituted with lactose-free formula (e.g. a soya-based formula) due to the strong possibility of lactose intolerance. Amasi and yoghurt are often also well tolerated by the children.
- Stool-microscopy and -culture should be done to identify infective causes of the diarrhoea, and treating them accordingly.

- Assessment for other infections, e.g. ruling out a urinary tract infection.
- Bowie regimen (oral cholestyramine and oral gentamycin with lactose free feeds) – this treats bacterial overgrowth in the gut, and binds bile salts and toxins.
- The child should be referred to the next level of care if the treatment is unsuccessful.
- Nutritional support should be continued after the diarrhoea has stopped, to ensure that the cycle of malnutrition and diarrhoea is broken in the child.

D. Recurrent bacterial infections

Many HIV-infected children suffer from recurrent bacterial infections, such as pneumonia, septicaemia, meningitis, abscess formation and chronic suppurative otitis media. These infections may be severe, but usually respond well to the standard antibiotic therapy. Bacterial infections should be diagnosed as accurately as possible, including culturing the organisms if possible, so that treatment can be tailored accordingly.

Recurrent salmonella infections are sometimes seen in HIV-infected children – an uncommon clinical picture in HIV-negative children.

E. Fungal infections

1) Candidiasis

Oral candidiasis is the most common fungal infection seen in HIV-infected children. It can be severe and very persistent. The recommended treatment is initially topical with Nystatin (Mycostatin®) (1ml six hourly orally) or Miconazole (Daktarin oral gel®) (apply oral gel 4-6 hourly to oral mucosa). Gentian violet can be used if these medications are not available. Oral Fluconazole (Diflucan®) (3mg/kg/day for 7 days) is used if the oral lesions do not respond to topical treatment, or if the patient is struggling to swallow, and spread of the candida into the oesophagus is suspected. Analgesia should be provided as needed.

Disseminated candidiasis can occur in children with HIV-disease. The biggest risk factors are the presence of oral candidiasis and the prolonged placement of a central venous catheter.

2) Other fungal infections

HIV-infected children are at risk of a large number of fungal infections, like histoplasmosis, aspergillus-infection, etc. *Cryptococcus neoformans* is an opportunistic pathogen, which usually presents as a subacute meningitis or meningo-encephalitis. Please refer to the module on opportunistic infections in adults.

F. Viral infections

Viral infections, especially with the herpes-group of viruses, can cause significant problems in HIV-positive children. Herpes simplex virus can cause recurrent gingivo-

stomatitis, with severe ulcer formation. Dissemination of the herpes simplex virus can also occur, with signs of pneumonia, jaundice or abnormal neurological features. The treatment consists of early initiation of acyclovir as well as supportive care.

Primary Varicella Zoster infection (chickenpox) can be prolonged, and complications may occur like pneumonia and secondary bacterial infections. Recurrent or chronic episodes of Zoster (shingles) may also occur. The treatment consists of early administration of acyclovir and pain relief.

Cytomegalovirus (CMV) can also disseminate in HIV-positive patients, causing retinitis, pneumonia, esophagitis, gastritis with pyloric obstruction, hepatitis, colitis and encephalitis. Ganciclovir or foscarnet are the drugs of choice.

Measles may occur despite immunization, and can present without the typical rash. Dissemination to the lung and the brain can occur, and there is a high mortality rate in these children.

Respiratory viruses like respiratory syncytial virus (RSV) and adenovirus may present with prolonged symptoms and prolonged viral shedding, increasing the risk of severe disease in the patient, as well as the infectious risk to the people around them.

G. Neurological disorders

HIV encephalopathy and other neurological problems have already been discussed in the module on the approach to paediatric HIV-infection.

H. Conclusion

The prevention and treatment of common and opportunistic infections in HIV-infected children has improved over the last few years, resulting in a decrease in the morbidity and mortality thereof. As more children receive antiretroviral therapy, fewer are likely to be at risk of opportunistic infections.

Despite these advances, health care workers who are caring for HIV-infected children should continue to anticipate the common as well as the opportunistic infections and their complications in HIV-positive children. The prophylaxis, diagnosis and treatment of these infections are likely to remain an integral part of the care for both the near and the distant future.

3. FURTHER READING

- National Department of Health, South Africa, 2004: National Antiretroviral Treatment Guideline.
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