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Editorial

The world's two billion children and adolescents are at the centre of the HIV/AIDS crisis. Today, more than half of all new HIV infections affect people under the age of 25. Girls are hit harder and younger than boys. Infant and child death rates have risen sharply, and 14 million children are now orphans because of the disease. And yet the young offer the greatest hope for defeating the epidemic. To make healthy and informed choices they need knowledge and life skills, youth-friendly and gender-sensitive services and a protective familial, social and legal environment.

The children of this world deserve proactive programmes to prevent mother-to-child transmission of HIV, and care, protection and support. Currently, only 5% of HIV-positive children in developing countries receive the treatment they need. Ann Veneman, executive director of Unicef, recently said: "Children are the missing face of HIV/AIDS", and Dean Hirsch, chairman of the Global Movement for Children, said the lack of treatment amounted to a death sentence for millions of children. He warned that most HIV-positive children die before their fifth birthday. Providing an HIV-infected pregnant woman with comprehensive care can reduce the risk of transmission to less than 2%, but not even 10% of HIV-positive pregnant women currently receive the necessary drugs.

Thomas Miller, chief executive officer of Plan International said: "Unless the world takes urgent account of the specific impact AIDS has on children, we will fail to meet the Millennium Development Goal - to halt and begin to reverse the spread of the disease by 2015." In response to these calls for action, the next four updAIDS columns will be dedicated to aspects concerning the prevention and comprehensive care of HIV exposed infants and children.

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What is in the news?

The UN General Assembly Special Session on HIV/AIDS (UNGASS) has ended with some civil society groups (including the TAC) accusing negotiators of reneging on HIV/AIDS prevention, treatment and funding targets set in the declaration drafted at the 2001 U.N. General Assembly Special Session on HIV/AIDS (http://www.org/ga/aids/coverage). The 2001 declaration laid out several goals, including the specific amount of money that should be spent on HIV/AIDS in developing countries in 2005, the percentage of pregnant women who should be receiving drugs to prevent mother-to-child transmission of HIV and the percentage of HIV-positive people with advanced stages of the disease who should be receiving antiretroviral drugs. Most of the goals in the 2001 declaration were not met, but a goal to spend $8.3 billion on HIV/AIDS in developing nations was met. The declaration is, however, not a binding document (Kaiser Daily HIV/AIDS Report, 6/1) (http://kaisernetwork.org/daily_reports?rep_hiv.cfu). In the debate over the 2006 document, several countries (including the USA, some Islamic countries such as Egypt, and other countries in Africa and Latin America) opposed a declaration that included references to condom distribution, needle-exchange programmes and vulnerable groups. Countries were also in conflict about the production of low-cost generic versions of patented antiretroviral drugs and about funding levels for each country. In addition, although UNAIDS wants to increase annual funding for HIV/AIDS from $8 billion to $22 billion by 2010, the US wants individual countries to set funding targets, rather than following targets set by the United Nations. UNAIDS Executive Director Peter Piot at the conference said that global HIV/AIDS programmes need at least $22 billion annually by 2008 to curb the pandemic. The agency projects that the need for resources will rise to $22.1 billion by 2008, including $11.4 billion for prevention (Kaiser Daily HIV/AIDS Report, 6/1) (http://kaisernetwork.org/daily_reports?rep_hiv.cfu).

HIV/AIDS advocates on the sidelines of UNGASS said that developed countries are not living up to commitments made on HIV/AIDS-related funding at the 2005 summit of the Group of Eight industrialised nations. In addition, Richard Burzynski of the International Council of AIDS Service Organizations (http://www.icaso.org/) said the Global Fund To Fight AIDS, Tuberculosis and Malaria (http://www.theglobalfund.org/en/) is facing a funding shortfall of $2.1 billion for this year and next year. The Global Fund had hoped to disburse at least $2.8 billion in grants for treatment in 2006 and $2.7 billion in 2007, but so far has received pledges of $1.9 billion for 2006 and $1.5 billion for 2007, according to Burzynski (Reuters UK) (http://today.reuters.co.uk/news/).

Preventing and diagnosing HIV infection in infants and children

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INTRODUCTION

Sub-Saharan Africa carries the brunt of the global Human Immunodeficiency Virus (HIV) epidemic. The vast majority of HIV transmission occurs through heterosexual contact with the highest infection rates occurring among women of childbearing age, therefore new born babies are frequently exposed to HIV. The World Health Organisation (WHO) reported at the end of 2005 that 2 million children lived with HIV in sub-Saharan Africa, and an additional 1 500 children in the region are newly infected each day.[1]

MODES OF TRANSMISSION

Mother-to-child transmission (MTCT) is the major route of HIV infection in infants and children. MTCT can occur before, during or after delivery.[2] In the absence of active intervention and with routine breast- and/or mixed feeding transmission rates are estimated to range from 15-34%.[3, 4] Under these circumstances an estimated 14-34% of transmission occurs in the pre-partum period, 65% intra-partum and 12% late post-partum.[5]

Risk factors for MTCT include:

Pre-partum

- High maternal viral load, low CD_4 count and/or advanced clinical disease
- Other maternal infections e.g. syphilis, malaria etc.
- Potentially traumatic procedures involving the foetus e.g. external version
- Absence of maternal antiretroviral treatment

Intra-partum

- High maternal viral load, low CD_4 and/or advanced clinical disease
- Vaginal delivery, rupture of membranes for >4 hours, assisted delivery, invasive foetal monitoring, prematurity
- Absence of MTCT preventive therapy

Post-partum

- High maternal viral load, low CD_4 and/or advanced clinical disease or maternal infection (seroconversion) during the time of breast-

Table 1: Strategies to reduce the risk of human immunodeficiency virus (HIV) transmission from mother to child

	Optimal management	Practical compromise - resource limited setting
Ante-partum	1) VCT in 1st trimester of pregnancy 2) Repeat VCT in the third trimester to identify mothers who may seroconvert during pregnancy 3) Counselling regarding infant feeding options 4) Provide HAART to the mother and aim to reduce the viral load to undetectable levels	1) VCT in 1st trimester of pregnancy or at 1st booking 2) HAART if mother's CD_4 count <200 or AIDS defining illness 3) Single dose NVP – remember that there are alternative and more effective ante-natal short course strategies 4) Optimal counselling regarding infant feeding options
Intra-partum	1) Caesarian section 2) Minimal invasive procedures - No invasive foetal monitoring - No suctioning in the absence of meconium stained liquor	1) Normal vaginal delivery 2) Minimal invasive procedures - Do not rupture membranes - No invasive foetal monitoring - No episiotomy - Limit assisted deliveries - No suctioning in the absence of meconium stained liquor 3) If the mother not on HAART give Nevirapine
Post-partum	1) If the mother is on HAART she should continue, in cases where mothers choose to stop there should be meticulous attention to the sequence of stopping drugs to accommodate the very long half-life of some antiretroviral drugs 2) If the mother received single dose NVP the use of a short course (7 days) of standard dose zidovudine and lamivudine may reduce the risk of NVP resistance(17) In the infant: 1) If the mother received single dose NVP only consider extending the use of AZT from 1 week to 4-6 weeks and adding 7 days of lamivudine ♦, (34) 2) No breast-feeding 3) A PCR at 48 hours (to be repeated at 6 weeks if negative) will identify intrauterine infection. If this is positive prevention can be stopped and a CD_4 count performed. ♦ 4) If the child becomes infected despite optimal MTCT prevention, drug resistance testing may assist to identify the optimal HAART regimen ♦	For the infant: 1) *NVP single dose with or without AZT for 1 week▲ 2) Formula milk only or exclusive breast-feeding with rapid weaning after 4-6 months (No mixed feeding) 3) Early infant diagnosis 4) Provide co-trimoxasole prophylaxis to all exposed infants

NVP - nevirapine, AZT – zidovudine, VCT – voluntary testing and counselling for HIV infection, HAART – Highly Active Antiretroviral Therapy

♦ Opinion of the authors; contact an experienced HIV clinician - the SAHIV Clinicians Society can be contacted at (011) 4535066

* Single dose NVP should be given as soon as possible after delivery, particularly in cases where the mother did not take her dose of NVP during labour

▲ Currently 1 week of AZT is used in the Western Cape

feeding together with breast and/or mixed feeding

Some children acquire infection through sexual abuse which should always be considered in cases where the mother is HIV-uninfected.[6] Other potential routes of HIV transmission include blood or blood product transfusion, exposure to contaminated medical waste products, and rarely, transmission may also occur through household contact.[7-9] In addition, there have been reports of children in whom no source could be identified and where nosocomial transmission may have occurred.[8,10]

Preventing mother to child transmission

MTCT prevention is the most cost effective way of managing paediatric HIV. With optimal intervention, the risk of MTCT can be reduced to <2 %.[11] However, optimal intervention is not widely accessible, and practical compromises have to be made in high burden settings with limited resources. Optimal and compromise strategies to reduce the risk of MTCT are summarised in Table 1.

It is imperative that all pregnant women should be offered voluntary counselling and testing (VCT), and this should be regarded as the only acceptable standard of care, both in the private and state sector. Achieving a low (undetectable) viral load in the mother is the best way to minimise the risk of vertical transmission; therefore, access to highly active antiretroviral therapy (HAART) for mothers is an important part of any prevention strategy.[11] According to the African National Prevention of MTCT programme, HIV-infected women who do not qualify for HAART (CD_4 count > 200 cells and or clinical stage < 4) should receive a single dose of nevirapine (NVP) during labour and an additional dose must be administered to the infant within the first 48 hours of life. The implementation of this simple strategy lowers the risk of transmission by 50% and is cost effective.[12,13] However, a negative long term consequence is that resistance to non-nucleoside reverse transcriptase inhibitors (NNRTI) develop in up to 80% of infected infants and/or their mothers, which may reduce the effectiveness of future treatment with NNRTI containing regimens.[14, 5]

Research is ongoing to identify optimal short course regimens that are more effective in reducing the risk of MTCT, while posing a reduced risk of acquired drug resistance. A more effective regimen is the provision of zidovudine (AZT) to the mother from 28 weeks in addition to single dose NVP during labour, together with single dose NVP to the baby in combination with AZT for 6 weeks.[16] A simplified version of this strategy has been implemented in the Western Cape Province of South Africa, where single dose NVP to the mother and baby is combined with one week of AZT to the baby; reported transmission rates are in the order of 5-8% (personal communication MF Cotton) . Researchers have shown that protecting the mother against NVP resistance by using a short course of zidovudine and lamivudine post partum is possible.[17] Similar strategies have not been investigated in infants but may be considered after consultation with an experienced clinician.

Infant feeding options

This is an emotive topic. A significant proportion of infants acquire HIV through breast milk. The risk of transmission is greatest during the first few months, but it is also proportional to the total duration of breast-feeding. Advanced maternal disease with high viral loads and maternal HIV infection (seroconversion) during the period of breast-feeding is associated with an increased risk of transmission.[18] Exclusive breast-feeding with early weaning poses a lower transmission risk than mixed feeding, but exclusive breast-feeding has a very strict definition that is difficult to enforce.[19] The definition of exclusive breast-feeding is; ONLY breast milk may pass the lips of the infant, with the only exceptions being the administration of routine oral polio vaccination and co-trimoxazole prophylaxis.

Mothers, who choose to breast feed exclusively, need adequate counselling on how to achieve rapid weaning around 6 months of age. Other strategies such as home pasteurisation may be helpful to reduce the infectivity of expressed breast milk, but this may not be sustainable in poverty stricken areas.[20] Breast milk pasteurisation seems most useful for premature babies who are likely to benefit most from its beneficial effects, while mothers of premature babies usually have access to kitchen facilities within the hospital under the supervision of nursing staff. It is important to note that maternal treatment with HAART does not fully suppress the secretion of HIV in breast milk.[21] In addition, the low concentrations of active drug excreted in breast milk may lead to acquired resistance in the HIV infected breast-feeding infant.[22]
Uptake of exclusive formula feeding is influenced by cost and availability as well as the stigma that is attached to a mother who does not breast feed.[23] Safe formula feeding requires access to clean water and the implementation of basic hygiene measures. Mothers who opt for formula feeding require counselling about additional feeding options from 4-6 months of age, especially in areas where formula milk is provided free of charge for a limited period of time only.

DIAGNOSING HIV INFECTION

When to test a child?

Children should be tested for HIV if the mother and/or a sibling is known to be HIV-infected (regardless of their age or symptoms), if there is a combination of non-specific symptoms suspect of HIV-disease or if specific conditions are present that indicate immune compromise and probable HIV-disease. (Table 2)

Table 2: When to test a child for HIV-infection*

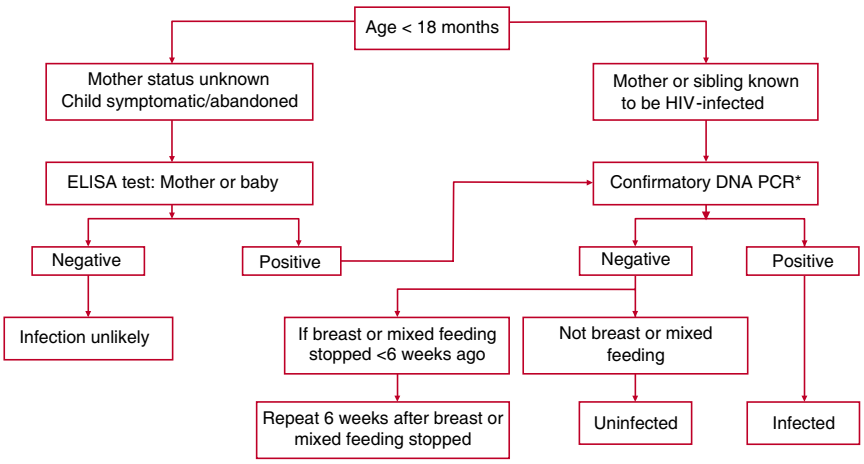
Suspected HIV exposure
- Mother with HIV
- Sibling with HIV

Symptoms indicative of possible HIV disease (3 or more)
- Pneumonia now
- Ear discharge ever
- Low weight for age
- Poor weight gain
- Persistent diarrhoea now or in the past 3 months
- Enlarged lymph glands at ≥2 sites
- Oral thrush
- Parotid enlargement

Symptoms indicative of probable HIV disease (1 or more)
- Poor weight gain despite nutritional support
- Neurodevelopmental delay
- Recurrent bacterial infections
- Herpes Zoster particularly if severe or affecting more than 1 dermatome
- Severe or repeated episodes of tuberculosis
- Probable or confirmed PJP
- Unexplained chronic lung disease
- Esophageal candidiasis
- Unexplained hepatosplenomegaly
- *Kaposi sarcoma*

HIV – Human Immunodeficiency Virus
PJP - *Pneumocystis jerovici* pneumonia
* (Adapted from Khomanani Guidelines for the management of HIV infected Children Ed 1 & IMCI guidelines)

Figure 1: Diagnostic algorithm for infants younger than 18 months of age (Adapted from Khomanani Guidelines Ed1)



*HIV-testing is routinely performed ≥ 6 weeks of age, but immediate testing is warranted if the child presents with suspect symptoms. Where clinical features and laboratory results are discordant, retesting is recommended.

How to establish the diagnosis?

It is important to establish a definitive diagnosis of HIV infection in all exposed infants and in those who present with a suggestive clinical picture (see Table 2). Establishing a definitive diagnosis in infancy is complicated by:

- The transfer of maternal antibodies across the placenta and therefore antibody tests may be false positive in infants <18 months of age.[24]
- The timing of HIV transmission (ante-partum, intra-partum or post-partum), as children who receive breast milk (exclusively or as part of mixed feeding) remain exposed and infection (seroconversion) can occur for an additional 6-8 weeks after exposure to breast milk has terminated.[18,25]

Given the poor performance of clinical diagnostic algorithms, particularly in infants <12 months, all exposed children and children suspected of infection should have access to the appropriate diagnostic investigations.[26] In children > 18 months the HIV Elisa antibody test can be used to establish infection. It is important to perform repeat testing at least 6 weeks after breast-feeding has stopped. In infants <18 months the diagnosis requires the use of assays that detect viral genomic material or antigens to confirm infection. These tests include; 1) HIV viral DNA (qualitative PCR), 2) HIV viral RNA (quantitive PCR/viral load) and 3) the ultrasensitive p24 antigen assay.[27-29]

Although PCR-based tests are expensive, performing a qualitative DNA PCR is accepted as the standard of care in South Africa. Current guidelines in the public sector recommend testing for viral DNA (Roche Amplicor 1.5 DNA PCR assay) at 6 weeks of age. This test has excellent sensitivity and specificity.[27] If the baby has been breast-fed, the test should be repeated 6 weeks after the last breast feed. The CD_4 count and/or percent should not be used as a surrogate marker of HIV infection. Where clinical features and laboratory results are discordant, retesting is recommended.

Disease progression in children

The natural history of disease in HIV-infected infants has been divided into three categories;

1) Those with rapid disease progression, progression to AIDS and/or death within the first year (20-30%)

2) Those with intermediate progression, progression to AIDS or death within 3-5 years (50-60%) and
3) The slow progressors or even long term non-progressors, who live beyond 8 years of age (5-20%)[30]

It seems that the prognosis of African children vertically infected with HIV is worse than that of HIV-infected children in industrialised countries, as a shorter median survival time and increased risk of developing AIDS has been reported.[31] An analysis of birth cohorts from African MTCT studies reported mortality rates of 35% and 52% at 12 and 24 months respectively.[32] Young infants often present with severe clinical disease and there may be discordance between the severity of clinical events and their immunological status (as measured by CD_4%). As soon as the diagnosis of HIV has been confirmed, all infants and children should have access to CD_4% determination and at regular intervals subsequently.

Basic management of the HIV-exposed infant

All infants with known exposure to HIV should be followed up regularly and the accepted standard of care includes the following:

1. Definitive determination of their HIV status as soon as possible.
2. Initiation of co-trimoxazole Pneumocystis jerovici (PJP or PCP) prophylaxis in all exposed infants at the age of 4-6 weeks; this should be continued until the diagnosis of HIV is excluded and probably for the first 6-9 months in all HIV-exposed children, irrespective of the child's HIV-status.
3. Regular clinical assessment for HAART eligibility and management of intercurrent infections.
4. Constant vigilance for documented tuberculosis exposure or symptoms suggestive of disease.
5. Basic child health promotion, including routine vaccinations, deworming and nutritional supplementation as needed.
6. Optimal care and support of the mother and/or care taker.

Performing the basic things well, remains essential to improve the outcome of both HIV-exposed and HIV-infected children.[33]

Conclusion

Paediatric HIV is a preventable illness and the main emphasis should remain on MTCT prevention. Optimal care includes early diagnosis of HIV-infection in all exposed infants and in those with suspect symptoms. Careful clinical assessment and follow-up in conjunction with co-trimoxazole prophylaxis is an essential part of the management of all HIV-exposed infants

Additional topics that will be covered in this series of articles include:

- Initiating ARV treatment in infants and children
- Maintaining infants' and children's ARV treatment
- Common opportunistic infections in HIV-infected infants and children

See CPD Questionnaire, page 42

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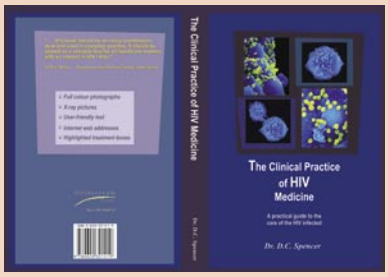
Recommended reading



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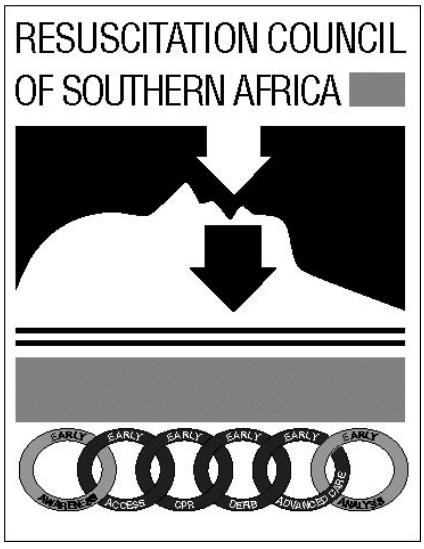
Latest editions of resuscitation algorithms (See page 43-45)



The eight updated algorithms of the Resuscitation Council of South Africa will be featured in the following editions of SA Family Practice. They incorporate the new international recommendations for resuscitation and emergency cardiovascular care.

This issue of SAFP includes the first three, namely:

- **Basic Life Support for Healthcare Providers (Adult and Child)**
  For simplicity and to aid memory retention, Adult, Child and Infant CPR sequences are combined into **one** algorithm rather than as three separate charts. Events that are proceeding unsuccessfully progress vertically downward, while encouraging developments proceed horizontally on the chart.

- **Advanced Life Support for Healthcare Providers (Adult and Child)**
  The management of all cardiac arrest rhuthms can be divided into just two categories: they are either **shockable** *VF or pulseless VT)* or **not-shockable** (**PEA or asystole**). The algorithm follows this simple concept.

- **Recommended Defibrillator Energy Settings in Cardiac Arrest (Adult and Child)**
  Current recommendations for both monophasic and biphasic defibrillators are tabulated. Users of the defibrillators are urged to ensure that the appropriate energy settings are clearly marked on all defibrillators that you may have access to, and that all AED's are upgraded as a matter of urgency.

What is the Purpose of an Algorithm?
An algorithm is a very simplified, summarised, sequentially structured memory aid for use by someone who already has the background in-depth knowledge of the relevant subject matter, but would like to revise the topic at a glance in an emergency. An algorithm does not replace sound clinical judgement, and cannot hope to cover all possibilities and situations. There are always exceptions, variations and alternatives in medical care. Just like a recipe, an algorithm is one suggested plan of action, which may result in a successful outcome, based on the best available current scientific evidence. An algorithm must never be seen as an alternative to proper education and training. It is hoped that anyone looking at an algorithm will indeed be tempted to immediately seek training in that particular skill and to only feel comfortable once practical competence has been successfully achieved.
You will note that algorithms issued by the Resuscitation Council of Southern Africa will always be dated. As new scientific evidence becomes available, these algorithms will be modified accordingly. You are encouraged to only use the most up-tod ate algorithm, and to discard previous outdated or undated charts. We hope you will enjoy this set of "memory joggers"!

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