Scaling up Early Infant Diagnosis and Linkages to Care and Treatment

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The Unite for Children, Unite against AIDS briefing series identifies and explores the latest information and analysis on subjects related to children and AIDS. Based on evidence and reports from the field, these briefs serve as a resource and advocacy tool to highlight some of the key issues shaping the global work in making a difference in the lives and life chances of children affected by HIV/AIDS. Unite for Children, Unite against AIDS is a call to action around the impact of HIV and AIDS on children. It focuses on four key areas - the “Four Ps”: preventing mother-to-child transmission of HIV, providing paediatric treatment for children infected with the virus, preventing new infections among adolescents and young people, and protecting and supporting children affected by HIV and AIDS.

For more information on Unite for Children, Unite Against AIDS, visit [www.uniteforchildren.org](http://www.uniteforchildren.org), or contact Shani Winterstein at swinterstein@unicef.org.

This Brief was produced in January, 2009.
Introduction

For over fifty years, UNICEF has been dedicated to improving maternal, newborn, and child health around the world. In the age of HIV, this commitment has translated itself into the work of partners in the Unite for Children, Unite against AIDS initiative to help governments strengthen their health systems’ response to HIV. Today, interventions for preventing mother-to-child transmission (PMTCT) of HIV and for treating HIV-infected children are established and functioning, to at least some extent, in nearly every country in the world. Progress is being seen in many of these countries in preventing HIV infections from mothers to their babies and putting children infected with HIV on life-saving treatment. However, in order for all children infected with HIV to receive essential treatment and care, few things are more important than early and accurate HIV diagnosis. Without care and treatment, about one third of children living with HIV will die in their first year of life and almost 50% by the second year of life. In 2007, only 8% of infants born to women with HIV were tested within the first 2 months of their life— a critical intervention to identify those who are infected and initiate them on treatment in a timely manner. Consequently, a small fraction of these children received the proper care and support needed. This paper provides an overview of the importance of ensuring that infants born to mothers living with HIV receive a timely HIV test and illustrates the various processes which need to be implemented in countries to make this possible. Through the identification of these infants, and all children living with HIV, countries can help provide essential health services, including HIV care and treatment services when needed, which will translate into real progress on child survival.
Background: the importance of early infant diagnosis

By the end of 2007, an estimated 33 million [30.3 million to 36.1 million] people were living with HIV. In 2007 alone, an estimated 370,000 (330,000-410,000) children younger than 15 years of age were newly infected with HIV, mainly through mother-to-child transmission. HIV can be transmitted from a mother to her child during pregnancy, at childbirth and through breastfeeding. Almost all infections in infants can be avoided by timely delivery of known, effective interventions to prevent mother-to-child transmission.

All infants who are exposed to HIV should be tested, even if their mothers received antiretrovirals (ARVs) for PMTCT. Evidence has shown that HIV infection follows a more aggressive course among infants and children than among adults. Without access to life-saving drugs, including antiretroviral therapy and preventive interventions such as cotrimoxazole prophylaxis, about one-third of infants will die by age 1 year, and 50% by age 2 years. In 2007, an estimated 270,000 [250,000-290,000] children younger than 15 years of age died of HIV-related causes. The vast majority of those children were under the age of five and over 90% were living in Sub-Saharan Africa. Many of the 270,000 children who died in 2007 never received an HIV diagnosis or entered into HIV care. Most of these deaths could have been avoided through early diagnosis of HIV and timely provision of effective care and treatment.

Box 1. The ‘Four Ps’: Goals of Unite for Children, Unite against AIDS

- Prevent mother-to-child transmission of HIV
  By 2010, offer appropriate services to 80 per cent of women in need
- Provide paediatric treatment
  Provide antiretroviral treatment, cotrimoxazole or both to 80 per cent of children in need
- Prevent infection among adolescents and young people
  Reduce the percentage of young people living with HIV by 25 per cent globally
- Protect and support children affected by HIV and AIDS
  Provide services that reach 80 per cent of children most in need

Preventing mother-to-child transmission: successes & challenges

The urgency of preventing mother-to-child infections is clear. At the end of 2007, 33% of pregnant women living with HIV received antiretrovirals to prevent mother-to-child transmission (491,000 of the total estimated 1.5 million pregnant women living with HIV). This represents a noteworthy increase from 23% in 2006, 15% in 2005 and 10% in 2004 (Fig. 1).

However in 2007, approximately one million pregnant women living with HIV gave birth without access to PMTCT services. At the end of 2007, 2 million [1.9 million to 2.3 million] children younger than 15 years were estimated to be living with HIV, with the vast majority having become infected perinatally.

The number of new infections in children under the age of fifteen years is starting to decline (Figure 2). It is likely that this drop has been driven by a combination of factors, including the progress being made in the scale-up of PMTCT, in treatment for adults, as well as falling HIV prevalence among pregnant women.

Figure 1. Percentage of pregnant women with HIV receiving antiretrovirals for preventing mother-to-child transmission of HIV in low and middle-income countries, 2004-2007

Figure 2. New infections among children under 15 years of age, 1990-2007

Background: the importance of early infant diagnosis
Providing treatment and care to HIV infected children: successes and challenges

The number of children who received antiretroviral treatment (ART) rose dramatically to almost 200,000 in 2007, up from around 127,000 in 2006 and 75,000 in 2005 (Figure 4). 9

In order for the Unite for Children, Unite against AIDS target of providing ART, cotrimoxazole, or both, to 80 per cent of children in need by 2010 to be met, the number of children reached will need to be greatly expanded (see box 1). Achievement of this target is dependant on significant scale-up of early infant HIV diagnosis.

Recent evidence demonstrates that early HIV diagnosis and ART is critical for infants, and a significant number of lives can be saved by initiating ART for HIV-infected infants immediately after diagnosis within the first 12 weeks of life. The Children with HIV Early Antiretroviral Therapy (CHER) study from South Africa demonstrates a 76 per cent reduction in mortality when treatment is initiated within this time period.10

Other studies have shown that late initiation of treatment results in a child’s immune system becoming severely compromised. One study showed that infants and children started on ART when they were already severely immunodeficient never regained normal levels of immune functioning even after five years on treatment.11,12 Another study showed that such infants and children are more likely to die than those children who received treatment at an earlier stage.13

Clinical guidelines issued by WHO therefore now recommend that all infants younger than one year of age with confirmed HIV infection should start antiretroviral therapy, irrespective of clinical or immunological stage. Previously, recommendations to initiate ART among children were based on an initial immunological and clinical assessment, and treatment was recommended only for the most severely affected children.

Even though it is widely known that early initiation of ART in children with HIV saves lives, and that children respond as well to ART in low and middle income countries as in high-income countries,14,15,16,17 very few children under the age of one are currently being diagnosed and subsequently receiving treatment. Several studies suggest that the median age at which children living in low-resource countries begin treatment is between five and nine years old,18 much later than children living in high-resource countries.

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Figure 3. Percentage of pregnant women living with HIV receiving antiretrovirals for preventing mother-to-child transmission of HIV in the 10 countries with the highest estimated number of pregnant women living with HIV, 2007

There are 13 high burden countries9 (figure 4) which account for 75 per cent of the estimated 1.5 million pregnant women living with HIV in 2007 in low and middle income countries and nearly 75 per cent of all children living with HIV. All but one of these countries (India) are in sub-Saharan Africa. The coverage of antiretrovirals for preventing PMTCT varies among the countries that have the largest number of pregnant women with HIV. This tells us two things: that the scale-up of PMTCT services is possible even in the most affected countries and that large numbers of children continue to be infected with HIV through mother-to-child transmission.
Scaling-up early infant diagnosis, identifying all infected children, and improving linkages to care and treatment

Identifying all children infected with HIV as early as possible is an essential component to child survival. As countries scale-up early infant diagnosis, the processes of identifying these children should be introduced as a package of services in order to strengthen overall health systems. This package of services should include all necessary HIV testing as well as infant feeding counselling and support, nutritional support and cotrimoxazole initiation. The process of ensuring that all exposed infants and children suspected of being infected with HIV receive an HIV test, and if infected, receive care and treatment, provides an important opportunity for health systems to deliver comprehensive interventions for women and children.

Optimizing follow-up of known exposed infants from PMTCT services

As stated earlier, many countries are moving towards national coverage of services for PMTCT; however, most children born to women with HIV are not being systematically monitored and followed up during the postpartum period and are thus missing out on life-saving services. Experience from South Africa reveals that without a systematic and structured plan that includes early testing at 6 weeks, up to 85% of HIV-exposed infants are lost to follow-up from clinics providing services for PMTCT by one year of age, with 75-80% already lost to follow-up at 6 months of age. The follow-up of known HIV-exposed children is not only necessary to identify infants with HIV and to ensure the timely initiation of treatment and care, but to also avoid postpartum HIV transmission and improve overall infant health outcomes.

Scaling up HIV PCR

Standard HIV antibody testing - as is done with adults and older children - cannot identify infected infants in their first year of life, as it also detects maternal HIV antibodies that are transferred to the baby during pregnancy (and subsequently decline slowly within the first year of life). More demanding testing methods that rely on detecting HIV virus, or virological tests (HIV DNA PCR, HIV RNA PCR, bDNA, NASBA), are required for diagnosing infants.

Virological testing detects HIV DNA or RNA. HIV DNA testing can also be reliably performed on specimens collected onto filter paper, or dried blood spots (DBS), and sent to laboratories with capacity for testing. The use of DBS requires only a few drops of blood from an infant. Once specimens are collected, they can be easily stored and transferred without cold-chain systems to centralized testing locations for analysis. The use of DBS permits blood samples to be collected in remote locations and allows countries with a limited number of specialized laboratories to expand access to virological testing. HIV RNA methods are also reliable and can be done on plasma and whole blood specimens and are well suited to inpatient or sick infants where specimens using DBS are not essential.

Figure 5 shows how a PCR network using DBS works. What it shows is that results can be analyzed and returned to the clinic within just two weeks. Rapid return of, and action on results, is essential to minimize morbidity and mortality in infants, considering the very rapid progression of disease in this population.

Figure 5. Example of PCR network using DBS, Kenya

Steps for using DBS for PCR testing, Kenyan example
1. Samples are collected from infant and placed on filter paper.
2. Samples placed in drying racks for a day to fully dry. They are placed in individual envelopes with desiccant and then placed in a larger airtight zip-lock bag with humidity indicators for transport.
3. Samples sent via courier to a laboratory where PCR testing capacity is in place.
4. Adequateness of samples is assessed upon arrival at the laboratory; adequate samples are analysed for the presence of HIV and determined to be either a positive or negative result.
5. Results sent back to the centres via courier or e-mail for quickest turnaround. In addition, all results sent via e-mail are also sent via courier to ensure good records.
6. Results provided to the caregiver of the infant at the next clinic visit, and follow-up continues in accordance with the national algorithm for early infant diagnosis.
Some countries have made great strides in providing access to early infant diagnosis of HIV. In 2007, 30 low- and middle-income countries used DBS filter paper to perform DNA PCR testing for HIV in infants, up from 17 countries in 2005 (Fig. 6). DBS has been used for transporting specimens to a centralized laboratory for HIV DNA testing in several countries in sub-Saharan Africa (Botswana, Côte d’Ivoire, Kenya, Rwanda, South Africa, Zambia and others).

Even where virological testing is available through DBS, transport time and logistics can still pose barriers to providing timely results. The first barrier is that specimens stay too long at the clinic before they are shipped to the laboratory for analysis, and the second is that even when results – positive or negative – reach the clinic, they are not communicated in a timely manner to the patient and caregiver so that appropriate action can be taken.

**Child Health Cards**

Many countries have high levels of immunization coverage. Maternal, newborn and child health clinics, where a child often receives his or her first set of vaccinations, provide important opportunities to identify and test infants and children who are known to be exposed to HIV. The age at which infants receive their first dose of the diphtheria, pertussis, tetanus immunization (DPT1) – at or around six weeks of age – is an ideal time for early virological testing for HIV as part of a comprehensive package of services essential for a child’s health. Several countries, including Cameroon, Malawi, Rwanda, Swaziland, United Republic of Tanzania and Zimbabwe (see box 2) have revised child health cards to include HIV-related information, making tracking of exposed children easier and increasing the likelihood that infants known to be exposed to HIV are referred for virological testing and put on treatment. These cards have also helped exposed children receive other critical interventions, such as cotrimoxazole prophylaxis and nutritional support.
Identifying all children living with HIV

In order to identify all children living with HIV, systems must be in place for children to have access to HIV testing through various entry points.

Provider-initiated testing and counseling of sick children

To-date, most children are entering HIV care and treatment programmes for children at an older age, after being identified in acute and chronic care facilities rather than as a follow-up of services for preventing mother-to-child transmission. A recent report from Malawi showed that 80% of children were referred to ART clinics as a result of provider initiated testing and counselling in acute and chronic care facilities.22

In countries such as Malawi and Zambia, provider-initiated testing and counselling of sick children has helped to substantially increase the numbers of HIV-infected infants and children who are detected. In 2007, 78 countries reported that they have a policy on provider-initiated testing and counselling for infants and young children, up from only 47 countries in 2005 (Fig. 6).23

Child Health Days

Another modality for scaling up HIV diagnosis of young children takes advantage of child health days, organized in many countries to deliver health and nutrition services on a large scale. During child health days in Lesotho in 2007, more than 4,400 children were tested for HIV (including some through DBS PCR) and screened for tuberculosis and malnutrition. Nearly 100 per cent of participants (adults and children) were tested. Overall HIV prevalence among children was 3 per cent, and children who tested positive were immediately referred to appropriate care at the nearest antiretroviral treatment clinic.24 As a model for provider-initiated HIV testing, the Lesotho experience is an important one to highlight and discuss, because of its high participation rate and seeming effectiveness.

Conclusion

The scale-up of programmes that provide early diagnosis of infants exposed to HIV and treatment for children who are infected is an essential component to child survival. Early initiation of treatment significantly reduces AIDS-related mortality in infants and young children, highlighting the urgent need to expand access to virological testing for infants and start them promptly on treatment. Scaling up in most countries will require a number of health systems strengthening interventions such as increasing laboratory capacity, provision of equipment, ensuring a reliable supply of reagents, the training of service providers and the establishment of networks that effectively link diagnosis with care. In some countries, policy level work will be necessary such as the revisions of national policies to include guidelines for early diagnosis and treatment targets. There is a need to develop and use innovative mechanisms to improve transport times and logistics that pose barriers to reaching families in a timely manner. Time is of particular importance for the youngest children, in whom rapid disease progression leads to early death.

Early infant diagnosis is a vital intervention which allows countries to provide essential health services for all children and to continue to make progress in keeping children alive and healthy.
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Notes


