Taking stock:

HIV in children

THE STATE OF AFFAIRS

Introduction

Each day, some 1500 children under 15 years of age become infected with HIV, an estimated 90% of whom live in sub-Saharan Africa. In 2005, there were 2.3 million (1.7–3.5 million) children living with HIV worldwide, most of whom acquired the virus in utero, during birth or while being breastfed, ways of contracting HIV that can be prevented.

For many children infected with HIV, the chances of survival are slim. Worldwide, AIDS now accounts for 3% of deaths in children under five years of age—and 6% of those in sub-Saharan Africa, where AIDS has become one of the major killers of young children.

One in seven people dying of HIV-related illness worldwide is a child under 15 years old. This is due largely to the failure to introduce programmes for preventing mother-to-child transmission of HIV on the scale needed.

Without HIV care, including antiretroviral therapy, the progression of HIV infection in children is particularly aggressive. In 2005, an estimated 380 000 (290 000–500 000) children died of HIV-related causes. It is likely that one half of them did not live past their second birthday. In hard-hit countries such as Botswana and Zimbabwe, HIV is the underlying reason for more than one third of all deaths among children under the age of five.

Yet paediatric HIV is almost entirely preventable. It has been virtually eliminated in high-income countries, where the ready availability of HIV prevention, testing and treatment services has lowered mother-to-child transmission rates to less than 2% and boosted the survival rates of HIV-infected infants (more than 80% of whom now live past the age of six).

However, the relatively simple services responsible for such achievements are largely absent in the places that need them most—particularly in sub-Saharan Africa and south Asia.

Figure 1

Estimated number of children
(0–14 years) living with HIV in 2005

Source: WHO/UNAIDS
**WHAT WE KNOW**

**How do young children acquire HIV?**

In 2005, an estimated 540 000 (420 000–670 000) children under 15 years of age became infected with HIV, mostly through mother-to-child transmission.

In sub-Saharan Africa, where the vast majority of children with HIV live, more than 95% of HIV-infected infants acquire HIV from their mothers in utero, during their delivery, or while being breastfed. A small fraction of HIV infections in children are caused by unsafe injections, the transfusion of infected blood or blood products, sexual abuse, sexual intercourse (a significant mode of transmission among adolescents) or scarification.

**How long do children with HIV survive?**

Between 25% and 30% of children who acquire HIV from their mothers die before their first birthday. Most of them will have acquired HIV in utero or around the time of birth. More than half (50-60% of the children) develop symptoms early in life and, in the absence of timely diagnosis and effective treatment, die by the time they are two years old. In a study of almost 3500 children enrolled in seven perinatal trials in sub-Saharan Africa, for example, 35% of HIV-infected children had died by age one year, and 53% had died before they reached the age of two years.

Without effective prevention measures, the risk of HIV transmission from an HIV-infected mother to her child, before or during the child’s birth, is 15–25%. If the mother breastfeeds her newborn until 18–24 months, that risk increases to 30–45%. This underscores the need to prevent HIV transmission in general, and to provide girls and HIV-positive women with better options for avoiding pregnancy.

**How can mother-to-child transmission of HIV be prevented?**

Pregnant women must have access to HIV testing and counselling so that they can learn their HIV status and make informed decisions about pregnancy,
delivery and feeding options. Those who are HIV-positive should have access to a package of services that can enable safe delivery and ensure safe postnatal care and support for the baby and the mother. In high-income countries, the use of antiretroviral drugs for treating the mother and preventing infection in the baby has become the standard of care and has led to the virtual elimination of mother-to-child transmission of HIV.

Widespread, effective services for prevention of mother-to-child transmission (PMTCT) could preclude an estimated 315 000 paediatric HIV infections annually with currently available technology. In North America and Europe, where such services are easily accessed, less than 2% of children born to HIV-positive mothers acquire the virus currently. In these areas, fewer than 300 new HIV infections were recorded in children less than 15 years old in 2005, not all of which were due to mother-to-child transmission.

Even in resource-poor settings, mother-to-child transmission can be limited to 2-4% when the necessary services are available, as recent experiences in Abidjan, Côte d’Ivoire have shown.

Does antiretroviral therapy work for children with HIV?

Antiretroviral therapy has proven to be highly effective in children, including for those in resource-poor settings. Rapid initiation of treatment restores and preserves immune functions, promotes normal growth and development, and prolongs life. Generally, some 80% of children with HIV die by age five years if they do not receive antiretroviral therapy. In high-income countries, where most children with perinatally acquired HIV infection are treated early with antiretroviral therapy, the treatment has been shown to reduce mortality by five-fold or more and results in survival rates of 80% and higher.

What else is needed?

The low-cost antibiotic co-trimoxazole can provide potentially life-saving protection against opportunistic and other childhood infections. In some settings, it has been shown to reduce mortality in children with HIV by more than 40%. Treatment costs about US$ 0.03 a day, or about US$ 10 a year per child. It has been estimated that up to 4 million children younger than age 15 years could benefit from treatment with co-trimoxazole, though only about 1% of those in need currently receive the drug.

CHALLENGES ...

Hardly anyone disputes children’s right to HIV prevention, care and treatment. Experiences in Brazil, South Africa and elsewhere demonstrate that early diagnosis of HIV in children is feasible in resource-poor settings, and that children respond well to antiretroviral therapy.

Nevertheless, in general, too little effort is being made to ensure that children receive the services they need, especially in sub-Saharan Africa, where most of the burden of paediatric HIV is concentrated. In 2005, some 380 000
(290 000–500 000) HIV-infected children younger than age 15 years died—almost of all them in sub-Saharan Africa. By contrast, according to the latest available data, fewer than 100 children with HIV died in the world’s high-income countries in 2004. Several factors cause this discrepancy:

- Many of the worst-affected countries are struggling with human resource constraints and weak health systems.
- There is limited screening for HIV in children many countries.
- Tools for diagnosing HIV in infants tend to be unaffordable or absent.
- Misconceptions persist about the effectiveness of antiretroviral therapy for children.
- In many places there is still limited experience with simplified, standardized treatment guidelines.
- Practicable paediatric antiretroviral formulations are either lacking or unaffordable in many of the countries that need them most.

Preventing mother-to-child transmission of HIV

Although about 100 countries have introduced efforts to prevent mother-to-child transmission of HIV, worldwide, about 10% and, in sub-Saharan Africa, fewer than 6% of pregnant women are currently offered PMTCT services. HIV transmission rates from mothers-to-children averaged at 20% in low- and middle-income countries in 2005, compared to less than 2% in high-income countries.

Expanding PMTCT programmes is vital if children are to be protected against HIV infection. Such an achievement would require meeting several other challenges, as well.

In many sub-Saharan African countries, pregnant women seldom visit an antenatal care clinic and less than half of all deliveries are attended by a suitably trained health professional. Those women who do visit antenatal clinics might never be offered HIV testing and counselling, the test might not be performed or they might not receive the test results. Thus, they are unable to know their HIV status and to prepare accordingly by seeking out services that can prevent their newborns from becoming infected and that can prolong their own lives.

In addition, few PMTCT programmes are properly linked with HIV services for HIV-positive mothers. Those mothers who do receive antiretroviral prophylaxis often get only a single-dose of nevirapine at time of birth; they themselves do not embark on the antiretroviral therapy that can protect or restore their own health. Even then, after giving birth, few mothers with HIV receive counselling or infant feeding support, thus increasing the chances that their uninfected newborns could become infected.

Diagnosis

As with adults, most HIV-infected children are diagnosed very late in the course of illness or not at all. The rapid progression of HIV in children means that many die in infancy or early childhood from common
childhood conditions and opportunistic infections that are preventable and treatable.

Prompt diagnosis of HIV infection is therefore vital so that antiretroviral therapy can be started as quickly as possible. However, achieving this can be complicated.

Usually, HIV testing entails comparatively inexpensive and readily available tests to detect the presence of antibodies to HIV (which, typically, appear in the blood within a few weeks of infection). However, all babies born to women with HIV acquire their mother’s antibodies, while their own immune system develops. Those antibodies usually are eliminated from the child’s system within the first year of life (though occasionally they can persist for up to 18 months). The presence of HIV antibodies in the blood of a baby younger than 18 months therefore does not necessarily mean that the child itself is infected with HIV. Accurate diagnosis of HIV infection in children younger than 18 months requires detecting the virus itself, which entails more sophisticated tests. Such virological tests require relatively expensive laboratory equipment that is not readily available in low-income countries. The equipment can cost up to US$ 140 000, and each test can cost up to US$ 40. In addition, in several countries the necessary technologies are licensed for patient monitoring but not for HIV diagnosis in infants.

Psychological barriers to testing infants can also delay diagnosis. Both the social stigma that HIV diagnosis might trigger for mother and child and the lack of treatment availability often discourage women from being tested and from having their children tested for HIV.

**Treatment**

Despite the recent progress in treating adults living with HIV, children are not getting the medicines that can prolong their lives. In low- and middle-income countries, about 60 000 to 100 000 of the more than 800 000 HIV-positive children needing antiretroviral therapy (most of them in sub-Saharan Africa) were receiving it in June 2006.

Not all the antiretroviral drugs approved for use in adults with HIV exist in an appropriate form, or are licensed and approved, for use in children—and those that are available often are unaffordable. In addition, the medicines are frequently unavailable in formulations that are suitable for children. Syrup formulations of antiretroviral drugs have been developed, but they tend to be foul-tasting, must be taken in large volumes, require refrigeration and have short shelf lives once opened—all of which can make them impractical.

Fixed-dose combination drugs, in which two or three different drugs are combined in a single pill to simplify treatment regimens, show excellent clinical, immunological and virological results when used in adults. Yet few such drugs are available currently for treating children.

Competition from generic manufacturers and pressure from lobby groups have led to lower prices for many antiretroviral
drugs for adults in recent years. However, the drugs for treating children can cost many times as much as those for treating adults. For example, in 2005, the drug Retrovir (zidovudine) cost US$ 260 per year for the 100 mg capsule used by children and US$ 183 annually for the adult 300 mg capsule—1.4 times the price for one third of the active ingredient. A one-year supply of a standard three-drug regimen ( stavudine, nevirapine and lamivudine) for adults cost on average about US$ 148 in 2005 in low-income countries, but the regimen for children cost US$ 2000 per child (and US$ 800 for a generic version).

Table 1

Percentage of people receiving antiretroviral therapy who are childrena
(in selected countries, end 2005)

<table>
<thead>
<tr>
<th>Sub-Saharan Africa</th>
<th>Asia</th>
<th>Latin America and the Caribbean</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ghana</td>
<td>China</td>
<td>Peru</td>
</tr>
<tr>
<td>Nigeria</td>
<td>India</td>
<td>Venezuela</td>
</tr>
<tr>
<td>Côte d’Ivoire</td>
<td>Viet Nam</td>
<td>El Salvador</td>
</tr>
<tr>
<td>Malawi</td>
<td>Cambodia</td>
<td>Brazil</td>
</tr>
<tr>
<td>Mozambique</td>
<td></td>
<td>Guyana</td>
</tr>
<tr>
<td>Rwanda</td>
<td></td>
<td>Haiti</td>
</tr>
<tr>
<td>Namibia</td>
<td></td>
<td>Argentina</td>
</tr>
<tr>
<td>Zimbabwe</td>
<td></td>
<td>Honduras</td>
</tr>
<tr>
<td>Kenya</td>
<td></td>
<td>Panama</td>
</tr>
<tr>
<td>South Africa</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zambia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Central African Republic</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Uganda</td>
<td></td>
<td></td>
</tr>
<tr>
<td>United Republic of Tanzania</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Median</strong></td>
<td><strong>Median</strong></td>
<td><strong>Median</strong></td>
</tr>
</tbody>
</table>


a Data on both children (<15 years) and adults (15–49 years) were available for about 500 000 people from 27 countries. Data for the other regions were not available.
Patent and regulation issues present an additional hurdle for the development, production and availability of paediatric formulations. Patents can also hinder the development and production of fixed-dose combinations. In addition, many developing countries encounter difficulties in obtaining information on the patent status of antiretroviral drugs. This lack of clarity about patent status creates uncertainties and can affect the procurement and production of generic versions of antiretroviral drugs. Meanwhile, high application costs discourage drug manufacturers from seeking country registration for paediatric drugs in many low-income countries.

Countries with serious AIDS epidemics are also struggling to forecast their paediatric HIV drug needs accurately, partly because of a shortage of precise epidemiological data.

Underlining the need for health systems strengthening generally is the lack of appropriate infrastructure and trained health-care personnel for treating children with HIV, and for supporting adherence to treatment regimens. Difficulties in assessing the types and quantities of drugs needed to treat children, and ineffective delivery systems limit scale-up of treatment. The problem is especially acute in east and southern Africa, where hospitals are being overwhelmed with caring for AIDS-affected patients and health systems are undermined by the loss of staff. The World Bank has estimated that countries with HIV prevalence of 15% can expect to lose about 3% of their health workers to AIDS each year.

---

**...AND SOME PROGRESS**

**Preventing mother-to-child transmission of HIV**

Many dozens of PMTCT pilot projects exist (see below), but only recently have national programmes begun to provide services at the scale required. In Jamaica and several eastern European countries, three quarters or more of HIV-infected women were receiving antiretroviral prophylaxis in 2005. Brazil and Thailand have sharply reduced mother-to-child transmission of HIV. At centres participating in a Brazilian Paediatric Society study, the infection rate in babies born to HIV-positive mothers decreased from 16% in 1995 to 2.4% in 2002 after receiving a package of basic PMTCT interventions. Overall, more than three quarters (8500) of the estimated 12 000 Brazilian children in need of antiretroviral therapy were receiving it in 2004. In Thailand, three out of four HIV-infected pregnant women now receive AZT to prevent mother-to-child HIV transmission. Almost all children born to HIV-infected mothers receive drug treatment, and just over half of the 12 000 children needing antiretroviral therapy are receiving it.

In sub-Saharan Africa, there has been progress as well. In that region, 11 of the worst-affected countries saw a 10-fold increase during the period 2002–2004 in the numbers of pregnant women tested for HIV and those given antiretroviral prophylaxis through PMTCT programmes. Botswana, in particular, has boosted its efforts (Box 1) massively, while countries such as Cameroon, Côte d’Ivoire, Kenya,
Rwanda, South Africa, Uganda and Zambia are trying to follow suit. The number of PMTCT sites in Cameroon, for example, increased from 64 in 2002 to 420 in mid-2005.

Such progress needs to be consolidated and extended. While many of these countries have been expanding their PMTCT programmes, coverage is still poor: the proportion of HIV-infected women receiving antiretroviral prophylaxis was only 16% in Zambia, 20% in Kenya and 22% in South Africa in 2004. Elsewhere, the corresponding coverage was dismal. In Nigeria, only 0.1% of HIV-infected women were receiving antiretroviral prophylaxis. At the same time, that figure was 1% in Ethiopia, 3%, in Mozambique, 2% in the United Republic of Tanzania and 5% in Zimbabwe.

**Treatment**

Globally, the number of children receiving antiretroviral therapy increased by 10 000 to 15 000 in 2004–2005, but it still constituted a mere 6% of the total number of people needing treatment. Just two countries—Brazil and Thailand—accounted for almost half of the children receiving treatment.

There has been some recent progress in developing fixed-dose combinations for children, with three producers of generics, based in Thailand and India, having developed such products. However, as of mid-2006, none had received the necessary approval from internationally recognized regulatory authorities.

Antiretroviral drug prices remain high, although some generic drug manufacturers appear ready to sell paediatric drugs at lower prices. Wider availability of low-cost paediatric fixed-dose combinations could trigger price reductions on single-drug formulations.

Meanwhile, Brazil, Chile, France and Norway have proposed the creation of an International Drug Purchasing Facility for HIV, tuberculosis (TB) and malarial drugs and diagnostics, with paediatric products an important focus. The aim is to use bulk purchasing power to influence market dynamics and encourage price reductions, as well as spur the development of new formulations and strengths (such as paediatric formulations). Some organizations, such as the Clinton Foundation, have already moved to lower prices by guaranteeing

**Where there’s a will, there’s a way**

Botswana is one of the few countries with a serious AIDS epidemic that has dramatically stepped up efforts to end mother-to-child transmission of HIV. Those services have been integrated with mother and child health-care services generally, and are available in all public antenatal clinics. Moreover, they are free. Some 92% of women delivering in hospitals were being tested for HIV in 2005, and at least 70% of those who tested HIV-positive received either zidovudine prophylaxis or nevirapine during pregnancy. Botswana funds most of its PMTCT programme with resources from the public purse.

Preliminary results of a pilot study on early diagnosis in Francistown (using HIV-DNA PCR, or rapid polymerase chain reaction, testing of babies) suggest that mother-to-child transmission has been reduced to less than 6%, and that early diagnosis is feasible. Without such programmes, an estimated 40% of infants born to seropositive mothers would be infected with HIV.
purchases of large stocks of paediatric drugs for HIV-infected children. Such an arrangement with the Indian generic drug manufacturer Cipla, for example, has lowered the prices of some drugs as much as 50%.

All this shows that when political, economic and public health entities have chosen to act, innovations and breakthroughs have followed. In the past few years, financial commitments have increased, greater political will is being marshalled, and more pieces of the technical puzzle are falling into place. The world seems poised for a breakthrough against paediatric HIV.

A REACHABLE GOAL

Eliminating transmission of HIV from mothers to children is not a pipe dream; the services for preventing perinatal HIV transmission are well understood. The challenge is to make them widely available where they are needed.

The starting point for reducing the burden of paediatric HIV is to prevent HIV infection in parents-to-be. Prevention efforts overall must be intensified and expanded.

Preventing unintended pregnancies in HIV-infected women will also reduce paediatric HIV. Reproductive health services should be strengthened so that all women can make informed decisions about planning their reproductive life. All pregnant women should have access to antenatal care, HIV diagnosis, antiretroviral prophylaxis or antiretroviral therapy, and appropriate feeding options. Children who do not benefit from such services and who become HIV infected must have access to antiretroviral therapy. Treating HIV-related infections in children is feasible. As many as 1.2 million child deaths could be prevented by providing antiretroviral therapy and the antibiotic co-trimoxazole by 2010.

IMMEDIATE PRIORITIES

The burden of paediatric HIV is unacceptably high, yet eminently avoidable. It can be virtually removed if solid progress is made on these four, long-term challenges:

- Programmes for preventing the transmission of HIV from mother to child must be drastically expanded in the countries with the biggest HIV burdens.
- Simpler and more affordable technologies for accurately detecting HIV in infants must be developed and put into wide use.
- Practical and affordable paediatric antiretroviral drug formulations must be made available.
- Health systems—especially the human resources, facilities and logistical systems that are needed to run such programmes efficiently—must be strengthened drastically.

Progress on these fronts will require a set of specific breakthroughs in the short term. Achieving them should be a priority in the immediate future.
**Intensify HIV testing and counselling**

- Prospective parents should know their HIV status.
- Routinely recommended HIV testing and counselling should be introduced in antenatal care settings, and rapid testing kits should be used more widely.
- Systematic approaches to diagnostic testing in infants and children should be introduced.

**Scale-up programmes for preventing mother-to-child HIV transmission**

- Governments must urgently scale up these programmes to ensure that quality national coverage is achieved, and that antiretroviral prophylaxis is available to all women who test HIV-positive as well as their children.
- In doing so, it is worth noting that in countries that have abolished user fees, women’s uptake of public health-care services has tended to rise.

**Speed-up diagnosis of HIV in children**

- It is essential that infants and children with HIV be identified rapidly as a first step in securing appropriate treatment and care for them. There should be wider use of rapid HIV antibody tests in infants older than 18 months, and these should be accessible to children in paediatric care units, therapeutic feeding centres, primary-care facilities, and at adult tuberculosis and antiretroviral care points.
- Standardized virological diagnostic services must be put in place within national programmes.
- More research and development of simple, affordable virological diagnostics could greatly improve programmes for prevention and care.

**Implement paediatric HIV treatment guidelines**

- Paediatric treatment guidelines, which provide reliable and practical guidance on how to diagnose and treat children with HIV, have been developed and must now be implemented.

**Add co-trimoxazole to the basic health-care package**

- Countries with generalized AIDS epidemics must ensure co-trimoxazole is provided to HIV-exposed and HIV-infected children, as part of a basic health-care package.

**Produce antiretroviral drugs in forms suitable for children**

- There is an urgent need for research into, and development of, improved antiretroviral products to treat younger children (in particular, more fixed-dose combinations for children).
- Because adult antiretroviral pills are too large for paediatric dosing, smaller scored pills (that can easily and accurately be divided into halves or quarters) are needed. Capsule sprinkle formulations that can be opened and mixed with food or tablets that can be crushed and dissolved in water would
also be useful. Such modifications could save hundreds of thousands of children’s lives.

Remove regulatory obstacles

- Ensure rapid prequalification or regulatory approval of suitable, new fixed-dose combinations that are submitted.
- Ensure rapid, in-country registration of paediatric drugs.

Make antiretroviral drug prices affordable

- Paediatric antiretroviral drugs must be priced at affordable levels. As a start, price differentials between adult and paediatric antiretroviral drugs should be removed.

Lift intellectual property barriers

- Greater efforts must be made to facilitate and increase transparency on the patent status of antiretroviral drugs and formulations in developing countries with the capacity to manufacture such products.
- Research and development pharmaceutical companies should clearly state their policies not to enforce patent rights on antiretroviral drugs or grant voluntary licenses to generic companies to enable the production of paediatric formulations (in particular, fixed-dose combinations) or both.
- More governments should use the Trade-Related Intellectual Property Rights (TRIPS) flexibilities when patents are hindering the production or procurement of paediatric formulations.

What is WHO doing?

WHO has developed a comprehensive set of guidelines on the diagnosis and treatment of HIV infection in children, and on the use of co-trimoxazole in children. In collaboration with its partners, WHO is working to ensure that the technical guidance is adapted and incorporated into countries’ child health and HIV programmes.

WHO is also providing simplified guidelines and implementation tools (for training, management, mentoring, supervision and evaluation) to facilitate rapid scale-up of paediatric and PMTCT interventions (the Integrated Management of Adolescent and Adult Illness (IMAI) and the Integrated Management of Childhood Illness (IMCI) tools).

WHO consistently reviews research findings on the safety and effectiveness of antiretroviral drugs that are used for preventing mother-to-child transmission of HIV and for treating HIV-infected pregnant women and their children. WHO’s recommendations and guidelines are revised accordingly, when necessary.

WHO is collaborating with partners, regulators and drug companies to develop practical guidance on what antiretroviral products are required, and to address regulatory obstacles that hinder reformulation and new product development. In particular, WHO is working to widen and improve the use of HIV diagnostics for young children, and is encouraging the development of safe and reliable fixed-dose combinations of recommended first-line regimens for children.

WHO is helping countries set themselves specific and measurable targets for treating HIV infection and for eventually eliminating HIV infection in infants and young children. It is also assisting countries in strengthening their monitoring and evaluation systems for tracking and analysing progress toward those targets.

With various partners, WHO promotes universal access to HIV prevention, care and treatment for children. Nationally and internationally, it works with partners to strengthen national capacities and build the health sector response to HIV.