HIV/AIDS

ADDRESSING THE MENTAL HEALTH NEEDS OF AFFECTED CHILDREN AND FAMILIES

Tami D Benton, Anusha Lachman & Soraya Seedat

'Amelia, 13, (right) and her sister Mamdiuana, 7, inside the door of their house near Mombane (Mozambique). The sisters now live alone, with the support of their community after both of their parents died of AIDS. Community support for HIV/AIDS orphans has become a priority for many communities. Leaders quickly realized that the effects of HIV related illness are felt by entire communities - not only those who are infected with the disease. As a result, community responses to the pandemic are necessary.'

Image and text: Andy Clark, PhotoSensitive

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AIDS: acquired immune deficiency syndrome.

AIDS-defining clinical condition: a list of diseases associated with AIDS (published by the United States Center for Disease Control and Prevention, CDC).

ARTs: antiretroviral drugs, term used to describe all medications used to treat HIV disease.

CCR5 antagonists: antiretroviral medications that bind to the CCR5 receptor on CD4 cells and prevent the HIV virus from entering lymphocytes, thus interfering with infectivity.

CD4: a glycoprotein found on the surface of helper T-cells which is a receptor for the HIV virus.

Cytotoxic T-lymphocytes (CTLs): killer T-cells that destroy cells infected by a virus.

Fusion inhibitors: class of antiretroviral medications that prevent the HIV virus from fusing with CD4+ cells, thus interfering with replication.

HAART: highly active antiretroviral therapy.

HIV: human immunodeficiency virus infection. HIV infects and destroys T-cells, eventually leading to an acquired immune deficiency syndrome (AIDS).

HIV-1 disease: the most prevalent strain of human immunodeficiency virus.

HIV-associated dementia (also known as AIDS dementia complex, HIV dementia, and HIV encephalopathy) is a rapidly progressive dementia associated with HIV infection and characterized by cognitive deficits in a variety of domains.

HIV-positive: refers to individuals who are infected with the HIV virus. HIV-positive denotes the confirmed presence of an HIV infection.

Integrase inhibitors: antiretroviral medications that prevent viral DNA from integrating with the CD4 cell's DNA thus preventing replication of the HIV virus.

Non-nucleoside reverse transcriptase inhibitors (NNRTIs): antiretroviral drug class that blocks reverse transcriptase of an HIV enzyme by binding to a different site than the NRTI's, but also results in inhibition of viral replication.

Nucleoside reverse transcriptase inhibitors (NRTIs): antiretroviral drug class that blocks reverse transcriptase of an HIV enzyme and thus inhibits replication of the HIV virus.

Progressive HIV-1 encephalopathy: a progressive neurological condition resulting from advanced HIV infection or AIDS, characterized by memory loss, slowed movements, and behavioral changes.

Protease inhibitors: class of antiretroviral medications that blocks activation of an HIV protease enzyme involved in the synthesis of new viral particles.

Reverse-transcriptase inhibitors (RTIs): a class of antiretroviral drugs that inhibit the activity of reverse transcriptase, a viral DNA polymerase that is required for replication of HIV and other retroviruses.

Viral load (VL): The amount of HIV in a sample of blood. Viral load (VL) is reported as the number of HIV RNA copies per milliliter of blood. An important goal of antiretroviral therapy is to suppress a person's VL to an undetectable level—a level too low for the virus to be detected by a VL test.

Viremia: presence of virus in the blood.
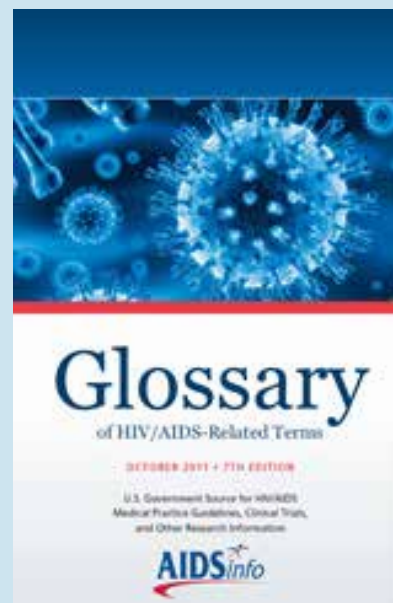
Click on the figure to access a comprehensive glossary of HIV/AIDS relevant terms

Progress in HIV/AIDS prevention and treatment over the last twenty years has been remarkable. A disease that initially resulted in rapid mortality has now become a chronic condition. So much so that an adolescent diagnosed with HIV can expect to live 60 years or more and will be more likely to succumb to diseases of aging such as heart disease rather than to their HIV infection (Insel, 2012). The HIV/AIDS pandemic has severely impacted the mental health of children and families worldwide. The World Health Organization (WHO) estimates that about 34 million people were living with HIV by the end of 2010 (WHO, 2011). Many of those affected are women and children. These data, though alarming, do not begin to reflect the impact of this illness on children, families and communities. HIV/AIDS is a biopsychosocial disease whose impact extends far beyond its physical symptoms. Stigma, social and economic factors, and political environment contribute to the burden of HIV/AIDS. Reports describing rates of new cases and the prevalence of HIV infection inform our understanding of the reach of this illness but they do not capture its actual burden. The number of HIV cases is not proportional to the impact of this illness. Efforts to identify cases, to treat HIV and prevent its progression—and in many instances, to decrease the number of new cases—have been effective. However, we have only begun to understand the mental health effects of HIV on children, adolescents and their families. Furthermore, recognition and treatment for those with the double stigma associated with HIV and mental illness has lagged far behind our knowledge about the HIV virus itself. In this chapter, we will describe what is known about psychiatric and neurologic comorbidities associated with HIV disease, psychosocial sequela of the illness in industrialized and in developing nations, and current evidence-based interventions for young people and families coping with this illness.

Drs Luc Montagnier, from the Pasteur Institute, France (top) and Robert Gallo, from the National Cancer Institute of the US are credited with the discovery of HIV. Luc Montagnier was awarded the 2008 Nobel Price in Physiology or Medicine.

Photos: Wikimedia Commons

EPIDEMIOLOGY

Despite significant advances in the prevention, detection and treatment of HIV, millions of men, women and children worldwide continue to be newly infected (see Table I.3.1). While the number of new cases is declining, they remain alarmingly high. Approximately 2.5 million adults and children acquired HIV in 2011, 20% lower than the global estimates of new infections reported in 2001. Children accounted for approximately 330,000 of these new cases, a decline of 24% since 2009. At the end of 2011, 0.8% of adults aged 15-49 were living with HIV, with considerable variation across regions (see Table I.3.2). The sharpest declines in newly acquired HIV have occurred in the Caribbean and Sub-Saharan Africa. Sub-Saharan Africa, however, accounts for 69% of individuals living with HIV. Despite the continued reduction in new cases of HIV globally, some regions have trended towards higher rates: a 35% increase in HIV infections were observed in the Middle East and North Africa since 2001, reflecting an increase from 27,000 new cases to 37,000 new cases through 2011 (UNAIDS, 2012).

Perinatal infection

Success in the reduction of new HIV infections has occurred principally through the prevention of transmission from mother to child; a 43% decline in vertical transmission has occurred since 2003. Sub-Saharan Africa—the region

Table I.3.1 Prevalence of HIV and new infections in adults and children

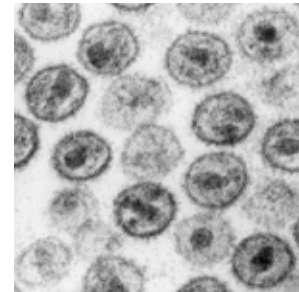| Region	Living with HIV (prevalence)	Newly Infected with HIV (incidence)
Sub-Saharan Africa	23.5 million	1.8 million
Middle East and North Africa	300,000	37,000
South and South-East Asia	4 million	280,000
East Asia	830,000	89,000
Oceania	53,000	2,900
Latin America	1.4 million	83,000
Caribbean	230,000	13,000
Eastern Europe and Central Asia	1.4 million	140,000
Western and Central Europe	900,000	30,000
North America	1.4 million	51,000
Global	34 million	2.5 million

Source: UNAIDS (2012)

burdened with more than 90% of the children with HIV globally—saw a 24% reduction in new cases from 2009 to 2011. Declines have also been achieved in the Caribbean, Oceania, Asia, Latin America, Eastern Europe and Central Asia. There has been no reduction in newly infected children in the Middle East and North Africa (UNAIDS, 2012).

Prenatal detection of HIV-infected women and highly active antiretroviral therapies (HAARTs) have produced significant reductions in new cases of congenitally acquired HIV. Use of HAARTs has resulted in decreased mortality in children acquiring HIV through vertical transmission. In many countries, children who were born with HIV are living into young adulthood and many are working, pursuing higher education and starting their own families (Donenberg & Pao, 2005).

HIV virus.
Hardin Library for the Health Sciences, University of Iowa, US.
http://hardinmd.lib.uiowa.edu/cdc/948.html

Youth

New infections are highest among older adolescents and young adults. Young women account for more than 60% of all young people living with HIV worldwide. This number is even higher in Sub Saharan Africa (71%). In 2010, adolescents aged 15-24 accounted for 42% of new HIV infections in people 15 years and older. Globally, women in the 15-24 years age group are infected at twice the rate of young men and account for 22% of all new HIV infections and 31% of new infections in Sub Saharan Africa. While new infections remain high, there has been progress in 21 of 24 countries that report HIV prevalence, especially in sub Saharan Africa. Women and girls are disproportionally burdened by HIV disease in part related to gender inequality and gender based violence in many countries. For example, rates of forced sex among adolescent girls younger than 15 years have been estimated at 11% to 48% globally (UNICEF, 2011).

Table I.3.2 Prevalence of HIV in people aged 15-24 years according to region (%)

Region	Women	Men
Sub-Saharan Africa	3.1	1.3
Middle East and North Africa	<0.1	<0.1
South and South-East Asia	0.1	0.1
East Asia	<0.1	<0.1
Oceania	0.1	0.1
Latin America	0.1	0.2
Caribbean	0.6	0.3
Eastern Europe and Central Asia	0.5	0.7
Western and Central Europe	<0.1	0.1
North America	0.2	0.3
Global	0.6	0.3

Source: UNAIDS (2012)

Deaths due to HIV

More than 20 million people are estimated to have died from HIV/AIDS since the discovery of the virus in 1981 (UNAIDS, 2004). The number of deaths related to AIDS began to decline during the 1st decade of the 21st century due to greater public education, a decline in new infections, and broader availability of antiretroviral drugs. The rate of AIDS-related deaths continues to decline. In 2011, 1.7 million people died from AIDS-related causes worldwide compared with 2.3 million in 2005 (UNAIDS, 2012). With access to antiretroviral drugs, AIDS has become a chronic condition, even in poorly resourced, hyper-endemic areas (UNAIDS, 2012).

MECHANISM OF INFECTION

Mother to child transmission of HIV can occur through pregnancy, delivery, and through breast milk. Transmission between individuals can occur through transfusions—advances in the detection of HIV in blood products has resulted in substantial transfusion-related reductions in transmission (CDC, 2011)—needle sharing or sexual contact. A decline in perinatal transmission of HIV has occurred globally due to efforts by international agencies—focusing on routine testing for HIV among pregnant women and treatment with antiretroviral drugs prepartum, intrapartum and during breast feeding (see box). Current guidelines recommending routine voluntary testing in all healthcare settings for individuals aged 13 to 64 years and annual testing of at risk individuals and their sex partners should further decrease new cases of HIV infection.

The mechanism of viral infection is well known. Following exposure, the HIV virus infects helper T-cells, replicating in the peripheral blood and lymphoid organs. Cytotoxic T-lymphocytes that recognize the virus are generated in an effort

Table I.3.3 CDC classification of AIDS defining illness in pediatric populations

HIV-associated immunodeficiency	Age-related CD4 values			
	<11 months (% CD4+)	12-35 months (% CD4+)	36-59 months (% CD4+)	>5 years (absolute number per mm² or % CD4+)
None or not significant	>35	>30	>25	>500
Mild	30-35	25-30	20-25	350-499
Advanced	25-29	20-24	15-19	200-349
Severe	<25	<20	<15	<200 or <15%

Source: WHO (2006).

Mother to baby transmission

HIV testing is recommended for all pregnant women. HIV can be transmitted from an HIV-positive woman to her child during pregnancy, labor, or by breastfeeding. In Europe and the US, about 15% to 20% of babies born to HIV-positive women who are not taking anti-HIV drugs are infected. Fewer than 2% of babies are infected if the mother is taking HIV medication.

Because HIV can be transmitted through breast milk, initial recommendations suggested that women infected with HIV should not breastfeed their babies. However, recently the WHO has produced guidelines for breastfeeding by HIV infected mothers that will optimize healthy survival of their children. These guidelines recommend breastfeeding for women who are receiving effective antiretroviral medications and who do not have alternatives available for feeding their infants.

Although the risk is very low, HIV can also be transmitted to a baby through food that was previously chewed (pre-chewed) by a mother or caretaker infected with HIV. To be safe, babies should not be fed pre-chewed food. HIV cannot be transmitted through casual contact, such as hugging and closed-mouth kissing. HIV also cannot be transmitted by items such as toilet seats, door knobs, or dishes used by a person infected with HIV.

Women who are receiving an antepartum combination antiretroviral drug regimen should continue this regimen as much as possible during labor and before delivery, including scheduled cesarean delivery. Intravenous zidovudine should be administered near delivery to HIV-infected women with HIV RNA ≥400 copies/mL (or unknown HIV RNA), regardless of antepartum regimen or mode of delivery. IV zidovudine is not required for HIV-infected women receiving a combination ARV regimens who have HIV RNA <400 copies/mL near delivery. For women who have received antepartum ARV drugs but have suboptimal viral suppression near delivery (that is, HIV RNA >1,000 copies/mL), scheduled cesarean delivery is recommended.

Women whose HIV status is unknown who present in labor should undergo rapid HIV antibody testing. If the results are positive, a confirmatory HIV test should be done as soon as possible and maternal (IV zidovudine)/infant (combination antiretroviral prophylaxis) antiretroviral drugs should be initiated pending results of the confirmatory test. If the confirmatory HIV test is positive, infant antiretroviral drugs should be continued for 6 weeks. If the test is negative, the infant ARV drugs should be stopped.

For some HIV-infected mothers (e.g., those who did not received anti-HIV medications during pregnancy or have a viral load greater than 1,000 copies/mL) a caesarean delivery at 38 weeks of pregnancy (2 weeks before the due date) can reduce the risk of mother to-child transmission. Either 6 weeks of zidovudine alone or zidovudine in combination with other agents is recommended for infants born to mothers reciving IV zidovudine at delivery.

Source: AIDS Info

Guidelines on **HIV and infant feeding** 2010
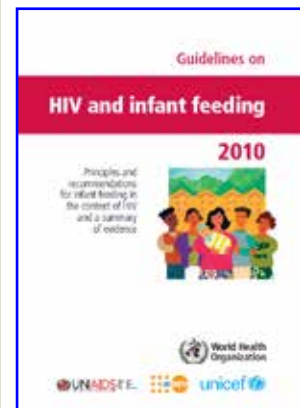
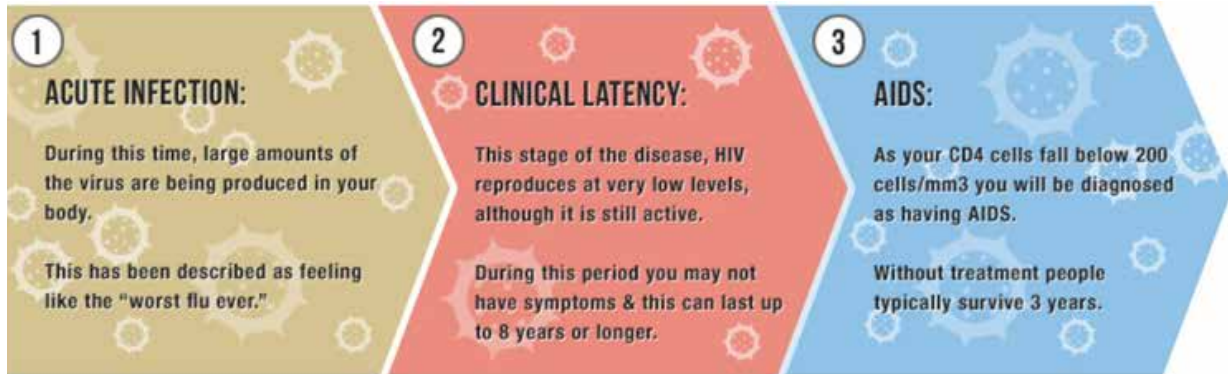Click on the image to access the WHO infant feeding guidelines.

Figure I.3.1 Stages of HIV infection (Source: Aids.Gov)

to kill viral particles. The initial viremia following infection is experienced as a flu-like syndrome by the infected individual. The cytotoxic T-lymphocytes generated at the start of the infection reduce the viremia and induces an asymptomatic phase (*clinical latency*) that can last for years. Eventually, however, the immune system deteriorates with increased viremia and an acquired immune deficiency syndrome (AIDS) develops. When the helper T-lymphocyte count falls below 200 cells/ml or one AIDS defining condition occurs, a diagnosis of AIDS is made.

Taking antiretroviral medications can significantly slow the progression of HIV infection to AIDS, thus early detection is critical to effective treatment. New and evolving technologies allow earlier, faster and more accurate detection of the HIV virus. Rapid diagnostic tests using saliva can provide screening results in as a little as 20 minutes. Serum samples however, are still required to confirm the presence of HIV infection, generally by detecting the virus or its antibody, 2-12 weeks after the initial infection (see Box). When vertically acquired HIV is suspected in infants, HIV antibody detection cannot be used to make a diagnosis of HIV. Virologic testing—to identify antibodies to the virus, DNA and RNA polymerase chain reaction—are made within 48 hours of birth, at 1-2 months and at 3-6 months to distinguish the infant's antibodies from maternal antibodies, which should decline over time. Criteria for defining AIDS in the pediatric population are similar to those for adults with some exceptions (Caldwell et al, 1994). An alternative classification system has been developed for infants exposed to HIV whose status remains to be determined (Table 1.3.4).

NEUROLOGIC EFFECTS

The primary targets for HIV infection of the central nervous system are the microglia and macrophages. HIV's neurotoxic effects are thought to result primarily from its ability to induce inflammatory factors that cause neuronal cell damage and eventual death. The late effects of the neuronal cell damage and death result in the HIV-associated dementia observed among adults infected with HIV. Two types of encephalopathy have been described in children and adolescents with HIV with CNS involvement:

Progressive HIV-1 encephalopathy, characterized by the classic triad of (a) acquired microcephaly, (b) delay or loss of developmental milestones (motor, cognitive and language) and (c) pyramidal tract motor deficits.

Testing for HIV

The most common HIV test is the **HIV antibody test**. Generally it takes the body about 3 months from the time of infection to produce enough antibodies to be detected by an HIV antibody test (for some people, it can take up to 6 months). The time period between infection and the appearance of detectable HIV antibodies is called the window period. Because HIV antibodies are not detectable yet, the HIV antibody test is not useful during the window period.

The **plasma HIV RNA test** (also called a viral load test) can detect HIV in a person's blood within 9 days of infection, before the body develops detectable HIV antibodies. The plasma HIV RNA test is recommended when recent infection is very likely—for example, soon after a person has had unprotected sex with a partner infected with HIV. Results of both tests are generally available within a few days.
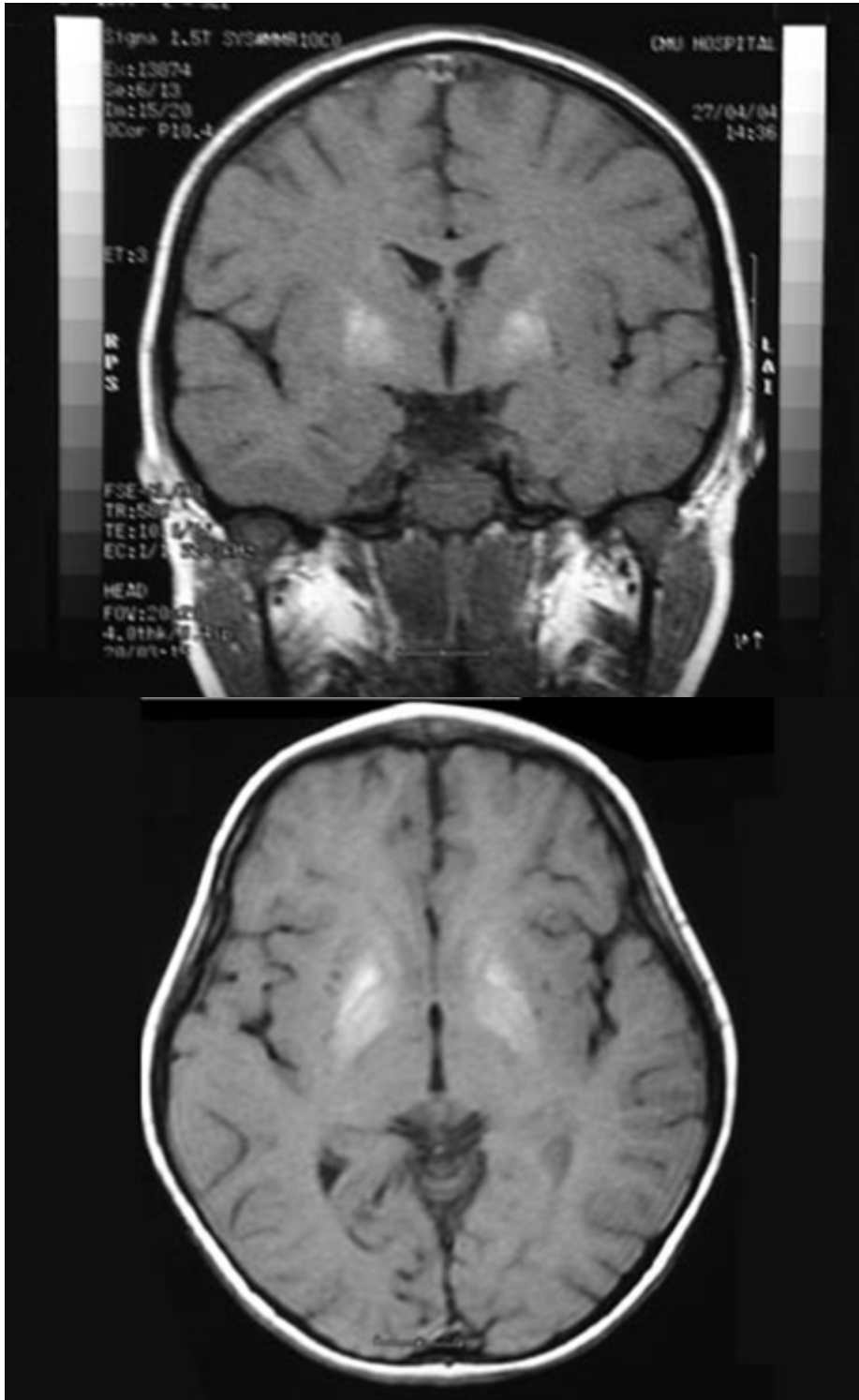
Source: AIDS Info

Figure I.3.2

Computed tomography scan of an 11-year-old child with progressive encephalopathy secondary to HIV infection showing diffuse atrophy and bilateral calcifications in the basal ganglia

Source http://www.rihes.cmu. ac.th/Ped_HIV/06-cli_present/ s4_09.html

A static encephalopathy involves no insidious deterioration of attained milestones and is characterized by significantly delayed development and acquisition of new skills at a much slower rate than would be anticipated based on the child's age. These children may display cognitive abilities ranging from low-average to markedly impaired. A subset of HIV-positive children has been observed to display mild neurocognitive deficits with average overall intellectual functioning but with specific learning problems, language and visuomotor deficits, attention dysregulation, and socio-emotional impairment.

At the beginning of the epidemic, severe progressive encephalopathy was the presentation in 50% to 90% of children born with HIV; however, improved treatment has altered this pattern (Tardieu et al, 2000). Recent estimates of HIV encephalopathy presenting with brain atrophy, cognitive delays and motor deficits among infected children are in the range of 13% to 23% (Tardieu et al, 2000). Radiologic findings associated with HIV encephalopathy include calcifications in the basal ganglia, global brain atrophy, enlarged ventricles and cortical sulci (see Figure I.3.2). Evidence further suggests that higher viral loads are associated with more severe cerebral atrophy (Brouwers et al, 2000).

The presentation of HIV infection of the nervous system is influenced by multiple interacting variables including duration of the illness, its severity and treatment. The pattern depends on the stage of brain development when infection occurs. Neurocognitive developmental delays may be due to multiple factors such as the direct effect of HIV, antiretroviral drugs toxicity, or psychological and socioeconomic factors (Willen, 2006). Many infected children may have no medical symptoms and their developmental progress may be more influenced by poverty and a lack of resources than the infection itself. For those presenting with behavioral and developmental symptoms, the specific etiology of these symptoms is often unclear. The determination of whether a child's neuro-behavioral deficit is related to HIV—as opposed to other environmental, social or medical reasons—is critical because of its implications for treatment.

Evaluating neurologic symptoms in the context of HIV requires considering many factors. Globally, the social context of many HIV positive children includes poverty, low socioeconomic status, lack of resources, and family losses interacting with environmental stressors and neglect. Low levels of maternal literacy, poor quality of interaction between caregivers and child, low birth weight and anemia are often more frequent in HIV-positive children (Brown et al, 2000). In developing countries, zinc deficiency, malnutrition, childhood encephalopathies such as cerebral malaria, and bacterial meningitis contribute an added burden. In areas heavily impacted by HIV, like sub Saharan Africa, few studies have examined other risks for neurologic disease, thus restricting the ability to draw firm conclusions regarding risk (Abubakar et al, 2008). The lack of measures of childhood neurocognitive outcomes standardized for Africa—and low-income countries in general—and insufficiently sensitive measures further limit the screening for deficits. This is especially important given data suggesting that some of the behavioral and emotional deficits present in HIV-positive children were noted among HIV-negative children who were living in the same social environment (Mellins et al, 2003).

Patterns of neurocognitive dysfunction

Untreated HIV infection in children has been associated with cognitive, motor, language, and psychological developmental deficits (Smith et al, 2006). Risk factors for CNS involvement in children include the timing of infection, advanced maternal disease at delivery, rapid progression with early advanced immune impairment. In the absence of antiretroviral treatment, children with a fast progression and a more aggressive illness are likely to die before the age of 2 years, a much more common event in resource limited settings.

Neuro-pathogenesis

The pattern of the disease depends on the stage of brain development when HIV infection occurs. As highlighted already, neurocognitive developmental delays may be due to the direct effect of HIV, antiretroviral toxicity, or psychological and socioeconomic factors (Willen, 2006). Neurological and developmental signs are often markers of HIV disease in infants and may precede other signs of disease progression. HIV infection in children impacts on an immature brain and manifests itself as a static or progressive HIV encephalopathy. A difference between adult and child (especially children under 1 year of age) is that CNS disease from HIV in children occurs more often *before* there is significant immunosuppression.

As a result of improved treatment, children are surviving into adolescence and neurocognitive deficits are now being noted. Adolescence is a critical period for brain development, nerve myelination and synaptic pruning—neural processes crucial for higher order functions (e.g., efficient information processing, decision making). The HIV virus affects subcortical white matter and frontostriatal systems that are important for the regulation of emotions and behavior, increasing the risk in adolescence of impaired decision making, poor impulse control, risky sexual behavior, and aggression. For perinatally infected youth exposed to early severe HIV, the psychosocial ramifications of the illness—including stigma, disclosure of HIV status to others, and the missed academic and social opportunities—may significantly impact on mental health outcomes. In low resource settings, this is often compounded by other factors such as poverty, exposure to violence, substance abuse, neighborhood gangs, parental psychiatric and substance use disorders, adjustment to parental illness and death, caretaking transitions, orphanhood, and family disintegration (Mellins & Malee, 2013).

Children are living longer, but often they do so with severe developmental delay or disability due to HIV encephalopathy. Children require motor skills to maintain levels of confidence and independence in daily activities and to interact with peers. Cognitive growth and social maturation have both been associated with motor skill development (Hilburn et al, 2010). Prevention of encephalopathy through early initiation of high CNS-penetrating HAART regimens is the treatment of choice (Violari et al, 2008). In poorly resourced settings where access to antiretrovirals is limited, developmental problems associated with HIV should be recognized and managed as early as possible.

Although the HIV-associated dementia found in adults has not been well described in adolescents, recent case studies describing dementia in adolescents suggest that this syndrome may be observed more frequently in the future (Scharko et al, 2006). Among adults, HIV associated dementia presents as subcortical dementia, a clinical syndrome characterized by slowing of cognition, memory disturbances, difficulty with complex intellectual tasks such as problem solving, visuospatial abnormalities, and disturbances of mood. Deterioration in attention, executive functioning and working memory have been associated with the progressive frontocortical thinning found in HIV-associated dementia. For adolescents, prevention of CNS disease requires adherence to antiretroviral therapy, which can be challenging for them. Poor adherence to antiretrovirals, which can require multiple doses daily, can lead to resistance, higher viral loads, and increased susceptibility to CNS infection. Among adolescents who acquire HIV disease

Click on the picture to access the lecture "HIV: Manifestations of Disease" by Lisa Hightow-Weidman, MD (51:22)

through risky behaviors or transfusions, antiretrovirals have prolonged survival. However, adolescents living longer with HIV are more likely to experience CNS sequela including attention, memory and cognitive processing deficits. Similar to adults, adolescents who develop AIDS show late neurocognitive changes with progressive bradykinesia, spasticity, and hallucinations (Watkins et al, 2000).

Antiretroviral therapies and neurocognitive outcomes

Highly active antiretroviral therapies and progressive HIV-1 encephalopathy

Evidence suggests that progressive HIV-1 encephalopathy is a potentially reversible complication with a high probability of neurobiological improvement. However, the literature disagrees regarding treatment. Though early initiation of HAARTs is considered to be neuroprotective, there is a high risk of relapse in patients with arrested encephalopathy if viral control is lost (Joska et al, 2010). There are higher rates of residual cognitive and scholastic deficits in children with previous diagnosis of progressive HIV-1 encephalopathy. Their IQ scores tend to improve but still remain lower than in the general population, than in HIV-negative children born to HIV-positive mothers (perinatally exposed but not infected), and lower than in HIV-negative children.

Highly active antiretroviral therapies in school aged children

Puthanakit et al (2010) have shown that school-aged HIV-positive children have lower cognitive functioning than age matched HIV-exposed and HIV-negative children. Long term treatment with HAARTs does not bring about improvement in baseline cognitive functioning despite virologic control and normal immune indices (normal CD4 counts). HIV positive children perform more poorly in cognitive tests regardless of stage of disease, immune status or medication (Van Loon, 2009). Thus, early initiation of HAART in infants and young children should be considered in order to *preserve* neurocognitive functioning.

Long term effects on cognitive functioning

Despite the overall benefits of HAARTs, their long term efficacy in reducing neurocognitive deficits remains to be demonstrated. Worldwide prevalence of neurocognitive impairment has been only marginally affected by widespread use of HAARTs. There have been few studies from low and middle income countries of the effects of antiretroviral initiation on neurocognitive outcomes in perinatally infected children and adolescents. Evidence to date from Thailand, Cambodia and South Africa suggests a failure of improvement of cognitive functions following antiretroviral initiation, even with virologic suppression and immunological recovery (Laughton et al, 2013). Benefits and *reversal* of deficits also vary significantly between individuals. The severity of cognitive impairment at the time of HAART initiation seems to be the strongest predictor of persistent deficits despite long-term HAART (Tozzi et al, 2007).

PSYCHIATRIC SYMPTOMS IN CHILDREN AND ADOLESCENTS WITH HIV/AIDS

The WHO recommends treatment for mental health conditions in individuals who are HIV-positive. To that end, recognition of psychiatric symptoms among young people at risk for HIV infection and those already infected is extremely

important. Psychiatric illness may be a predisposing factor for HIV infection or a perpetuating factor for risky behaviors in HIV infected youth. HIV infection can also occur as a consequence of the psychiatric disorder itself. Psychiatrically ill adolescents are more likely to become sexually active at a younger age, to engage in unprotected intercourse, to have multiple sexual partners, to have history of sexually transmitted diseases, to use drugs or alcohol and less likely to use condoms (Donenberg & Pao, 2005; Brown et al, 2000).

As with neurologic symptoms, recognition of psychiatric disorders is complicated by multiple interacting factors. Symptoms may occur as a result of direct or indirect effects of the virus upon the CNS, genetic factors, opportunistic infections, prenatal substance exposure, poor nutrition, limited access to medical treatment, and other psychosocial and environmental factors. Other aspects that may impact on the presentation of behavioral symptoms in youth living with HIV include the fact that most live in distressed areas affected by poverty, violence, family conflict, substance use or in low income countries with limited access to care.

Estimates of the prevalence of psychiatric disorder in youth infected perinatally or who acquired HIV infection vary widely, with clinic-based reports suggesting high rates of mental health problems (Gaughan et al, 2004). Children with lower CD4 nadir counts (the lowest CD4 cell count measured after HIV infection), higher viral loads, and AIDS-defining diagnoses seem to be at a higher risk of poorer neurodevelopmental and cognitive outcomes, underscoring the need for earlier initiation of antiretroviral treatment. Scharko and colleagues (2006) reviewed published studies of psychiatric diagnosis among perinatally infected youth; they found high rates of ADHD (29%), anxiety disorders (24%) and depression (25%). However, the authors note that studies had serious limitations such as small sample sizes, differing diagnostic methods, a variety of ages and lack of a control group. Other studies have also found high rates of psychiatric disorder, ranging from 48% to 61% (Wood et al, 2009, Mellins et al, 2009). However, a controlled study of behavioral problems in perinatally infected children found rates of behavioral problems that did not differ from those of a control group of children who were perinatally exposed but not infected with HIV, suggesting that the observed behavioral problems were not the result of HIV infection (Mellins et al, 2003).

In one of the few studies using a structured diagnostic interview to obtain psychiatric diagnosis, Pao and colleagues (2000), examined a sample of 34 HIV positive adolescents attending an urban clinic. The investigators found very high rates of lifetime psychiatric diagnosis with 68% meeting criteria for depression, 59% for substance abuse and 29% for conduct disorder. However, the majority had a psychiatric disorder preceding their HIV diagnosis, with approximately half of them having a current affective disorder.

Studies of psychiatric diagnosis among children in low income nations are scarce, and the few existing studies are hampered by small sample sizes and the use of diagnostic instruments that have not been validated in those settings. However, studies in children infected with HIV suggest higher rates of psychiatric symptoms. One study from Kenya examining psychiatric syndromes among congenitally

'One of the most effective ways of getting a message out to your target audience is to print it loud and clearly on the back of a t-shirt. That's what these young Kenyans have done, "HIV/AIDS - chill and live longer" is their message; it's an abstinence message, which they feel is one tool that should be employed in their community.'

Text and image: Patti Gower, PhotoSensitive

acquired HIV infected children and adolescents reported overall rates of 48% for any disorder (major depression, social phobia, oppositional defiant disorder, and ADHD) with 25% having more than one diagnosis (Kamau et al, 2012). A Ugandan study of HIV positive adolescents found high rates of anxiety, depression, somatization and mania (Musisi & Kinyanda, 2009). Studies are emerging from South Africa and India which show associations between psychosocial factors and HIV/AIDS (Collins et al, 2006). Studies in Brazil found high rates of psychiatric symptomatology among adolescents seeking HIV testing who were HIV-positive (Bassols et al, 2007). While more research is needed, current data suggests there is a high prevalence of psychiatric disorders among children infected perinatally or through other mechanisms, pointing to the need for screening, early identification and treatment. Mellins et al's (2003) finding that behavior problems observed in perinatally infected youth were no different than in youth exposed to HIV but not infected highlights the challenges faced when making diagnosis of mental health conditions in the context of HIV disease. It is notable that there have been few studies of evidence-based mental health interventions in perinatally infected youth and no published randomized controlled trials of treatment for specific psychiatric disorders in this population.

TREATMENT OF HIV

Effective treatments for HIV infection have transformed the lives of individuals living with HIV throughout the world, in developed and developing nations. The neurologic sequela of HIV infection that occurred at the beginning of this epidemic are now observed much less frequently. The encephalopathy that develops with progression of HIV disease can be prevented or reversed with HAARTs (McCoig et al, 2002; Brouwers et al, 1990)
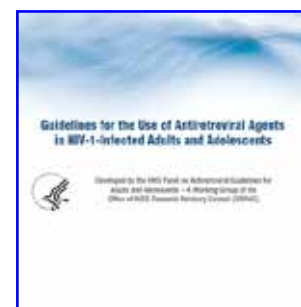
Click on the picture to access the US Office of AIDS Research Advisory Council guidelines for the use of antiretroviral agents.

Antiretroviral treatment is based on the use of six major classes of medication, determined by their mechanisms for fighting the HIV virus:

- Nucleoside reverse transcriptase inhibitors (NRTIs)
- Non-nucleoside reverse transcriptase inhibitors (NNRTIs)
- Protease inhibitors
- Fusion inhibitors
- CCR 5 antagonists, and
- Integrase inhibitors.

Highly active antiretroviral therapy disrupts the HIV virus ability to infect and reproduce by interrupting its mechanisms of infection at more than one site, thus decreasing the virus' effectiveness. Use of three or more HAARTs from at least two different drug classes is recommended to maximize therapeutic benefits (OARAC).

Adherence

Though effective, there are many challenges associated with adherence to HIV treatment. Failure to completely adhere to treatment regimens can result in treatment failure and the development of resistance to medication, particularly a problem for adolescents (Williams et al, 2006). HAART regimes, though simplified by the development of combination pills, remain complicated by the need to take medication several times a day, significant side effects, and interactions with other medications, especially psychotropic drugs, and food items that could interfere with their effectiveness. HAARTs can also exacerbate the symptoms initially. For example, nucleoside reverse transcriptase inhibitors (NRTIs) have been reported to exacerbate progressive encephalopathy and neuropathy (Tamula et al, 2003; Church et al, 2001).

Optimal benefit of treatment requires nearly 100% compliance. Inconsistent adherence can result in drug resistance, increasing viral loads and progression to AIDS (Feingold et al, 2000). In developing nations, the presence of psychiatric illness has been shown to negatively impact adherence to antiretrovirals (Murphy et al, 2005). A systematic review examining the relationships between mental illness and HIV disease in adults did not find similar relationships between mental disorder (depression) and adherence to ARTs (Nachega et al, 2004). A south African study found that fear of rejection, stigma and violence by a sexual partner to be associated with less than 95% adherence to HAARTs (Nachega et al, 2004). Studies examining adherence among HIV-positive adolescents who were not congenitally infected have found an association between the presence of depression and poor adherence to antiretrovirals (Donenberg & Pao, 2005; Murphy et al, 2005). Studies of children perinatally infected with HIV found that non-adherence increased with increasing age, female gender, detectable viral load, recent stressful life events, failing a grade, and the presence of depression or anxiety (Williams et al, 2006). In summary, factors found to reduce adherence among children and adolescents include increasing age, complexity and palatability of the treatment regimen, symptomatic HIV disease, caregivers' mental health, family belief systems, disclosure status, and family social support (Dodds et al, 2003; Wiener et al, 2004). There are a number of successful evidence-based interventions

Without proper treatment, half of the 370,000 children newly infected with HIV in 2010 will die before they reach their second birthday. But very few medicines are designed and adapted specifically for children, and are affordable and practical to use in the places where they live. Click on the figure to watch a podcast by *Doctors without Borders* discussing these issues, particularly as they refer to very young children (under 3 years of age), from the size of the pills to taste and affordability (13:51).

for improving antiretroviral adherence for adults and youth using behavioral approaches (Rotheram-Borus et al, 2001a).

Impact of antiretroviral treatment

Antiretroviral therapy in children is associated with enhanced survival, improved neurocognitive function, reduction in the incidence of opportunistic infections, and better quality of life. Yet, despite the initiation of antiretroviral treatment, children with HIV continue to fall behind their HIV non-infected peers in terms of growth and development. Clinical trial data in high, middle and low income countries have confirmed the immunologic and virologic benefits of antiretroviral drugs (Ciaranello et al, 2009).

There is a higher risk of death and disease progression in infancy than in adulthood and it is well known that CD4 counts and viral load are poor predictors of disease progression in infants. The results of the CHER trial demonstrated that early treatment with antiretrovirals reduced mortality by 76% and HIV progression by 75% (Violari et al, 2008). This resulted in a change in guidelines, now recommending that all HIV infected children under 12 months of age receive antiretrovirals immediately. These guidelines present particular challenges in low income countries where access to care after birth is limited and where there is a lack of early infant testing, mother to child transmission prevention programs, and monitoring of treatment. Providing antiretrovirals to infants in resource poor countries demands a *holistic* approach that goes beyond the simple administration of pills.

TREATMENT OF PSYCHIATRIC SYMPTOMS

Treating psychiatric symptoms in the context of HIV disease requires a careful assessment and consideration of the interacting organic and psychosocial factors contributing to an individual's presentation (Brown et al, 2000). For example, differentiating the medical symptoms of HIV disease from depressive symptoms manifesting as somatic concerns or symptoms of depression itself can be difficult (Benton, 2008). Furthermore, cultural factors influence the psychological response to HIV infection (Ponton & Lees, 1998). As mentioned earlier in this chapter, HIV-positive youth may exhibit depression, attention deficits, mania, and even psychotic symptoms resulting in distress, resistance to taking or poor adherence to antiretroviral treatment, and disregard for safe sex behaviors (Lightfoot et al, 2005). Thus, treatment of psychiatric symptoms may alleviate distress, improve adherence to treatment and overall functioning.

Psychosocial interventions

While most controlled psychological and behavioral therapy studies have focused upon HIV prevention in developing nations, some treatment studies suggest that evidence based psychotherapies that are effective for non-medically ill individuals can be effective for mental conditions in HIV-positive persons as well (Donenberg & Pao, 2005; Olatunji et al, 2006). Studies suggest that psychosocial and behavioral treatments that utilize a wide variety of interventions including social support, interpersonal therapy, CBT, and behavioral stress management in individual or group formats are effective in both adults and adolescents (Olatunji et al, 2006; Harding et al, 2011). A systematic review of adults and adolescents with

HIV concluded that individual, family and group-based treatments all demonstrated efficacy in improving coping, family functioning and in reducing psychological distress and social isolation. The interventions were effectively delivered in an individual or group format—particularly relevant for resource poor countries (Harding et al, 2011). A study in Uganda tested the efficacy of interpersonal psychotherapy for depression in rural communities with high HIV prevalence and high AIDS related mortality. In this study, 30 villages were randomized to 16 weeks of interpersonal psychotherapy or a control condition. The results showed significant reductions in depressive symptoms for the intervention group when compared with controls, suggesting that evidence based interventions are feasible in communities with limited resources and few mental health professionals (Bolton et al, 2003). Among pediatric populations, family focused mental health services have been found useful for improving family functioning, reducing social isolation and increasing utilization of other support services (Brown et al, 2000), reducing problem behaviors and emotional distress (Rotheram-Borus et al, 2001a).

Substantial data support the efficacy of behavioral interventions for the prevention of HIV transmission among adults and youth. More than 144 interventions have demonstrated efficacy in randomized controlled trials conducted in both high income and resource poor nations (Rotheram-Borus et al, 2009). For HIV-positive adolescents, prevention programs usually focus on adherence to medication and lifestyle changes, prevention of transmission, improved self-care and quality of life, partnering with medical providers, managing medication side effects, disclosure, and positive health behaviors (Rotheram-Borus et al, 1995; 1998; 2001a; 2001 b).

Using psychotropic medication

Limited data exist regarding medication treatment for psychiatric symptoms in children and adolescents infected with HIV. Recommendations are largely empirical and mostly extrapolated from adult studies (Evans et al, 2005). However, caution is warranted when prescribing any psychotropic medication to HIV-positive youth who are using antiretrovirals. Both HAARTs and psychotropics are largely metabolized by the 3A4 and 2D6 enzymes of the cytochrome (CYP) p450 system with the subsequent high potential for drug interactions. As a result, blood levels of antiretrovirals and psychotropic medications may be increased, decreased or both, by inhibition or induction of these enzymes. Certain antiretrovirals are known to have a particular impact and to pose risks for individuals with HIV. The protease inhibitors, especially *ritanovir*, are potent inhibitors of 3A4 and to a lesser extent 2D6. *Efavirenz* is a potent inducer of CYP 3A4, decreasing plasma levels of other medications that are metabolized by this pathway.

Some of the antiretrovirals can also cause psychiatric symptoms. The most concerning in this regard is *efavirenz*. Early reports suggested that sudden onset of suicidal ideation and depression were potential side effects. Reports further suggest that more than 50% of individuals using *efavirenz* might experience depression, suicidal ideation, vivid nightmares, anxiety, insomnia, psychosis, cognitive dysfunction and antisocial behavior. More recent data suggests that vivid dreams and vestibular dysfunction were much more frequent with *efavirenz* than in patients treated with a triple nucleoside regimen. However, these unwanted effects were transient and resolved within 4 weeks (Ferrando, 2013)

HIV-positive individuals tend to be more sensitive to the side effects of pychotropic drugs and often respond to lower doses.

Table I.3.4 Common interactions between antiretroviral drugs and psychotropic medications

Drug	Interaction
Citalopram	• Lopinavir/ritonavir (ritonavir increases citalopram levels)
Fluoxetine and fluvoxamine	• Increase levels of amprenavirdelavirdine, efavirenz, indinavir, opinavir/ritonavir, nelfinavir, ritonavir, saquinavir. • Nevirapine decreases fluoxetine levels
Paroxetine	• Lopinavir/ritonavir (ritonavir increases paroxetine levels)
Sertraline	• Lopinavir/ritonavir (ritonavir increases sertraline levels)

Click on the picture to access detailed information about HIV drug interactions.

When considering   psychotropic use in the context of pediatric HIV and antiretroviral tretament, clinicians must examine factors beyond the presenting behavioral complaint. A thorough psychiatric and psychosocial assessment including ascertaining developmental factors, environmental issues, and social and family circumstances must occur. Recent stressors must also be elucidated. Collateral information from school, primary care providers, specialists, counselors and family members must be obtained before reaching diagnostic conclusions. Neurologic disorders must also be evaluated as a potential cause of behavioral symptoms and as a risk factor for medication side effects. A thorough review of the antiretroviral regimen should identify potential precipitants of behavioral changes.

Given the absence of evidence to guide the prescribing of psychotropic medication in this population, caution is warranted. When choosing medication and dosing, the clinician should consider Tanner stage, body weight and body mass index, as well as the child's medical condition. Medications should be selected taking into consideration their side effect profiles, starting with the lowest therapeutic dose, and titrating gradually to minimize adverse effects. HIV-positive individuals tend to be more sensitive to side effects and often respond to lower doses (Benton, 2010).

Mood disorders

Depression and bipolar disorder increase in frequency from childhood to adolescence among HIV-positive and HIV-negative youths (Geller et al, 2002; Lewinsohn et al, 1993). Criteria for a depression diagnosis in adolescents who are HIV-positive are the same as for adolescents who are not HIV-positive. However, making a diagnosis of depression is complicated in the young person with HIV by the overlap of the vegetative symptoms of depression with HIV symptoms themselves or side effects of antiretroviral treatment. Symptoms common in depression such as fatigue, anorexia, anhedonia and other somatic complaints may also suggest progression of HIV disease. Clinical assessment must include an evaluation of worsening medical status, poor adherence to antiretrovirals resulting

in drug resistance, and recent stressors (e.g., adjustment disorders) or grief due to the loss of family members or friends.

SSRIs are the most commonly used antidepressants for young people living with HIV; they are the antidepressants of choice due to their efficacy in adolescents and their favorable side effect profile. Although no data exist supporting differential efficacy among the SSRIs, fluoxetine has the strongest evidence base and is approved in the US and other countries for treatment of depression in children older than 8 years of age (Emslie et al, 1997). Tricyclic antidepressants have not been shown to be superior to placebo in controlled trials in youth and are toxic, particularly in overdose. Other agents commonly used for the treatment of depression in the context of HIV disease include mirtazapine due to its safety profile and lesser risks for drug interactions. Mirtazapine has been helpful for sleep and in promoting weight gain although controlled trial data is still lacking. Similar to other groups with depression, careful monitoring of the emergence of suicidal ideation is warranted (Benton, 2010). The prevalence of bipolar disorders in HIV-positive youth has not been systematically studied and recommendations for treatment are based on current pediatric and adult treatment guidelines.

Pediatric HIV: The reality of a neglected disease. Click on the figure to watch a video clip discussing some of the problems facing the treatment of young children with HIV in low income countries (4:42).

Attention deficit hyperactivity disorder

While high prevalence rates of attention deficit hyperactivity disorder in HIV infected youth have been reported (Mellins et al, 2009; Scharko, 2006), few medication treatment trials exist among HIV-positive youth. Psychostimulants are well studied in youth with ADHD who are not medically ill, being the treatment of choice for this disorder in those who are HIV-positive also. Efficacy of stimulants for ADHD in HIV-positive youth has not been studied, even though they are commonly prescribed in this population. The current practice is that children who exhibit ADHD symptoms in the context of HIV disease can be treated with stimulant medication at the recommended dosages for non-HIV-positive children. Because stimulant medications have few drug-drug interactions, they are relatively safe in combination with antiretrovirals.

Anxiety disorders

High rates of anxiety disorder have been reported among HIV-positive youth, however, prevalence of specific disorders is unclear (Mellins et al, 2009). Social phobias, specific phobias, separation anxiety, agoraphobia, panic disorder, and obsessive compulsive disorder have been reported in this population as well as high rates of comorbidity with other psychiatric conditions (Mellins et al, 2009). As with other anxiety disorders, treatment should be initiated when symptoms interfere with normative functioning. Cognitive and behavioral therapies have demonstrated efficacy in children and adolescents for the treatment of anxiety and should be the first line of treatment for HIV-positive youth with anxiety disorders (Brown et al, 2000). SSRIs should be considered for anxiety disorders that do not respond to behavioral interventions.

Another source of anxiety for HIV-positive children and adolescents relates to medical procedures occurring during treatment for their illness. Distraction techniques and psychotherapies have been helpful, often used in conjunction with benzodiazepines in low doses, such as lorazepam. Clonazepam has also been used for children with more prolonged anxiety. However, benzodiazepines may cause

sedation and behavioral disinhibition, especially in patients with CNS disease or other cognitive effects of HIV disease or its treatment and should be monitored closely. Antihistamines are commonly used for calming anxiety or sedation for anxious children, but are not recommended for the treatment of anxiety. The anticholinergic properties of antihistamines may worsen delirium.

Post-traumatic stress disorder

The epidemiology of HIV in industrialized and low income nations increases the risk of exposure to trauma in youths. For example, the majority of perinatally exposed youth in the US live in inner cities where stress, poverty, and trauma are endemic (Havens et al, 2008). Both traumatic events and medical procedures further increase the risk for post-traumatic stress disorder or traumatic stress (Stuber et al, 2003). This is very relevant given the association between trauma exposure and adherence to safe sex practices and to antiretroviral treatment for HIV-positive youth (Radcliffe et al, 2006). In a study examining PTSD and post-traumatic stress in 30 HIV-positive adolescents and young adults, rates of PTSD (13%) and post-traumatic stress syndrome (23%) were high in response to being diagnosed with HIV infection, but even higher when examining other traumatic events occurring among the same young people, giving further support to the impact of ongoing trauma in the lives of HIV-positive youth (Radcliffe et al, 2006).

Trauma focused cognitive behavioral therapies have been found to be effective for PTSD symptoms. Medications may be helpful for some youth; however, empirical support for medication use is weak (Foa et al, 2000)

Delirium

The clinical presentation of delirium in adolescents is similar to adults. Impaired attention and responsiveness, disorientation, confusion, affective lability, alterations in level of consciousness, and sleep disturbance can be present. Although paranoia, perceptual disturbances and memory impairment are less common in younger children, the diagnostic criteria for delirium are applicable across the lifespan. In most cases of pediatric delirium the etiology is a medical condition or medication (Turkel & Tavare, 2003).

Click on the picture to view a lecture on 'Pediatric HIV Prevention, care and treatment in Lesotho' by Lindy C Fenlason MD, from the Baylor International Pediatric AIDS Initiative (BIPAI) (48:17).

Treatment consists of strategies to maintain orientation and environmental cueing. Pharmacologic treatment for delirium in HIV infection relies primarily on second generation antipsychotic agents in low dose. Adverse effects of the antipsychotics, including extrapyramidal, are limited; both typical and second generation antipsychotic agents are equally efficacious. Lorazepam causes a worsening of delirium with disinhibition, ataxia, confusion and oversedation, suggesting that benzodiazepines should not be used for delirium in this population (Ferrando, 2013).

OTHER PSYCHOSOCIAL FACTORS AFFECTING TREATMENT FOR FAMILIES AFFECTED BY HIV/AIDS

Bereavement

UNICEF reports that 15.2 million children had been orphaned by AIDS worldwide by 2005 and that 13.7 million children had lost one or both parents

to AIDS in South Africa alone. The number of orphans is predicted to reach 2.3 million by 2020 (Dorrington et al, 2005). Parental loss poses further mental health risks for the children and adolescents left behind. Evidence suggests that children who have been orphaned by HIV/AIDS have multiple risks for poor outcomes including poor medical care and nutrition. Further, orphaned children aged 16 to 24 show lower educational achievement, are more likely to be abused and have higher rates of HIV (Cluver et al, 2007). In addition, children and adolescents with HIV often face the dual misfortune of living with their own life-limiting illness and facing the death of loved ones (Roth et al, 1994). Frequently, the loss multiplies the burden because of HIV disease. The stigma and secrecy commonly surrounding death by HIV/AIDS may complicate the grieving process by depriving these youngsters of the support they need and by reinforcing a sense of shame about their parents' death. Disclosure of an AIDS-related cause of death may result in stigmatization, shaming by family members, and ostracism and teasing by peers, thus interfering with the grieving process and further impairing a child's ability to cope with the loss (Siegel & Gorey, 1994).

In addition to the loss, extended family members are often counted upon to provide care and support for the remaining children. The impact of orphanhood has been most profoundly experienced in low income nations. It is estimated that about 9% of children in Sub-Saharan Africa have lost at least one parent to HIV/AIDS during the 1990's (Monasch & Boerma, 2004). In most cases, the extended family assumes the roles of caretaking, shouldering the financial and emotional burden of caring for these children with multiple medical and emotional needs (Earls et al, 2008). Further, longitudinal studies suggest that both HIV/AIDS in orphans and in their caregivers predicts increased rates of depression, anxiety, and posttraumatic stress symptoms in HIV/AIDS orphans years later, highlighting the need to focus interventions on infected youth and their caregivers (Cluver et al, 2012).

Disclosure

Reasons influencing the decision to tell a child or adolescent their HIV-positive status are complex. Cultural issues, misperceptions and misinformation about the disease—by relatives, teachers, health care providers, and the community—are all factors impacting on the disclosure (Bakeera-Kitaka et al, 2008). Additionally, disclosure of a child's HIV status may also reveal the HIV status of the parents, who may experience stigma and discrimination themselves as a result (Pinzon-Iregui et al, 2013).

The WHO, the American Academy of Pediatrics (AAP, 1999) and the International Center for AIDS Care and Treatment Programs (Abrams et al, 2004) have endorsed disclosure to older children (10 years of age or older) of their HIV status (see box). These organizations have also published guidelines to assist clinicians and families who are struggling with this complicated issue. Despite these recommendations, most studies about disclosure worldwide suggest that many HIV-positive children and adolescents are unaware of their HIV status (Pinzon-Iregui et al, 2013). The proportion of children who know their HIV status is lower in low and middle income countries (20.4%) when compared with industrialized countries (43.1%) (Pinzon-Iregui et al, 2013; Vreeman et al, 2010). For example, one study in Thailand found that only 1 in 5 HIV infected youths
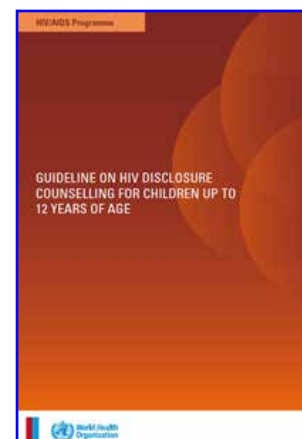
Click on the figure to access the WHO Guideline on HIV Disclosure Counseling for Children up to 12 Years of Age.
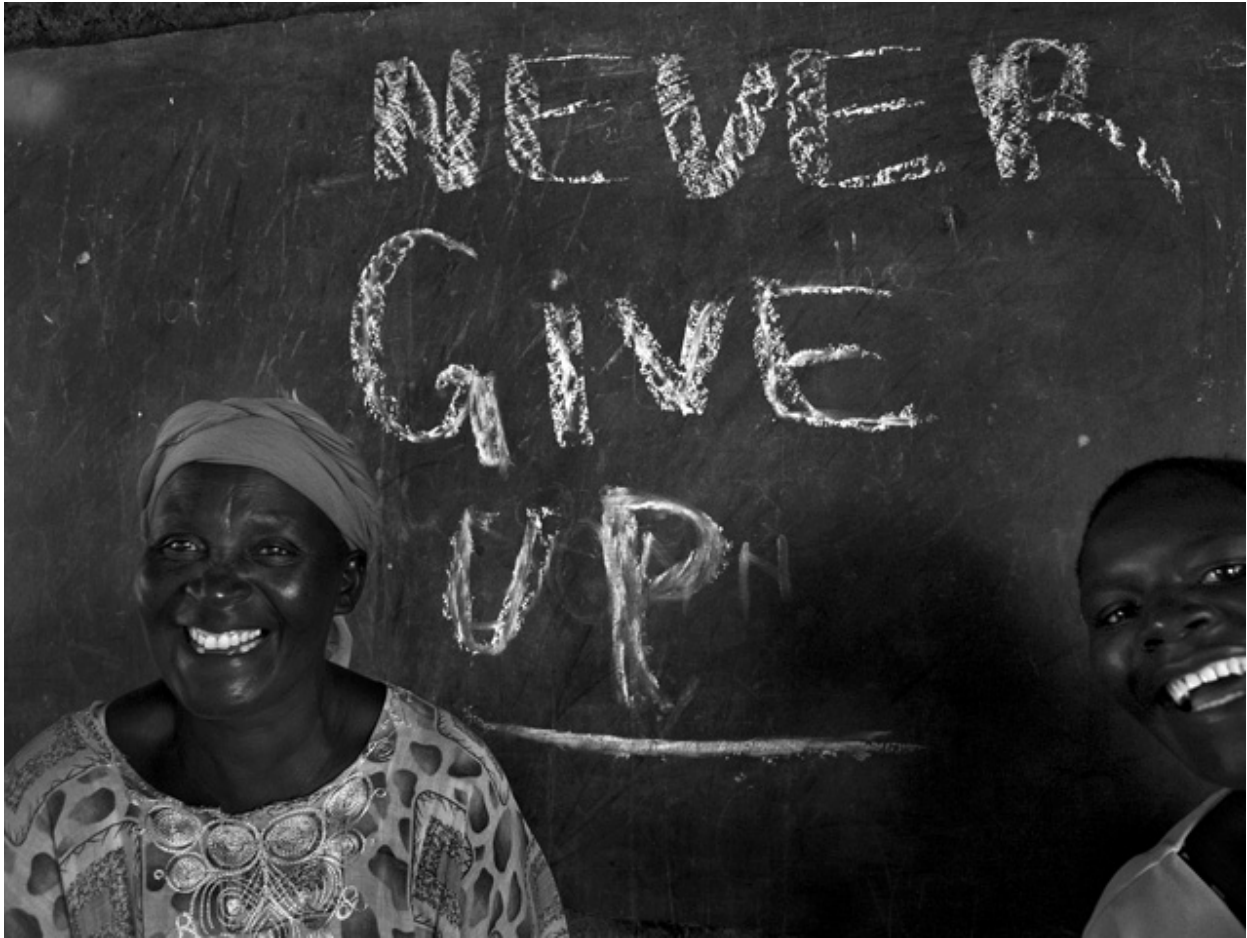
Image: Patti Gower, PhotoSensitive

between the ages of 5-16 years had been told of their HIV diagnosis (Boon-Yasidhi et al, 2005).

The ambivalence of caretakers and providers to disclose a child's HIV status is fueled by realistic concerns about the potential consequences of disclosure. Some of the reasons commonly cited for failure to disclose are fear of emotional trauma to the child, fear that the child is too young to understand and cannot keep a secret, fear of disclosure to others because of the stigma, that children do not express interest in knowing, and caregivers not knowing how to initiate the discussion (Domek, 2010). Pinzon-Iregui et al (2013) provide a comprehensive review of disclosure practices globally. The most commonly cited fear was that of psychological trauma to the child. Further complicating this issue are the conflicting results of studies examining disclosure. Some studies report higher self-esteem, promotion of trust, improved adherence to treatment, and better health and well-being (Mellins et al, 2002). Studies further suggest that disclosure may decrease psychological distress and depression and improve the overall mental health of caregivers compared with those who do not disclose (Wiener et al, 1998). Other studies have suggested that disclosure may increase distress and contribute to anxiety, depression, and behavioral problems (Tubman et al, 2003). However, most have found a positive association between disclosure and quality of adherence to antiretroviral treatment (Vreeman et al, 2010). Children's knowledge of their HIV status has been associated with lower CD4 counts and viral loads, lower likelihood of being classified as non-adherent (Vreeman et al, 2010), better adherence to

WHO (2011) recommendations about disclosure of HIV status to children*

- Children should be told their HIV positive status; younger children should be told their status incrementally to accommodate their cognitive skills and emotional maturity, in preparation for full disclosure (strong recommendation, low quality of evidence).
- Children should be told the HIV status of their parents or caregivers; younger children should be told this incrementally to accommodate their cognitive skills and emotional maturity (conditional recommendation, low quality of evidence)
- The decision on who will disclose to the child should be guided by the intent to improve/promote the child's welfare and minimize the risk to his or her well-being and to the quality of the relationship between child and parent/caregiver (conditional recommendation, absence of evidence)
- Initiatives should be put in place to enforce privacy protection and institute policy, laws and norms that prevent discrimination and promote tolerance and acceptance of people living with HIV. This can help create environments where disclosure of HIV status is easier (strong recommendation, low quality of evidence).

*6 to 12 years of age.

WHO (2011) Guideline on HIV Disclosure Counselling for Children up To 12 Years of Age. WHO Press, Geneva, Switzerland

Click on the image to access the education resources of the Baylor International Pediatric AIDS Initiative.

antiretroviral treatment (Blasini et al, 2004), and decreasing vulnerability to risky behaviors (Bakeera-Kitaka et al, 2008).

A well planned discussion about a child's HIV status can have many benefits. Ideally, the discussion should occur in a structured setting with coordination between parents or caregivers and their health care team. The information should be conveyed to the child in a developmentally appropriate, socio-culturally sensitive way. Parents and caregivers must also be prepared for the child's reaction to the disclosure. Children may not respond immediately but have a delayed reaction, which can range from no signs of distress to severe distress. Caregivers must also keep in mind that most children and adolescents adjust and learn to cope with their illness (Weiner et al, 2003).

Disclosure to adolescents

Disclosure to adolescents who are HIV-positive is even more complicated. Adolescents are beginning to make decisions about sexual activity, other risk behaviors such as experimentation with drugs and planning about their future including relationships and parenting. Realistic concerns about rejection by peers can impact an adolescents' willingness to adhere to antiretroviral treatment and safe sex practices to avoid raising suspicion about their HIV status. It is essential that adolescents know their HIV status and understand its treatment in order to maximize their health-promoting behaviors and decrease risk of transmission. Disclosure and open discussion about their illness can enhance adolescents' acceptance of guidance, support and skills needed to cope with their illness (Benton, 2011).

Disclosure of parental HIV status

Another unique issue for HIV-positive youth concerns parental HIV status and parental disclosure of their HIV status. Reasons for parents to disclose are often for parental custody planning and the moral imperative of doing the right thing for their child (Pilowsky et al, 2000). Studies of the impact of maternal disclosure of HIV status upon youth have produced conflicting results. Some studies suggest increased behavioral problems and distress, increased sexual risk taking and substance use, while others suggest no effect on psychological functioning. A positive parent child relationship appears to be a better predictor of a child or adolescent's response to disclosure than the act of disclosing (Donenberg & Pao, 2005).

An AIDS free world is within our reach.

CONCLUSIONS

Progress is being made towards the global vision of a world in which AIDS has been eliminated. Reduction in new cases worldwide, decreasing mother-child transmission, and increased access to antiretroviral treatment strongly suggest that UNAIDS' vision for zero new HIV infections and zero AIDS related deaths is achievable. Antiretroviral treatments have been successful in prolonging lives and transforming AIDS into a chronic disease.

Increasing data continue to demonstrate the effectiveness of antiretroviral treatment. The discrepancies between effective antiretroviral treatment and low rates of viral suppression can be partially explained by behavioral factors. Even the most effective treatments are useless if the patient does not take the medication. Achieving an AIDS free generation will require universal testing integrated into primary medical care so that everyone knows their status, treating those who are found to be positive and ensuring that individuals remain engaged in their treatment, adhere to recommendations and remain in HIV care (Cohen et al, 2011).

Treatment for mental health conditions in these patients requires a similar approach in HIV-positive individuals as in other groups: early detection, early treatment and patient engagement. Both HIV and psychiatric disorder require behavior changes before treatment success is possible. Effective behavioral interventions in the context of HIV/AIDS and its treatment can be lifesaving.

The best treatment approach for children and adolescents with HIV/AIDS involves multidisciplinary, integrated care that includes pediatric AIDS care, mental health care, outreach, case management providing linkages to services, and a comprehensive continuum of care within the primary care setting. Although this treatment approach is recommended, access to such programs is limited in industrialized countries and to a much greater extent in low income countries where mental health services are much more limited or non-existent. This has been recognized by the WHO, which has developed a five part series of training materials and resources for integrating mental health care with HIV care (Collins et al, 2010).

An AIDS free world is within our reach but not without addressing the mental health needs of individuals at risk of becoming infected with HIV, those who are already infected, and the families of HIV-positive individuals. Recognizing

psychiatric disorders, treating them, and being able to intervene in a culturally sensitive and cost effective way in low income countries will be essential to prevent transmission of HIV and improve the lives of young people living with HIV/AIDS.

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