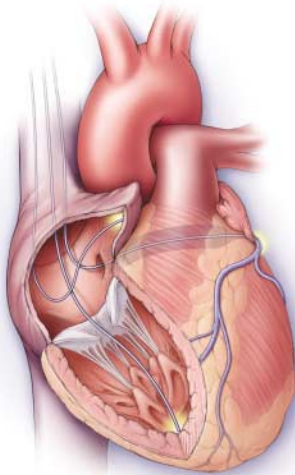




This Week in the Journal

June 13, 2002



Cardiac Resynchronization in Heart Failure

About a third of patients with chronic heart failure have an intraventricular conduction delay, which may lead to dyssynchrony of cardiac contraction and further clinical impairment. The patients in this clinical trial were randomly assigned to a group receiving resynchronization therapy with an atrial–biventricular pacemaker or to a control group. As compared with the control group, the resynchronization group had improved functional capacity, quality of life, and ejection fraction over a six-month period.

Resynchronization therapy has considerable promise in patients with heart failure, but there are limitations. It is applicable to only about a third of patients, and it requires the insertion of a complex pacing device that may be associated with a variety of technical problems and complications. This technique should be reserved for experienced centers.

see page 1845 (editorial, page 1902)



Ventricular Pacing or Dual-Chamber Pacing for Sinus-Node Dysfunction

In patients with sinus-node dysfunction who require permanent pacing for bradycardia, single-chamber ventricular pacing and dual-chamber atrioventricular pacing are alternative options. In this randomized trial, the frequency of the primary end point (death or nonfatal stroke) was not significantly different in the two groups. However, the dual-chamber group had a lower incidence of atrial fibrillation and end points related to heart failure, as well as a slightly better quality of life.

Dual-chamber pacing is more expensive and more technically complex than single-chamber ventricular pacing. Nevertheless, the maintenance of atrioventricular synchrony with dual-chamber pacing provides enough additional clinical benefit to justify its use in patients with sinus-node dysfunction.

see page 1854

PERSPECTIVE

Preventing HIV Infection in Children

For a child, the risk of becoming infected with the human immunodeficiency virus (HIV) is a stark example of the difference between being born in a rich country and being born in a poor country. In the United States, the acquired immunodeficiency syndrome (AIDS) is a vanishing disease among children. Throughout the world, however, the number of new HIV infections in children continues to increase (see Figure). In 2001, an estimated 800,000 children under 15 years of age were newly infected, 2.7 million children were living with HIV infection, and 580,000 died of AIDS, according to UNAIDS and the World Health Organization.

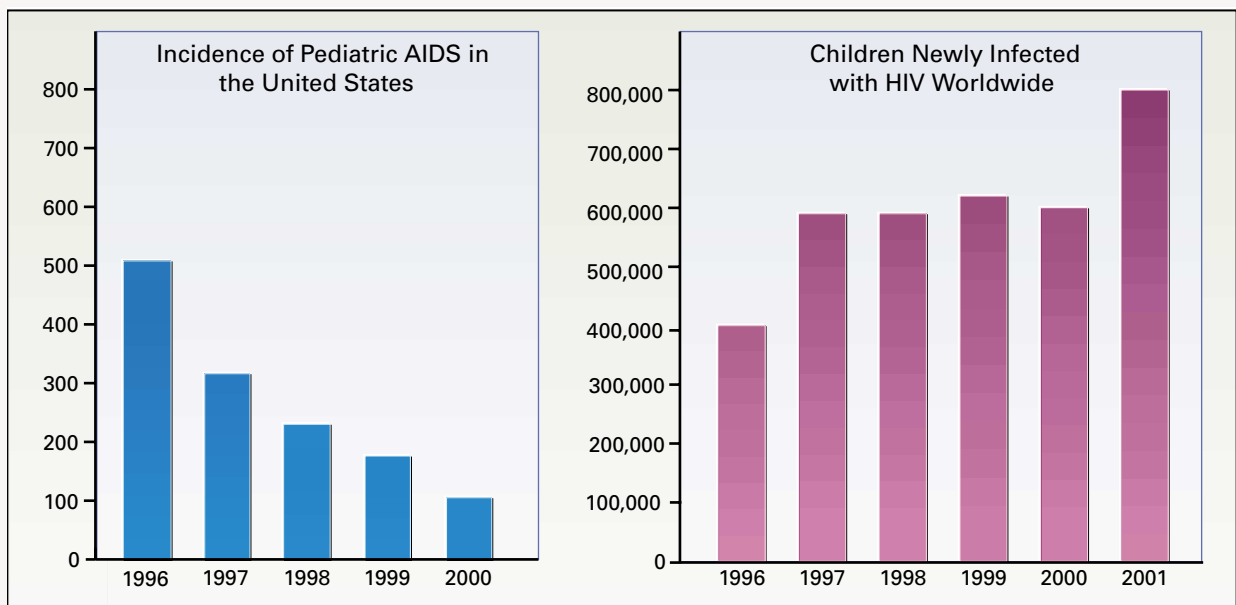
Most children who are infected with HIV acquire the virus

through mother-to-child transmission. Worldwide, half these children are likely to die before their first birthday, and most of the rest before their fifth birthday. These infections are largely preventable with antiretroviral therapy, careful obstetrical management, and the use of alternatives to breast-feeding. However, these interventions are still largely unavailable in Africa and some other parts of the world. Many women receive no prenatal care or give birth at home or in settings where antiretroviral medicines are not available. Counseling, testing, and treatment to prevent mother-to-child transmission of HIV infection are possible only as part of an organized health care system. Despite sharp price reductions, many antiretroviral agents are still prohibitively expensive for poor countries. The World Health Organization estimates that less than 5 percent of the 6 million people with HIV infection or AIDS who require treatment with antiretroviral medications have access to them.

Preventing HIV infection in chil-

dren is only part of what needs to be done. A short course of antiretroviral treatment for mother and child does nothing to stop the progression of AIDS in an HIV-infected mother. When parents die, they leave orphans, most of whom are not infected with HIV. In 2010, more than 44 million children under the age of 15 years in 34 developing nations will have lost one or both parents, according to an estimate prepared for the U.S. Agency for International Development. AIDS and related illnesses are projected to account for about two thirds of these parental deaths. Thus, nearly 13 percent of the children in these countries will be orphans.

In this issue of the *Journal*, three articles address aspects of the problems that HIV infection creates for children. Tuomala et al. (see pages 1863–1870) studied the safety of antiretroviral therapy during pregnancy. They found that the use of multiple antiretroviral medications, as compared with no therapy or treatment with one medication,



U.S. data are from the Centers for Disease Control and Prevention, and international data are from the Joint United Nations Program on HIV/AIDS (UNAIDS) and the World Health Organization.

“The risks of adverse outcomes of pregnancy that are attributable to antiretroviral therapy are low.”

Antiretroviral Therapy during Pregnancy

This report describes an analysis of combined data from seven studies of pregnant women with human immunodeficiency virus type 1 (HIV-1) infection to assess whether antiretroviral therapy during pregnancy is associated with an increased risk of premature delivery (<37 weeks of gestation) and other adverse outcomes. Rates of premature delivery, low birth weight, low Apgar scores, and stillbirth were similar whether or not the women received antiretroviral therapy and whether the treated women received combination therapy or monotherapy. As compared with combination regimens that did not include protease inhibitors, regimens that included these medications were associated with a greater risk of very low birth weight, after adjustment for several confounding factors, but this finding was based on small numbers of women.

These data provide reassurance that the use of combination antiretroviral therapy is not associated with an increased risk of premature delivery or other adverse outcomes in late pregnancy. Although the risk of very low birth weight appears to be higher with combination therapy that includes protease inhibitors than with regimens that do not include them, this finding requires confirmation, and the overall risks appear to be small in relation to the recognized benefits of these agents.

see page 1863

was not associated with increased rates of preterm labor, low birth weight, low Apgar scores, or stillbirth. These findings should be reassuring, although some aspects of the safety of antiretroviral therapy during pregnancy warrant further study. In another article, Watts (see pages 1879–1891) reviews the management of HIV infection in pregnant women. In the third article, Foster (see pages 1907–1910) discusses the global problem of orphans and how best to respond to it from local and international perspectives.

The burden of HIV infection for both infected and uninfected children threatens to dwarf the capacity and willingness of nations to respond to it. Nonetheless, there are hopeful signs. Some drug companies, in response to public pressure, are discounting the prices of medications or donating them to countries that cannot afford to buy them. South Africa has more people in-

fectured with HIV than any other country but has lagged in providing medications to prevent pediatric infections. In April, South Africa's government announced that it would make medications available to a larger number of pregnant women — although much more needs to be done. The World Health Organization has issued guidelines for treating HIV infection and AIDS with combinations of medications in poor countries and has also included 10 new antiretroviral agents on its revised list of essential medicines.

The Global Fund to Fight AIDS, Tuberculosis and Malaria is an independent nongovernmental organization based in Geneva that accepts donations from governments and other sources. The Global Fund will distribute up to \$616 million over the next two years to programs in more than 40 countries. Although these distributions are substantial they are small in comparison with

the estimates of the additional resources that are needed. UNAIDS has calculated that a total of \$7 billion to \$10 billion each year is needed, just for HIV infection and AIDS.

Further progress depends as much on the sustained commitment of governments, the private sector, and philanthropic leaders as on clinical advances. The United States is already the largest contributor to the Global Fund to Fight AIDS, Tuberculosis and Malaria. Yet considerably more money and technical support are needed for this and other efforts, both from the United States and from other countries. Congress is pushing the Bush administration to spend more money on global AIDS. The challenge is not only to eliminate mother-to-child transmission of HIV but also to provide effective treatments for mothers and fathers.

ROBERT STEINBROOK, M.D.

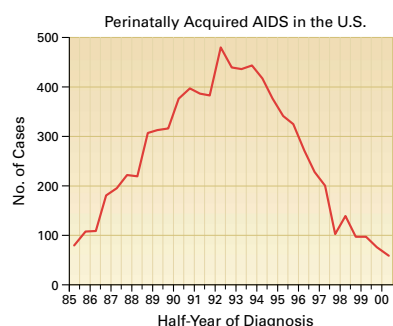
“Carriage of S. aureus was eliminated from 81.3 percent of carriers.”

Intranasal Mupirocin to Prevent Postoperative Infections

In this double-blind trial, the rate of *Staphylococcus aureus* wound infections was similar among patients treated with mupirocin ointment (2.3 percent) and those who received placebo (2.4 percent). However, 23.1 percent of 3864 patients were identified as having nasal carriage of *S. aureus*, and among these patients there were fewer nosocomial *S. aureus* infections in the mupirocin group than in the placebo group (4.0 percent vs. 7.7 percent, $P=0.02$).

Nasal carriage of S. aureus is common, and carriers have a higher risk of staphylococcal infection after invasive medical or surgical procedures than those who do not carry this organism. This large study found an effect of topical antibiotic treatment only in the subgroup of patients who were carriers.

see page 1871 (editorial, page 1905)



Drug Therapy: Management of HIV Infection in Pregnancy

Globally, more than 16 million women are living with human immunodeficiency virus (HIV) infection. Each year, 600,000 children are infected, most of them through mother-to-child transmission. This review focuses on the management of HIV infection during pregnancy in developed countries in which antiretroviral therapy, scheduled cesarean delivery, and alternatives to breast-feeding are available; it discusses strategies for obtaining the best possible outcomes.

Intrapartum and postpartum care of the mother and infant can reduce the risk of HIV transmission and improve maternal health.

see page 1879

“The scale of the AIDS epidemic in Africa makes its repercussions qualitatively different from those in other parts of the world.”

Sounding Board: Supporting Community Efforts to Assist Orphans in Africa

As a result of the AIDS epidemic, an increasing number of children throughout the world have lost their parents. Africa has been hardest hit by the pandemic, and millions of children have been left orphaned. In this Sounding Board article, Foster, who works in a hospital in Zimbabwe, describes the scope of the problem and argues that external aid agencies must work with local communities to distribute resources effectively to assist children who have been orphaned.

see page 1907