ty study also reported results suggesting that regular use of aspirin (taken mostly in the low doses advised for cardiovascular prophylaxis) had a protective effect, although the effect was less than that afforded by the use of nonaspirin NSAIDs. Because most aspirin is purchased without a prescription, it is not surprising that no effect of aspirin was observed in the study by in ‘t Veld et al., which relied on pharmacy-dispensing records. The observation that low doses of NSAIDs or aspirin may protect against Alzheimer’s disease challenges the presumption that these agents work by suppressing inflammation. More important, low-dose NSAIDs carry much lower risks of gastrointestinal bleeding and other serious side effects that would otherwise contraindicate long-term use of NSAIDs for the prevention of Alzheimer’s disease.

Like all observational studies, the current report remains vulnerable to unsuspected sources of confounding. A definitive evaluation of the efficacy of NSAIDs or other antiinflammatory treatments for the primary prevention of Alzheimer’s disease will require lengthy and expensive randomized, controlled trials of these agents among persons who are cognitively intact but at risk for Alzheimer’s disease. One such trial, the Alzheimer’s Disease Anti-inflammatory Prevention Trial (http://www.2stopAD.org), has recently been initiated with funding from the National Institute on Aging. This trial will evaluate the ability not only of the conventional NSAID naproxen but also of the selective cyclooxygenase-2 inhibitor celecoxib to prevent Alzheimer’s disease. New epidemiologic studies on this topic should provide further insights while we await results of the prevention trial.

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THE CHANGING FACE OF PEDIATRIC HIV-1 INFECTION

It has been nearly 20 years since the first cases of AIDS were reported in children in the United States, and the face of pediatric human immunodeficiency virus type 1 (HIV-1) infection has changed markedly. During the first 15 years of the epidemic, approximately 15,000 infants acquired HIV-1 infection in the United States, mainly through vertical, or mother-to-child, transmission of the virus. Over the same period, about 3000 children died of AIDS. More recently, the development of effective prophylactic and therapeutic strategies has markedly reduced the number of newly infected infants and has changed clinical outcomes in infected children.

In 1994, Connor et al. reported that the use of zidovudine therapy in mothers and infants markedly reduced the risk of mother-to-child transmission. An improved understanding of the pathogenesis of vertical HIV-1 transmission and the availability of additional antiretroviral agents have made possible further refinement of our clinical strategies. Through the mid-1990s, there were approximately 6000 to 7000 pregnancies each year among HIV-1–infected women, and the rate of mother-to-child transmission in the absence of antiretroviral therapy was 25 percent. In 2001, the combination of routine prenatal screening for HIV-1 and antiretroviral therapy in mothers and infants has markedly reduced the incidence of mother-to-child transmission. The recently completed Pediatric AIDS Clinical Trials Group Protocol 316 trial reported an overall transmission rate of 1.4 percent in a cohort of HIV-1–infected pregnant women receiving standard antiretroviral therapies; more than 40 percent of these women received combination regimens that included a protease inhibitor.

The availability of potent combination therapies has also altered the clinical course of HIV-1 infection in children. In the United States today, fewer than 200 children acquire HIV-1 infection each year, and these infections are in large part the result of the failure of HIV-1–infected pregnant women to obtain prenatal care or adhere to prescribed regimens. Current diagnostic methods permit the identification of the majority of vertically infected infants by one month of age.
age, and the current guidelines recommend the initiation of combination antiretroviral therapy as soon as the diagnosis is confirmed. This recommendation is based on the recognition that it is difficult to distinguish between infants whose disease will progress rapidly and those whose disease will progress slowly. Recent studies show that the initiation of combination therapy within the first three months of life can result in the complete cessation of viral replication and the preservation of normal immune function—a condition that may last for years with adherence to therapy. These results can be achieved with combination therapies including nucleoside reverse-transcriptase inhibitors and nonnucleoside reverse transcriptase inhibitors, as well as with combinations containing protease inhibitors.

In this issue of the Journal, Gortmaker et al. report on the effect of combination therapy including protease inhibitors on mortality among HIV-1–infected children and adolescents in the United States between 1996 and 1999. Most of the children in this cohort were born before combination therapies began to be used for early treatment. At the inception of this Pediatric AIDS Clinical Trials Group study, funded by the National Institutes of Health, only 7 percent of HIV-1–infected infants and children were receiving protease inhibitors as part of their treatment regimens, and the annual mortality rate was 5.3 percent. By 1999, however, 73 percent of the study subjects were receiving combination regimens containing protease inhibitors, and the mortality rate had declined to 0.7 percent per year. These results are similar to those reported in adults by Palella et al. The most dramatic reductions in mortality associated with the increased use of protease inhibitors have occurred among adults and children with markedly reduced CD4+ T-helper cell counts.

Along with these successes come several challenges. Realization of the benefit of antiretroviral therapy requires adherence to complex and demanding regimens. Toxic effects limit the use of antiretroviral therapies in some children. Early suppressive therapy was not available to the majority of the 10,000 to 12,000 HIV-infected children currently alive in the United States, and in many, resistance to multiple agents has developed. Fortunately, several promising second-generation drugs as well as new classes of antiretroviral agents are currently in phase 1 and 2 trials.

Of critical importance is the fact that more than 90 percent of the estimated 1700 new pediatric infections that occur each day around the world occur in developing countries. Advances in the developed world have been difficult to replicate in resource-poor settings. Although safe, simple, and inexpensive regimens can substantially reduce mother-to-child transmission, the infrastructure necessary for the delivery of these regimens in the developing world is just beginning to be created. The United Nations AIDS Summit has set the modest goal of a 20 percent reduction in mother-to-child transmission by 2005.

Similarly, combination antiretroviral therapies are unavailable to millions of HIV-1–infected children in developing countries. Our efforts must focus on devising simple, relatively inexpensive, triple-combination regimens for the treatment of all HIV-1–infected pregnant women and all HIV-1–infected children. Such a regimen could be provided for $5 per day and would have a substantial effect on the prevention and treatment of HIV-1 disease in the developing world. These efforts would represent an important step toward changing the face of pediatric HIV-1 infection for the many millions who are affected by it around the world.

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PREIMPLANTATION GENETIC DIAGNOSIS BY COMPARATIVE GENOMIC HYBRIDIZATION

Currently, the most common techniques for prenatal diagnosis are amniocentesis, performed between 14 and 22 weeks’ gestation, and chorionic villus sampling, performed between 14 and 20 weeks’