**TABLE 226-19 INITIAL EVALUATION OF THE PATIENT WITH HIV INFECTION**

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| History and physical examination |
| Routine chemistry and hematology |
| AST, ALT, direct and indirect bilirubin |
| Lipid profile and fasting glucose |
| CD4+ T lymphocyte count |
| Two plasma HIV RNA levels |
| HIV resistance testing |
| HLA-B5701 screening |
| RPR or VDRL test |
| Anti-*Toxoplasma* antibody titer |
| PPD skin test or IFN-γ release assay |
| Mini-Mental Status Examination |
| Serologies for hepatitis A, hepatitis B, and hepatitis C |
| Immunization with pneumococcal polysaccharide; influenza as indicated |
| Immunization with hepatitis A and hepatitis B if seronegative |
| Counseling regarding natural history and transmission |
| Help contacting others who might be infected |

***Abbreviations:*** ALT, alanine aminotransferase; AST, aspartate aminotransferase; PPD, purified protein derivative; RPR, rapid plasma reagin; VDRL, Venereal Disease Research Laboratory.

RNA levels, an HIV resistance test, a rapid plasma reagin or VDRL test, an anti-*Toxoplasma* antibody titer, and serologies for hepatitis A, B, and C. A PPD test or IFN-γ release assay should be done and an MMSE performed and recorded. A pregnancy test should be done in women in whom the drug efavirenz is being considered, and HLA-B5701 testing should be done in all patients in whom the drug abacavir is being considered. Patients should be immunized with pneumococcal polysaccharide, with annual influenza shots, and, if seronegative for these viruses, with HPV, hepatitis A, and hepatitis B vaccines. The status of hepatitis C infection should be determined. In addition, patients should be counseled with regard to sexual practices and needle sharing, and counseling should be offered to those whom the patient knows or suspects may also be infected. Once these baseline activities are performed, short- and long-term medical management strategies should be developed based on the most recent information available and modified as new information becomes available. The field of HIV medicine is changing rapidly, and it is difficult to remain fully up to date. Fortunately there are a series of excellent sites on the Internet that are frequently updated, and they provide the most recent information on a variety of topics, including consensus panel reports on treatment **(Table 226-20)**.

### ANTIRETROVIRAL THERAPY

Combination antiretroviral therapy (cART), also referred to as highly active antiretroviral therapy (HAART), is the cornerstone of management of patients with HIV infection. Following the initiation of widespread use of cART in the United States in 1995–1996, marked declines were noted in the incidence of most AIDS-defining conditions (Fig. 226-33). Suppression of HIV replication is an important component in prolonging life as well as in improving the quality of life in patients with HIV infection. Adequate suppression requires strict adherence to prescribed regimens of antiretroviral drugs. This has been facilitated by the coformulations of antiretrovirals and the development of once-daily regimens. Unfortunately, many of the most important questions related to the treatment of HIV disease currently lack definitive answers. Among them are the questions of when therapy should be started, what the best initial regimen is, when a given regimen should be changed, and what it should be changed to when a change is made. Notwithstanding these uncertainties, the physician and patient must come to a mutually agreeable plan based on the best available data. In an effort to facilitate this process, the U.S. Department of Health and Human Services makes available on the Internet (*www.aidsinfo.nih.gov*) a series of periodically updated guidelines, including *"Guidelines for the Use of Antiretroviral Agents in HIV-Infected Adults and Adolescents"* and "*Guidelines for the Prevention of Opportunistic Infections in Persons Infected with Human Immunodeficiency Virus*." At present, an extensive clinical trials network, involving both clinical investigators and patient advocates, is in place attempting to develop improved approaches to therapy. Consortia comprising representatives of academia, industry, independent foundations, and the federal government are involved in the process of drug development, including a wide-ranging series of clinical trials. As a result, new therapies and new therapeutic strategies are continually emerging. New drugs are often available through expanded-access programs prior to official licensure. Given the complexity of this field, decisions regarding cART are best made in consultation with experts.

**TABLE 226-20 RESOURCES AVAILABLE ON THE WORLD WIDE WEB ON HIV DISEASE**

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| *www.aidsinfo.nih.gov* | AIDSinfo, a service of the U.S. Department of Health and Human Services, posts federally approved treatment guidelines for HIV and AIDS; provides information on federally funded and privately funded clinical trials and CDC publications and data |
| *www.cdcnpin.org* | Updates on epidemiologic data and prevention information from the CDC |

***Abbreviation:*** CDC, Centers for Disease Control and Prevention.

Currently available drugs for the treatment of HIV infection as part of a combination regimen fall into four categories: those that inhibit the viral reverse transcriptase enzyme (nucleoside and nucleotide reverse transcriptase inhibitors; nonnucleoside reverse transcriptase inhibitors), those that inhibit the viral protease enzyme (protease inhibitors), those that inhibit the viral integrase enzyme (integrase inhibitors), and those that interfere with viral entry (fusion inhibitors; CCR5 antagonists) **(Table 226-21; Fig. 226-45)**.

The FDA-approved reverse transcriptase inhibitors include the *nucleoside analogues* zidovudine, didanosine, zalcitabine, stavudine, lamivudine, abacavir, and emtricitabine; the *nucleotide analogue* tenofovir; and the *nonnucleoside reverse transcriptase inhibitors* nevirapine, delavirdine, efavirenz, and etravirine (Table 226-21; Fig. 226-45). These represent the first class of drugs licensed for the treatment of HIV infection. They are indicated for this use as part of combination regimens. It should be stressed that none of these drugs should be used as monotherapy for HIV infection due to the relative ease with which drug resistance may develop under such circumstances. Thus, when lamivudine, emtricitabine, or tenofovir is used to treat hepatitis B infection in the setting of HIV infection, one should ensure that the patient is also on additional antiretroviral medication. The reverse transcriptase inhibitors block the HIV replication cycle at the point of RNA-dependent DNA synthesis, the reverse transcription step. While the nonnucleoside reverse transcriptase inhibitors are quite selective for the HIV-1 reverse transcriptase, the nucleoside and nucleotide analogues inhibit a variety of DNA polymerases in addition to those of the HIV-1 reverse transcriptase. For this reason, serious side effects are more varied with the nucleoside analogues and include mitochondrial damage that can lead to hepatic steatosis and lactic acidosis as well as peripheral neuropathy and pancreatitis. The use of either of the thymidine analogues zidovudine and stavudine has been associated with a syndrome of hyperlipidemia, glucose intolerance/insulin resistance, and fat redistribution often referred to as *lipodystrophy syndrome* (discussed in "Diseases of the Endocrine System and Metabolic Disorders," above). The reverse transcriptase inhibitors preferred for use according to the DHHS Panel on the use of antiretroviral drugs are lamivudine, emtricitabine, abacavir, tenofovir, and rilpivirine.

*Lamivudine* (3TC; 2′,3′-dideoxy-3′-thiacytidine) is the fifth of the nucleoside analogues to be licensed in the United States. It is the negative enantiomer of a dideoxy analogue of cytidine. In actual practice, lamivudine or the closely related drug emtricitabine (see