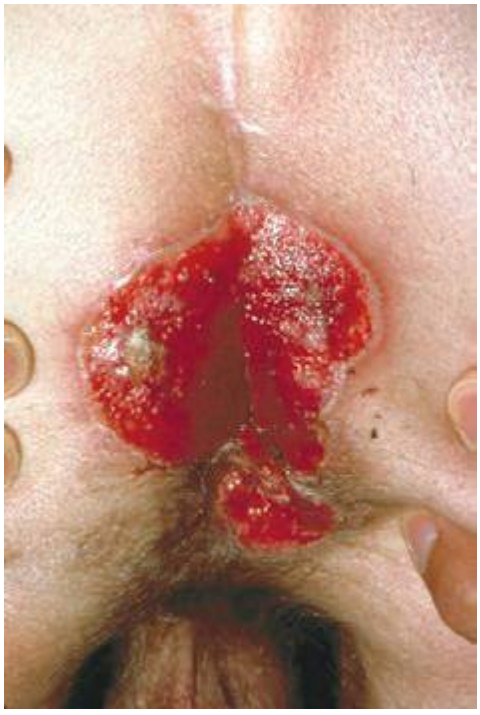

FIGURE 226-37 Severe, erosive perirectal herpes simplex in a patient with AIDS.

(Fig. 226-37). These lesions may appear quite atypical, as denuded skin without vesicles. They typically respond well to treatment with acyclovir, famciclovir, or foscarnet. Other rectal lesions encountered in patients with HIV infection include condylomata acuminata, KS, and intraepithelial neoplasia (see below).

Hepatobiliary Diseases Diseases of the hepatobiliary system are a major problem in patients with HIV infection. It has been estimated that approximately 15% of the deaths of patients with HIV infection are related to liver disease. While this is predominantly a reflection of the problems encountered in the setting of co-infection with hepatitis B or C, it is also a reflection of the hepatic injury, ranging from hepatic steatosis to hypersensitivity reactions to immune reconstitution, that can be seen in the context of cART.

The prevalence of co-infection with HIV and hepatitis viruses varies by geographic region. In the United States, ~90% of HIV-infected individuals have evidence of infection with HBV; 6–14% have chronic HBV infection; 5–50% of patients are co-infected with HCV; and co-infections with hepatitis D, E, and/or G viruses are common. Among IV drug users with HIV infection, rates of HCV infection range from 70% to 95%. HIV infection has a significant impact on the course of hepatitis virus infection. It is associated with approximately a threefold increase in the development of persistent hepatitis B surface antigenemia. Patients infected with both HBV and HIV have decreased evidence of inflammatory liver disease. The presumption that this is due to the immunosuppressive effects of HIV infection is supported by the observations that this situation can be reversed, and one may see the development of more severe hepatitis following the initiation of effective cART. In studies of the impact of HIV on HBV infection, four- to tenfold increases in liver-related mortality rates have been noted in patients with HIV and active HBV infection compared to rates in patients with either infection alone. There is, however, only a slight increase in overall mortality rate in HIV-infected individuals who are also hepatitis B surface antigen (HBsAg)–positive. IFN-α is less successful as treatment for HBV in patients with HIV co-infection. Lamivudine, emtricitabine, adefovir/tenofovir/entecavir, and telbivudine alone or in combination are useful in the treatment of hepatitis B in patients with HIV infection. It is important to remember that all the above-mentioned drugs also have activity against HIV and should not be used alone in patients with HIV infection, in order to avoid the emergence of quasispecies of HIV resistant to these drugs. For this reason, the need to treat hepatitis B infection in a patient with HIV infection is an indication to treat HIV infection in that same patient, regardless of CD4+ T cell count. HCV infection is more severe in the patient with HIV infection; it does not appear to affect overall mortality rates in HIV-infected individuals when other variables such as age, baseline CD4+ T cell count, and use of cART are taken into account. In the setting of HIV and HCV co-infection, levels of HCV are approximately tenfold higher than in the HIV-negative patient with HCV infection. There is a 50% higher overall mortality rate with a five-fold increased risk of death due to liver disease in patients chronically infected with both HCV and HIV. Use of directly acting agents for the treatment for HCV leads to cure rates approaching 100%, even in patients with HIV co-infection. Successful treatment of HCV in HIV-infected patients decreases mortality. Hepatitis A virus infection is not seen with an increased frequency in patients with HIV infection. It is recommended that all patients with HIV infection who have not experienced natural infection be immunized with hepatitis A and/or hepatitis B vaccines. Infection with hepatitis G virus, also known as GB virus C, is seen in ~50% of patients with HIV infection. For reasons that are currently unclear, there are data to suggest that patients with HIV infection co-infected with this virus have a decreased rate of progression to AIDS.

A variety of other infections also may involve the liver. Granulomatous hepatitis may be seen as a consequence of mycobacterial or fungal infections, particularly MAC infection. Hepatic masses may be seen in the context of TB, peliosis hepatis, or fungal infection. Among the fungal opportunistic infections, *C. immitis* and *Histoplasma capsulatum* are those most likely to involve the liver. Biliary tract disease in the form of papillary stenosis or sclerosing cholangitis has been reported in the context of cryptosporidiosis, CMV infection, and KS. When no diagnosis can be made, the term AIDS cholangiopathy is used. Hemophagocytic lymphohistiocytosis of the liver has been seen in the setting of Hodgkin's disease.

Many of the drugs used to treat HIV infection are metabolized by the liver and can cause liver injury. Fatal hepatic reactions have been reported with a wide array of antiretrovirals including nucleoside analogues, nonnucleoside analogues, and protease inhibitors. Nucleoside analogues work by inhibiting DNA synthesis. This can result in toxicity to mitochondria, which can lead to disturbances in oxidative metabolism. This may manifest as hepatic steatosis and, in severe cases, lactic acidosis and fulminant liver failure. It is important to be aware of this condition and to watch for it in patients with HIV infection receiving nucleoside analogues. It is reversible if diagnosed early and the offending agent(s) discontinued. Nevirapine has been associated with at times fatal fulminant and cholestatic hepatitis, hepatic necrosis, and hepatic failure. Indinavir may cause mild to moderate elevations in serum bilirubin in 10–15% of patients in a syndrome similar to Gilbert's syndrome. A similar pattern of hepatic injury may be seen with atazanavir. In the patient receiving cART with an unexplained increase in hepatic transaminases, strong consideration should be given to drug toxicity.

Pancreatic injury is most commonly a consequence of drug toxicity, notably that secondary to pentamidine or dideoxynucleosides. While up to half of patients in some series have biochemical evidence of pancreatic injury, <5% of patients show any clinical evidence of pancreatitis that is not linked to a drug toxicity.

Diseases of the Kidney and Genitourinary Tract Diseases of the kidney or genitourinary tract may be a direct consequence of HIV infection, due to an opportunistic infection or neoplasm, or related to drug toxicity. Overall, microalbuminuria is seen in ~20% of untreated HIV-infected patients; significant proteinuria is seen in closer to 2%. The presence of microalbuminuria has been associated with an increase in all-cause mortality rate. *HIV-associated nephropathy* (HIVAN) was first described in IDUs and was initially thought to be IDU nephropathy in patients with HIV infection; it is now recognized as a true direct complication of HIV infection. Although the majority of patients with this condition have CD4+ T cell counts <200/μL,