Although intravenous drug use is the major route of transmission in several countries, sexual transmission is the dominant mode of HIV spread globally, with a concomitant epidemic in infants borne to HIV-infected mothers. The HIV epidemic varies substantially from one geographic area to another, and three broad epidemic categories describe the diversity of features observed globally: low epidemic settings, concentrated epidemics, and generalized epidemics. The introduction of highly active antiretroviral therapy in industrialized countries has transformed AIDS from an inevitably fatal condition to a chronic, treatable condition, but this goal has yet to be realized in most resource-constrained settings that bear a disproportionate burden of infection. This article describes the modes of HIV transmission, geographic distribution of the evolving AIDS pandemic, and case studies of each of the three types of HIV epidemics, and presents global trends in AIDS and mortality.

HIV infection starts as an acute, systemic infection, followed by a chronic period of clinical latency, usually lasting 3 to 10 years, which precedes the eventual collapse of the immune system. It is increasingly recognized that events occurring during acute HIV infection may determine the natural course of the disease. The very dynamic events of acute HIV infection provide multiple opportunities for biologic interventions, such as anti-retroviral or immune-based therapies. Similarly, the implementation of public health measures during acute HIV infection could help control epidemics or outbreaks. Many of the dramatic possibilities for
intervention in acute HIV infection remain unproved, not the least because of traditional difficulty of diagnosing patients during this early period. This article reviews the natural history, pathogenesis and clinical presentation of acute HIV infection, and suggests a diagnostic and therapeutic approach to guide clinicians dealing with patients with suspected or confirmed acute HIV infection.

Primary Care Issues for HIV-Infected Patients 49
Daniel E. Cohen and Kenneth H. Mayer

HIV primary care is determined by the intersection of the unique aspects of the infection and its treatment, the unique aspects of the populations affected by HIV, and the challenges of disease prevention and health maintenance in the general population. Any primary care provider may be called on to care for a patient living with HIV, and it is incumbent on all medical providers to become proficient in the management of this complex infection. This proficiency includes an awareness of local resources for referral, including medical and surgical specialists, mental health providers, and social service organizations. Given the complexity of HIV care in the twenty-first century and the potential for involvement of multiple consultants, the role of primary care provider is perhaps more critical for the HIV-infected patient than for the average patient.

Antiretroviral Management of Treatment-Naive Patients 71
Roy M. Gulick

Antiretroviral management of treatment-naive patients begins with the decision of when to start treatment. Current treatment guidelines suggest starting therapy in anyone with AIDS, HIV-related symptoms, or a CD4 cell count less than 200/mm$^3$ regardless of symptoms. Starting treatment in asymptomatic patients with CD4 of more than 200 requires consideration of a number of pros and cons, and individualization is the key. Recommended first-line antiretroviral regimens consist of two nucleoside reverse transcriptase inhibitors together with either a nonnucleoside reverse transcriptase inhibitor or a protease inhibitor (with or without ritonavir boosting). The goal of antiretroviral therapy is maximally to suppress viremia, enhance or improve immune function, and prevent clinical progression.

Approach to the Treatment-Experienced Patient 85
Joel E. Gallant

The management of treatment-experienced patients is complex and challenging. Fortunately, new agents continue to be developed that offer hope to those who have developed resistance to currently available agents. Knowing when, how, and in whom to use new agents is never easy and highlights the importance of expert care for HIV-infected patients. The management of treatment-
experienced patients requires considerable expertise, especially now that patients with highly resistant virus can hope to achieve full virologic suppression.

Management of Antiretroviral Treatment–Related Complications 103
Risa M. Hoffman and Judith S. Currier

Antiretroviral therapy for HIV restores immune function, controls viral replication, decreases opportunistic infections, and extends lifespan to near-normal for infected individuals. However, successful HIV therapy has been accompanied by the emergence of treatment-related complications, with an impact not yet fully understood. This article reviews six common complications of antiretroviral therapy, including hyperlactatemia/lactic acidosis, hypersensitivity reactions, abnormal glucose metabolism, dyslipidemia, body composition changes, and cardiovascular disease. A comprehensive approach to management of antiretroviral-related complications includes awareness of (1) risk factors for adverse reactions, (2) clinical syndromes suggestive of an evolving complication, and (3) evidence-based monitoring and treatment strategies. Fluency in options for preventing and managing complications can provide maximal opportunity to balance treatment effects with quality of life.

Special Care Issues of Women Living with HIV-AIDS 133
Erna Milunka Kojic and Susan Cu-Uvin

Many HIV-infected women are benefiting from highly active antiretroviral therapy and living longer. Their reproductive choices vary over the life cycle, and there is a need to understand the appropriate contraceptives for those not intending pregnancy. There are specific gynecologic issues relevant to HIV-infected women, such as genital tract infections, risk for cervical cancer, and menstrual irregularities. More women are expected to reach menopause. Health care providers should be aware of these unique needs of HIV-infected women.

Clinical Care of the HIV-infected Drug User 149
R. Douglas Bruce and Frederick L. Altice

HIV/AIDS and chemical dependency, the latter often intertwined with mental illness, are complex, overlapping spheres that adversely influence each other and the overall clinical outcomes of the affected individual. Each disorder individually impact tens of millions of people adversely, with explosive epidemics described worldwide. This article addresses the adverse consequences of HIV/AIDS, drug injection, the secondary comorbidities of both, and the impact of immunosuppression on presentation of disease as well as approaches to managing the HIV-infected drug user.
Behavioral Aspects of HIV Care: Adherence, Depression, Substance Use, and HIV-Transmission Behaviors
Carla J. Berg, Susan E. Michelson, and Steven A. Safren

A variety of psychosocial stressors are involved in living with HIV, maintaining a regimen of highly active antiretroviral therapy, and negotiating necessary self-care behaviors. Because health care providers are in regular contact with HIV-infected individuals in care, these contacts allow for the opportunity to assess and intervene on important variables related to quality of life and HIV outcomes. This article reviews information about four important behavioral aspects of HIV care: treatment adherence, depression, high-risk sex, and substance abuse. Efforts by health care providers to address these factors may result in better treatment outcomes, enhanced quality of life among HIV patients, and decreased HIV transmission.

HIV Vaccine Efficacy Trials: Towards the Future of HIV Prevention
Denny Kim, Marnie Elizaga, and Ann Duerr

Past efficacy trials of HIV vaccines have attempted to generate neutralizing antibodies. With the failure of these trials to demonstrate protection, the focus for HIV vaccine development has shifted to inducing a cytotoxic T-lymphocyte response (CTL). A CTL response is not expected to produce sterilizing immunity, but may delay progression to AIDS or reduce the transmission of HIV. Adenovirus vector-based regimens that induce CTLs are currently in efficacy trial testing. These efficacy trials are using surrogate end points in an innovative Phase 2B trial design.

The Future of HIV Prevention: Prospects for an Effective Anti-HIV Microbicide
Jeremy Nuttall, Joseph Romano, Karen Douville, Caroline Galbreath, Annaléne Nel, William Heyward, Mark Mitchnick, Saul Walker, and Zeda Rosenberg

Topical microbicides are self-administered products for prevention of HIV transmission, and they present one of the most promising strategies for combating the HIV-AIDS epidemic. The development of microbicides is a long and complicated process, with many hurdles that are unique to this class of product, including challenges in product design, in the conduct and design of clinical trials, and in obtaining licensure of a new class of products intended for use almost exclusively in developing countries. Once they have been registered, there are additional challenges to the marketing and distribution of microbicides. An overview of the types of microbicide currently in development, and a summary of the issues and the approaches being taken to address them, are provided.
Prevention and control of sexually transmitted infections (STIs) has proven effective in reducing HIV infection when treatment is available promptly for symptomatic persons in conditions of an emerging epidemic. Biologically, it is assumed that reduced genital tract inflammation reduces infectiousness for HIV as well as reducing susceptibility in HIV-uninfected persons. Male circumcision has been demonstrated effective in reducing risk for HIV infection in three separate trials from South Africa, Kenya, and Uganda. Global expansion of STI treatment and male circumcision programs are vital tools for control of HIV infection; current evidence is reviewed and research priorities are presented.