Preface: Nearly Two Decades Later, Exciting Progress in HIV, But Challenges Remain  
Paul E. Sax  

HIV Diagnostics: Current Recommendations and Opportunities for Improvement  
Bernard M. Branson  

Profound changes in technology have revolutionized laboratory testing for human immunodeficiency virus (HIV) since the first laboratory enzyme immunoassays that detected only immunoglobulin G (IgG) antibodies. Instrumented fourth-generation random-access chemiluminescent assays are now recommended for initial screening because they become reactive in as little as 2 weeks after infection. Using HIV-1 RNA viral load assays after a reactive initial test could confirm infection and provide useful clinical information. Early initiation of antiretroviral therapy and use of preexposure prophylaxis can alter the evolution of biomarkers and assay reactivity, leading to ambiguous test results.

Antiretroviral Medications for the Prevention of HIV Infection: A Clinical Approach to Preexposure Prophylaxis, Postexposure Prophylaxis, and Treatment as Prevention  
Amila Heendeniya and Isaac I. Bogoch  

Preventing new human immunodeficiency virus (HIV) infections is essential to halting the global pandemic. HIV prevention strategies include integrating both nonpharmacologic (eg, safe sexual counseling, circumcision) and pharmacologic approaches. Several pharmacologic HIV prevention strategies are increasingly used globally and include postexposure prophylaxis, preexposure prophylaxis, and treatment as prevention. These prevention modalities have enormous clinical and public health appeal, as they effectively reduce HIV acquisition in individuals and also may lower HIV incidence in communities when integrated and implemented broadly. Efforts are now underway to scale HIV prevention programs using these techniques in both high- and low-resource settings.

HIV Initial Assessment and Routine Follow-up: What Tests to Order and Why  
Daniel A. Solomon  

Laboratory tests are an important tool in the care of patients with human immunodeficiency virus. An organized approach to laboratory ordering helps clinicians to understand the utility of each test, ensure a comprehensive evaluation, and decrease use of unnecessary tests. Tests are organized around the following goals of care: confirm the diagnosis, assess for immune suppression, guide antiretroviral therapy, screen for coinfections and latent infections, monitor response to therapy, and provide preventative care. This article reviews appropriate testing for patients with human immunodeficiency virus to accomplish these goals with a focus on how each test is useful in clinical practice.
Since 2014, a consensus of landmark studies has justified starting antiretroviral therapy (ART) regardless of CD4 count. The evidence for immediate and universal ART is strong, clearly showing individual and population-level benefits, and is supported by all major guidelines groups. Altogether, improvements in ART and recognition of its clinical and epidemiologic benefits justify near-universal ART, preferably as soon after the diagnosis of human immunodeficiency virus (HIV) as possible. Case-based discussions provide a framework to explore the evidence behind the current recommendation for ART for all HIV-positive persons and specific scenarios are discussed in which ART initiation may be delayed.

With the second-generation integrase inhibitors (dolutegravir and bictegravir) extending the attributes of earlier integrase inhibitors, three-drug regimens containing integrase inhibitors plus two nucleos(t)ide reverse transcriptase inhibitors are now widely recommended for first-line (initial) treatment of human immunodeficiency virus-1 infection. Led by dolutegravir plus lamivudine, two-drug therapy is emerging as a way to reduce antiretroviral therapy cost and adverse effects without compromising treatment options should virologic failure occur. Initial two-drug therapy has limitations, including the relative incompatibility with the coemerging concept of same-day antiretroviral therapy initiation.

This review provides a synopsis of key clinical considerations for switching antiretroviral therapy (ART) for individuals with human immunodeficiency virus who have maintained a routinely suppressed viral load. There may be benefits but also risks involved in every ART regimen change, so strategies for prioritizing individuals for a switch based on the specific antiretroviral agents in the regimen are discussed, along with approaches to ensure maintenance of viral suppression after treatment modifications. Controversial and evolving questions in the area of ART switches and simplifications are also considered.

Approximately 20% of people with HIV in the United States prescribed antiretroviral therapy are not virally suppressed. Thus, optimal management of virologic failure has a critical role in the ability to improve viral suppression rates to improve long-term health outcomes for those infected and to achieve epidemic control. This article discusses the causes of virologic failure, the use of resistance testing to guide management after failure, interpretation and relevance of HIV drug resistance patterns,
considerations for selection of second-line and salvage therapies, and management of virologic failure in special populations.

Management of Advanced HIV Disease 743

Nathan A. Summers and Wendy S. Armstrong

Great progress has been made in caring for persons with human immunodeficiency virus. However, a significant proportion of individuals still present to care with advanced disease and a low CD4 count. Careful considerations for selection of antiretroviral therapy as well as close monitoring for opportunistic infections and immune reconstitution inflammatory syndrome are vitally important in providing care for such individuals.

HIV and Aging: Reconsidering the Approach to Management of Comorbidities 769

Kristine M. Erlandson and Maile Y. Karris

Health care for older adults with human immunodeficiency virus can be highly complex, resource intensive, and carry a high administrative burden. Data from aging longitudinal cohorts and feedback from the human immunodeficiency virus community suggest that the current model is not meeting the needs of these older adults. We introduce the 6 Ms approach, which acknowledges the multicomplexity of older adults with human immunodeficiency virus, simplifies geriatric principles for non-geriatrics-trained providers, and minimizes extensive training and specialized screening tests or tools. Implementing novel approaches to care requires support at local/national levels.

Key Principles of Antiretroviral Pharmacology 787

Brandon Dionne

Antiretroviral therapy has advanced significantly since zidovudine was first approved. Although 31 antiretrovirals have been approved by the FDA, only about half of those are commonly used. Newer, more tolerable agents have made human immunodeficiency virus into a chronic condition, which can be managed with medication. The most common antiretroviral regimens consist of 2 nucleoside reverse transcriptase inhibitors plus a third agent, often an integrase inhibitor because of better tolerability and fewer drug interactions than other regimens. Understanding the dosage forms, adverse effects, and drug interactions of antiretrovirals allow clinicians to choose the most appropriate regimen for their patient. New developments, such as branded generic regimens and long-acting intramuscular injections, may play a larger role in the future.

How Big Data Science Can Improve Linkage and Retention in Care 807

Aadia I. Rana and Michael J. Mugavero

Ending the HIV Epidemic: A Plan for America” (EtHE), launched by the Department of Health and Human Services (DHHS), is predicated on actionable data systems to monitor progress toward ambitious goals and to guide human immunodeficiency virus (HIV) testing, prevention, and treatment services. Situated on a status-neutral continuum of HIV prevention and care, EtHE relies on coordination across DHHS agencies and utilization of data systems established for
programmatic purposes. Improving efficiencies and timeliness of existing data systems and harnessing the potential of novel data systems, including those afforded by social media, require big data science approaches and investment in technological and human resources.

The Reproductive Years of Women with Perinatally Acquired HIV: From Gynecologic Care to Obstetric Outcomes 817
Saba Berhie, Lynn Yee, and Jennifer Jao

Women with PHIV have distinct medical and social concerns in the context of lifelong immunosuppression, complex HIV care, and stigma because of with HIV from an early age. This article reviews the gynecologic and obstetric concerns experienced by women with PHIV. Cervical cancer screening is suboptimal, and data suggest higher rates of unintended pregnancy. Pregnant women with PHIV are younger and exposed to more antiretroviral therapy regimens compared with women with NPHIV. Although obstetric outcomes are similar between women with PHIV and NPHIV, there are concerns that infant morbidity may be increased in infants of women with PHIV.

HIV and Substance Use Disorder: Role of the HIV Physician 835
Christopher M. Bositis and Joshua St. Louis

The ongoing syndemic of substance use disorder and human immunodeficiency virus infection threatens progress made in preventing new infections and improving outcomes among those infected. To address this challenge effectively, human immunodeficiency virus physicians must take an increased role in the screening, diagnosis, and treatment of substance use disorders. Such treatment decreases human immunodeficiency virus risk behaviors and improves human immunodeficiency virus and substance use disorder-related outcomes. An effective response to this syndemic requires increased access to adjuvant interventions and a radical movement away from the current stigmatization and criminalization of those suffering from substance use disorders.

On the Road to a HIV Cure: Moving Beyond Berlin and London 857
Nikolaus Jilg and Jonathan Z. Li

The Berlin patient, a famous example for human immunodeficiency virus (HIV) cure, had received a bone marrow transplantation with an HIV resistance mutation. The authors describe his case and others that had shown HIV control, like the Mississippi baby who was started on antiretroviral therapy very early after birth, and posttreatment controllers, like the VISCONTI cohort. Moreover, the authors outline various strategies, oftentimes informed by these individuals, that have been tried in vitro, in animal models, or in human trials, to deplete the latent reservoir, which is considered the basis of HIV persistence and the obstacle to cure.