

Contents

Preface

xiii

Kristina Crothers, Laurence Huang, and Alison Morris

Abnormalities in Host Defense Associated with HIV Infection

143

James M. Beck

The broad variety of pulmonary infections encountered in human immunodeficiency virus (HIV)-infected individuals demonstrates that the host defense network is impaired. An improved understanding of these events in the lung can lead to specific interventions aimed at restoration of deficient function. This review summarizes the pulmonary host defense deficits in HIV-infected individuals, focusing on lymphocytes, alveolar macrophages, and neutrophils.

Impact of Antiretroviral Therapy on Lung Immunology and Inflammation

155

Homer L. Twigg III and Kenneth S. Knox

Human immunodeficiency virus (HIV) infection causes profound changes in the lung compartment characterized by macrophage and lymphocyte activation, secretion of proinflammatory cytokines and chemokines, and accumulation of CD8 T cells in the alveolar space, leading to lymphocytic alveolitis. Because many of the changes seen in the lung can be attributed to the direct effect of HIV on immune cells, therapy to reduce the HIV burden should have significant beneficial effects. Indeed, antiretroviral therapy rapidly reduces the viral burden in the lung, number of CD8 T cells in the alveolar space, and amount of proinflammatory cytokines and chemokines in bronchoalveolar lavage.

Epidemiology of Human Immunodeficiency Virus–Associated Pulmonary Disease

165

John F. Murray

HIV/AIDS was initially characterized as a progressively worsening disorder of cellular immunosuppression. In 1996, HIV/AIDS was separated into 2 diagnostic, management, prognostic categories: high-income and low-income groups. High-income people with HIV have had access to antiretroviral therapeutic agents, which have transformed HIV from a lethal to an indolent disease, with life expectancy comparable with other chronic conditions. About 50% of low-income people with HIV who are candidates for antiretroviral therapy actually receive it. Since 1996, the principal HIV-associated pulmonary disease in high-income countries has changed from *Pneumocystis pneumonia* to community-acquired pneumonia; tuberculosis has predominated in low-income countries as long as HIV has prevailed.

Tobacco Use and Cessation in HIV-Infected Individuals

181

Kristine K. Browning, Mary Ellen Wewers, Amy K. Ferketich, and Philip Diaz

Smoking prevalence estimates among HIV-infected individuals range from 40% to 84%, much higher than the overall US adult prevalence. To date, few tobacco dependence treatment trials have been conducted among HIV-infected smokers. Recommendations for future research include examining underlying factors that contribute to persistent smoking and barriers to abstinence, identifying ways to increase motivation for quit attempts, increasing the number of multicentered

2-arm tobacco dependence treatment trials, and using highly efficacious first-line pharmacotherapy in tobacco dependence treatment intervention studies. Addressing these research gaps will help to reduce the tobacco-related disease burden of HIV-infected individuals in the future.

Evaluation of Respiratory Disease

191

Sofya Tokman and Laurence Huang

The spectrum of HIV-associated pulmonary diseases is broad. Opportunistic infections, neoplasms, and noninfectious complications are all major considerations. Clinicians caring for persons infected with HIV must have a systematic approach. The approach begins with a thorough history and physical examination and often involves selected laboratory tests and a chest radiograph. Frequently, the clinical, laboratory, and chest radiographic presentation suggests a specific diagnosis or a few diagnoses, which then prompts specific diagnostic testing and treatment. This article presents an overview of the evaluation of respiratory disease in persons with HIV/AIDS.

HIV-Associated Bacterial Pneumonia

205

Charles Feldman and Ronald Anderson

Community-acquired bacterial pneumonia (CAP) remains one of the most common opportunistic infections in patients who are infected with the human immunodeficiency virus (HIV). The risk of CAP increases as the CD4 cell count decreases. The common bacterial pathogens that cause CAP in HIV-infected persons are similar to those in HIV-uninfected individuals, with the pneumococcus being the most common pathogen. Prevention of CAP remains critical and necessitates a comprehensive approach addressing, among many other factors, cigarette smoking cessation strategies, antiretroviral therapy adherence, and immunization against those infections for which effective vaccinations are available.

Human Immunodeficiency Virus–Associated Tuberculosis: Update on Prevention and Treatment

217

Kerry L. Dierberg and Richard E. Chaisson

Tuberculosis (TB) is the leading cause of opportunistic infection and mortality among HIV-infected persons. Screening for symptoms of TB in people with HIV infection, use of isoniazid preventive therapy for those with latent TB infection, earlier diagnosis and treatment of active TB disease, and early initiation of antiretroviral therapy are essential for controlling the spread of TB. Treatment of HIV-related TB is complicated by overlapping drug toxicities and drug-drug interactions between antiretroviral therapy and anti-TB therapy and risk for development of immune reconstitution inflammatory disease. This review provides an overview of the prevention and treatment of TB in HIV-infected persons.

Pneumocystis Pneumonia Associated with Human Immunodeficiency Virus

229

Robert F. Miller, Laurence Huang, and Peter D. Walzer

Pneumocystis pneumonia (PCP) is caused by the yeastlike fungus *Pneumocystis*. Despite the widespread availability of specific anti-*Pneumocystis* prophylaxis and of combination antiretroviral therapy (ART), PCP remains a common AIDS-defining presentation. PCP is increasingly recognized among persons living in Africa. *Pneumocystis* cannot be cultured and bronchoalveolar lavage is the gold standard

diagnostic test to diagnose PCP. Use of adjunctive biomarkers for diagnosis requires further evaluation. Trimethoprim-sulfamethoxazole remains the preferred first-line treatment regimen. In the era of ART, mortality from PCP is approximately 10% to 12%. The optimal time to start ART in a patient with PCP remains uncertain.

Other HIV-Associated Pneumonias

243

Jakrapun Pupaibool and Andrew H. Limper

The incidence, mortality, and epidemiology of human immunodeficiency virus (HIV)-associated pulmonary infections have changed as a result of effective antiretroviral and prophylaxis antimicrobial therapy. The clinical presentation, radiographic abnormalities, and treatment of pneumonia from various uncommon pathogens in patients with AIDS can be different from those in immunocompetent patients. Advances in invasive and noninvasive testing and molecular biological techniques have improved the diagnosis and prognosis of pulmonary infections in patients infected with HIV. This review focuses on pulmonary infections from nontuberculosis mycobacteria, cytomegalovirus, fungi (aspergillosis, cryptococcosis, endemic fungi), and parasites (toxoplasmosis), and uncommon bacterial pneumonia (nocardiosis, rhodococcosis) in these patients.

Human Immunodeficiency Virus–Associated Lung Malignancies

255

Allison A. Lambert, Christian A. Merlo, and Gregory D. Kirk

This review of lung malignancies in human immunodeficiency virus (HIV) briefly highlights key epidemiologic and clinical features in the pulmonary involvement of AIDS-defining malignancies of Kaposi sarcoma and non-Hodgkin lymphoma. Then, focusing on non-AIDS defining lung cancer, the epidemiology and mechanisms, clinical presentation, pathology, treatment and outcomes, and prevention of HIV-associated lung cancer are discussed. Finally, the important knowledge gaps and future directions for research related to HIV-associated lung malignancies are highlighted.

Human Immunodeficiency Virus–Associated Obstructive Lung Diseases

273

Matthew R. Gingo, Alison Morris, and Kristina Crothers

In the era of effective antiretroviral therapy (ART), epidemiologic studies have found that persons infected with human immunodeficiency virus (HIV) have a higher prevalence and incidence of chronic obstructive pulmonary disease than HIV-uninfected persons. In comparison with HIV-uninfected persons and those with well-controlled HIV disease, HIV-infected persons with poor viral control or lower CD4 cell count have more airflow obstruction, a greater decline in lung function, and possibly more severe diffusing impairment. This article reviews the evidence linking HIV infection to obstructive lung disease, and discusses management issues related to the treatment of obstructive lung disease in HIV-infected patients.

Human Immunodeficiency Virus–Associated Pulmonary Arterial Hypertension

283

Christopher F. Barnett and Priscilla Y. Hsue

Antiretroviral therapy has greatly increased longevity for individuals with human immunodeficiency virus (HIV) infection. About 0.5% of patients with HIV infection develop moderate to severe pulmonary arterial hypertension, which is several thousand times higher than the incidence of idiopathic pulmonary arterial hypertension. As more than 30 million individuals are chronically infected, HIV infection could soon

become one of the most common causes of pulmonary arterial hypertension worldwide. Pulmonary arterial hypertension is a relentlessly progressive disease leading to right heart failure and death. In this article the available data on epidemiology, hemodynamics, mechanisms, and therapeutic strategies for HIV-associated pulmonary arterial hypertension are reviewed.

Interstitial Lung Disease in HIV

293

Sarah R. Doffman and Robert F. Miller

A spectrum of noninfectious, nonmalignant lymphocytic infiltrative disorders, including nonspecific interstitial pneumonitis and lymphocytic interstitial pneumonitis, was frequently described in HIV-infected adults in the precombination antiretroviral therapy (ART) era. With the advent of ART, these conditions are less commonly encountered when caring for HIV-infected adults, possibly as a consequence of the effects of HIV treatment on pulmonary immunology. By contrast, reports of sarcoidosis among HIV-infected persons were uncommon in the pre-ART era, but sarcoidosis is increasingly recognized since the introduction of ART and may represent an immune reconstitution phenomenon. Other causes of interstitial pneumonitis are infrequently encountered among HIV-infected persons.

Critical Care of Persons Infected with the Human Immunodeficiency Virus

307

Anuradha Ganesan and Henry Masur

Antiretroviral therapy (ART) has transformed the prognosis for patients infected with the human immunodeficiency virus (HIV). With effective ART, these individuals can expect to live almost as long as their HIV-negative counterparts. Given that more than a million people infected with HIV currently live in the United States, the likelihood that the practicing intensivist will manage a patient infected with HIV is high. This review discusses the challenges associated with management of critically ill patients infected with HIV, including the immune reconstitution inflammatory syndrome (a complication associated with ART initiation), ART-related toxicities, and the management of some common opportunistic infections.

Future Directions: Lung Aging, Inflammation, and Human Immunodeficiency Virus

325

Meghan Fitzpatrick, Kristina Crothers, and Alison Morris

Chronic lung diseases, including chronic obstructive pulmonary disease (COPD) and pulmonary hypertension (PH), are unusually prevalent among persons infected with human immunodeficiency virus (HIV). Often these disease states are identified at younger ages than would be expected in the general population. Recent epidemiologic, basic scientific, and cross-sectional clinical data have implicated immune dysfunction and cellular senescence as potential drivers of advanced presentations of age-related diseases in HIV-infected persons. This article describes how HIV-associated COPD and PH may fit into a paradigm of immunosenescence, and outlines the hypothesized associations among chronic HIV infection, immune dysfunction and senescence, and cardiopulmonary outcomes.