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THE PRESENT AND FUTURE

REVIEW TOPIC OF THE WEEK

Stimulating High Impact HIV-Related Cardiovascular Research

Recommendations From a Multidisciplinary NHLBI Working Group on HIV-Related Heart, Lung, and Blood Disease

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ABSTRACT

The clinical challenges confronting patients with human immunodeficiency virus (HIV) have shifted from acquired immunodeficiency syndrome (AIDS)-related illnesses to chronic diseases, such as coronary artery disease, chronic lung disease, and chronic anemia. With the growing burden of HIV-related heart, lung, and blood (HLB) disease, the National Heart, Lung, and Blood Institute (NHLBI) recognizes it must stimulate and support HIV-related HLB research. Because HIV offers a natural, accelerated model of common pathological processes, such as inflammation, HIV-related HLB research may yield important breakthroughs for all patients with HLB disease. This paper summarizes the cardiovascular recommendations of an NHLBI Working Group, Advancing HIV/AIDS Research in Heart, Lung, and Blood Diseases, charged with identifying scientific priorities in HIV-related HLB disease and developing recommendations to promote multidisciplinary collaboration among HIV and HLB investigators. The working group included multidisciplinary sessions, as well as HLB breakout sessions for discussion of disease-specific issues, with common themes about scientific priorities and strategies to stimulate HLB research emerging in all 3 groups. (J Am Coll Cardiol 2015;65:738–44) © 2015 by the American College of Cardiology Foundation.

Tremendous progress in the treatment of human immunodeficiency virus (HIV) has led to increased survival and a dramatic evolution of the disease (1). The clinical challenges confronting the population have now shifted from acquired immunodeficiency syndrome (AIDS)-related illnesses to chronic diseases, such as coronary artery disease, chronic obstructive lung disease, and chronic anemia (2–7). Many studies have demonstrated that the risk of developing cardiovascular (CV) disease in the HIV-positive population is significantly higher, and disease progression may be accelerated compared with in the general population (8–14). Factors that potentially contribute to the pathophysiology of HIV-related CV disease include the HIV virus itself, adverse effects of antiretroviral therapy (ART), and processes such as aging, inflammation, immune activation, microbial translocation, endothelial injury, and disordered coagulation (15–19). These unique features, along with a large burden of traditional risk factors that include cigarette smoking, hypertension, metabolic syndrome, and dyslipidemia, contribute to the increased CV risk in the HIV population (20–26).

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With the growing burden of HIV-related heart, lung, and blood (HLB) disease, the National Heart, Lung, and Blood Institute (NHLBI) recognizes that it must stimulate and support research that addresses how the chronic phase of HIV affects the HLB systems. Also, because HIV offers a natural, accelerated model of common pathological processes, such as inflammation, HIV-related HLB research has the potential to yield important breakthroughs for all patients with HLB disease. Recently, the NHLBI assessed its AIDS scientific portfolio and determined that it needed to stimulate more peer-reviewed research in HIV-related HLB disease. The first step to encourage more peer-reviewed research was to identify the scientific priorities in the field to guide investigators. Although a small group of investigators has been pioneering this field for years, the NHLBI also recognized the need to develop a larger multidisciplinary scientific community to carry out research in the future. This paper and the Online Appendix summarize the CV recommendations of an NHLBI Working Group (WG), entitled Advancing HIV/AIDS Research in Heart, Lung, and Blood Diseases, which was charged with both identifying scientific priorities in HIV-related HLB disease and developing recommendations to promote multidisciplinary collaboration among HIV and HLB investigators (27).

OVERVIEW OF THE NHLBI WG. The WG included basic and clinical researchers with scientific expertise in HIV and HLB disease, as well as representatives from the NHLBI, the National Institutes of Health (NIH) Office of AIDS Research, the Center for Scientific Review, and other NIH institutes and centers. WG participants were asked to identify the top scientific priorities in HIV-related HLB disease, recommend research approaches to address identified critical research gaps, and develop strategies to promote collaboration and partnerships among the HIV and HLB scientific communities.

The group addressed specific HIV-related HLB diseases, as well as on cross-cutting multiorgan and multidisciplinary themes. The CV group focused on HIV-related coronary artery disease (CAD), the pulmonary group centered on HIV-related chronic obstructive pulmonary disease and pulmonary hypertension, and the hematology group addressed HIV-related anemia and the role of hematopoietic stem and progenitor cells, both as potential reservoirs and potential cures for the disease. Common themes that emerged from the conference included the role of inflammation, direct effects of organisms and medications, and barriers to multidisciplinary and cross-institutional collaboration.

The CV group focused on the specific question "Why does CAD occur at such high rates in patients with HIV?" In the following sections, we review the scientific priorities in HIV-related CV disease identified by the WG and the strategies that they proposed to advance research in the field.

METHODS

During the 2-day meeting, participants were charged with refining the primary question, identifying the related scientific gaps, and developing research approaches to address the gaps. The participants were encouraged to consider basic, clinical, and population science research approaches. The preliminary recommendations were presented to the larger group, and further refined and consolidated into a final set of CV recommendations.

In addition, the WG was asked to provide recommendations on how to stimulate more HIV-related CV research to further develop this emerging field, including identifying operational challenges to multidisciplinary research, developing strategies to enhance collaboration and engage new investigators, and highlighting ways to leverage existing research resources.

RESULTS

SCIENTIFIC THEMES. The top scientific priorities focused on epidemiology, pathogenesis, and prevention and treatment. The scientific recommendations are discussed by category in the following text and listed in the **Central Illustration**.

Epidemiology. The WG observed that although there is growing evidence that the incidence and prevalence of CAD in HIV patients may be higher than in noninfected people, the actual rate of CAD in the HIV-infected population, and how it compares with the noninfected population, is still not well established (28–31). Some of the limitations of previous studies included small numbers of HIV-infected patients, a deficiency of rigorously adjudicated of CV events, and inconsistent adjustment for confounding factors, such as smoking, that occur at much higher rates in the HIV population. The WG also noted that there was not enough information to fully understand the contributions to HIV-related CAD of traditional risk factors, such as hyperlipidemia, hypertension, and smoking versus the detrimental effects of the HIV virus itself, associated inflammation, ART, and coinfections (32,33).

The WG identified the following major knowledge gaps in the epidemiology of HIV-related CAD: 1) the

ABBREVIATIONS AND ACRONYMS

AIDS = acquired immunodeficiency syndrome

ART = antiretroviral therapy

CAD = coronary artery disease

CV = cardiovascular

HIV = human immunodeficiency virus

HLB = heart, lung, and blood

NHLBI = National Heart, Lung, and Blood Institute

NIH = National Institutes of Health

WG = working group