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Cardiometabolic Disease in the Human Immunodeficiency Virus: The Tip of the Iceberg?

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Infection with the human immunodeficiency virus (HIV), use of highly active antiretroviral drug therapies (HAART), undesirable lifestyle/behavioral choices, genetic background, and other factors all contribute to adverse metabolic and morphometric changes in appreciable numbers of adults and children with HIV. At least in the developed world, HIV/AIDS has transitioned from certain death to a chronic, manageable condition, with the potential for long-term salubrious survival, due to therapeutic advances over the past 10 years.

Many challenges remain, however, as outlined by the articles in this issue of the *Journal of the CardioMetabolic Syndrome (JCMS)*. With longer-term survival, will HIV-infected persons succumb to the causes of death that are most common among aging humans in the industrialized world, especially components of the cardiometabolic syndrome (CMS) (heart disease, stroke, lung disease, diabetes), but at an earlier age? Does HIV infection and the accompanying chronic proinflammatory processes impart increased risk for these most common causes of death? Are there HIV-specific risk factors for CMS? Recent observational data indicate that death from cardiovascular disease, diabetes, non-HIV-related cancer, and drug abuse may be increasing among HIV-infected persons.^{1–5} In addition, socioeconomic and demographic data from the Centers for Disease Control and Prevention suggest that low-income, poorly educated, young minority men and women with poor access to health care constitute a disproportionate percentage of individuals with newly infected HIV.^{6,7} Are these not the same groups in the general population that are at greater risk for developing diabetes, obesity, heart disease, and cancer? Likewise, the HIV epidemic is most serious in resource-limited areas of the world. As these regions become more developed and industrialized, we anticipate a “collision of epidemics” of HIV and CMS, and recent analyses support this notion.⁸ The issues are complex and will require multidisciplinary teams and approaches to resolve them.

The more fundamental questions are left to be resolved by the biomedical scientists (ie, the contributing authors of this issue of *JCMS* and their peers) and include: Are we being alarmist? After all, we only have 10 years of experience with antiretroviral medications. Maybe newer medications and treatment paradigms will have fewer toxicities. What are the underlying mechanisms that link HIV, HAART, lifestyle habits, and genetic predisposition to the development of CMS? Do these mechanisms point us to established or novel therapeutic interventions for CMS in HIV? By studying CMS in HIV, can we learn more about the pathogenesis of CMS in the general population? Are there interactions between the immune and cardiovascular systems that we are overlooking? Can technologic and analytic advances

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(eg, imaging, “omics,” RNA knockdown) help us identify, characterize, or treat the evolving CMS in HIV? How can we develop, test, and implement better screening, monitoring, and treatments for CMS in HIV in all parts of the world? Does the research and knowledge gained about HIV and HAART in developed countries properly inform providers about how to treat and manage HIV-infected individuals in resource-limited regions of the world?

These are all difficult questions. They strongly suggest that research on HIV and CMS must continue to receive support. We propose that research efforts have only scraped the tip of the iceberg. Given our limited experience with HAART and the complexities of HIV replication, combined with our extensive knowledge of the proatherogenic disposition of dyslipidemia, inflammation, visceral adiposity, insulin resistance, poor eating behaviors, and physical inactivity, one can only envision that this is the tip of the iceberg for a future epidemic of CMS in persons with HIV. We hope that scientists and clinicians continue to seek unbiased knowledge and the truth about these issues, and that granting agencies and policymakers appropriately respond to this knowledge.

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