Chronic Respiratory Disease in HIV-Infected Adolescents

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(See the HIV/AIDS Major Article by Ferrand et al, on pages 145–52.)

The study by Ferrand et al in the current issue of *Clinical Infectious Diseases* draws attention to the frequency and severity of lung disease in adolescents with human immunodeficiency virus (HIV) infection [1]. In this clinic-based cohort of adolescents with presumed vertically acquired HIV infection, 86% had clinical evidence of chronic respiratory disease. Nearly half of the participants were hypoxic at rest or minimal exertion, a marker of severe lung disease in the absence of primary cardiac pathology. In addition, this damage occurred in many of the adolescents without severe immunosuppression. More than 40% of adolescents with a CD4 count ≥350 cells/µL had clinical and radiologic evidence of chronic respiratory disease. This highlights the inadequacy of immunological criteria alone as indication for initiating antiretroviral therapy (ART). These data are consistent with reports from the United States regarding preuse of highly active ART, when more than one-third of perinatally HIV-infected children were shown to have chronic lung damage, as indicated by persistent radiologic changes at 4 years of age [2]. Clinicians and program directors involved in the care of HIV-infected children and adolescents should be aware of these data and ensure that clinical care includes careful assessment of respiratory disease and that simple equipment needed for appropriate assessment of respiratory disease is given priority.

Chronic respiratory illness (CRI) is a common problem faced by clinicians working with HIV-infected children and adolescents [3]. Research that investigates the spectrum, severity, and potential preventive and management options has been lacking. Given the substantial number of children and adolescents potentially affected, this has particular public health import in Southern Africa and similarly affected areas [4]. The few published studies of CRI in HIV-infected children describe disease in much younger cohorts and, with the exception of Jeena et al, describe children from high-income settings [2, 5–7]. Southern Africa, a low- and middle-income area with the highest HIV prevalence globally, has a high incidence of many additional factors known to be associated with CRI in children and young adults, such as poverty, overcrowding, exposure to indoor air pollution, and differing infective exposures, most notably tuberculosis. These factors are likely to play a role in the etiology and management strategies for CRI in HIV-infected children living in low- to middle-income areas, hence the value of research from similar settings.

Ferrand et al used high-resolution computed tomography (CT) to more sensitively delineate lung damage in a subset of 56 children. Although chest CT has been used previously in young HIV-infected children with persistent respiratory symptoms, the predominant findings were those of interstitial pneumonitis and tuberculosis [6]. This difference likely reflects the much younger age of the children investigated (mean age, 36 months) who were in an earlier stage of their disease. In addition, the chest CT reporting criteria in this article did not mention mosaic attenuation. In a selected group of HIV-infected children, median age 3.6 years, with subacute and chronic respiratory disease, high-resolution CT findings of mosaic perfusion were reported in children with varying respiratory pathology [8]. The finding of extensive damage to the small and, in many, large airways is not unexpected in the setting of long-standing untreated HIV infection. The pathophysiology of lung damage in HIV-infected adolescents is probably one of recurrent infective and inflammatory insults. Whether from HIV infection itself, intercurrent infections, or abnormal immune responses, the outcome is that of extensive
A statement that ART does not alter respiratory disease progression, as is made in this article, has the potential to undermine the crucial role ART plays in preventing ongoing infections and lung damage and potentially improving chronic respiratory symptoms. From the data presented, one is not able to conclude if ART improves respiratory disease, prevents further damage, or does not halt the relentless progression of respiratory damage, as this was a cross-sectional review of selected children. Moreover, because children in this study were a selected group of adolescent survivors, it is highly probable that those with more severe immunosuppression and HIV disease would have, without access to ART, died before reaching adolescence. ART has been shown to reduce acute respiratory illnesses and hence likely to play a role in preventing ongoing airflow damage [12, 13]. Its role, if any, in improving lung function in the setting of established CRI requires longitudinal follow-up and has yet to be established.

Uptreated pediatric HIV infection can lead to extensive respiratory damage, even in children and adolescents with mild or moderate immunosuppression. Regular assessment of chronic respiratory symptoms and assessment of respiratory function are important in the management of these young people. Respiratory symptom history and examination should be undertaken regularly in all HIV-infected children and adolescents. The diagnosis of HIV infection should be considered in all children who have chronic respiratory symptoms and who live in HIV-endemic areas. ART should be considered in any HIV-infected child with persistent respiratory symptoms irrespective of CD4 count. Future research is needed to assess the role of ART in preventing lung damage and the impact of management strategies such as antimicrobial and anti-inflammatory therapies, immunizations, avoidance of inhaled pollutants, and maximization of growth and nutrition in established lung disease.

Note

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References