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Hot News

The new face of advanced HIV infection

The World Health Organization and UNAIDS estimate that 39 million people were living with HIV by the end of 2022. Only in Sub-Saharan Africa were living at least 26 million. Approximately 1.5 million were children (< 15 years old). Women and girls represented 53%. New HIV infections occurred in 1.3 million people during the previous year. Antiretroviral therapy was taken by nearly 30 million people with HIV (76% of all people with HIV). Overall, 71% of HIV persons were virally suppressed (*https://www.hiv.gov/hiv-basics/overview/data-and-trends/global-statistics/*). These figures are still far from the 95-95-95 goal that pursues having more than 95% of people with HIV diagnosed, more than 95% of them under antiretroviral treatment, and more than 95% of treated patients virologically suppressed.

Approximately 86% of people with HIV knew their HIV status. The remaining 14% (about 5.5 million people) do not know that they have HIV due to lack of access for testing or that they do not consider themselves at risk for HIV infection and fail to be tested. Most of these people are viremic and the major source of new HIV infections.

In the early decades of the global response to HIV/AIDS the focus was on saving lives. However, over the past two decades, attention has shifted to virological control. Treating HIV could not only benefit the infected person but also eliminate transmission. In 2015, two large randomized trials, START and TEMPRANO, showed that antiretroviral treatment should be started as soon as possible after knowing HIV infection. Guidelines adapted soon to the new paradigm. However, an indirect consequence of this major step was that CD4 testing was no longer essential.

In spite of a wider use of antiretroviral therapy, reductions in AIDS-related deaths have been smaller and slower than expected. The proportion of people with advanced HIV disease (defined by a CD4 count < 200 cells/mm^3) remains high. Indeed, it is estimated that more than 4 million people have advanced HIV disease nowadays. Each year more than 600,000 of them are expected to die (*Rajasingham et al. Lancet Infect Dis 2022; 22: 1748-55*).

Until recently, advanced HIV disease was viewed as a problem of late presentation, so the solution was thought to be testing more people and diagnosing the infection earlier. However, in many regions, especially in the Third World, advanced HIV infection is now predominantly seen among people who started care but were not effectively engaged or have disengaged for any reason (*Kaplan et al. PLoS Med 2017; 14: e1002407*), returning only when they are ill. In this regard, we should keep in mind that stopping antiretroviral therapy suddenly may be followed by a precipitous drop in CD4 T-cell counts within the first 2 months (*SMART Study Group. N Eng J Med 2006; 355: 2283-96*).

Although HIV is not a neglected disease, tens of billions of dollars have been invested in scaling up access to prevention and treatment, advanced HIV has become neglected (*Ford et al. N Engl J Med 2024; 390: 487-9*). As global HIV targets have shifted attention on viral suppression, the focus on mortality has diminished. Neglect of advanced HIV disease is an unintended consequence of the global shift in objectives from treating the sickest people to treating all who are infected.

There is a need to continue supporting CD4 testing for diagnosing advanced HIV infection. As in the past, the most frequent opportunistic infections in those presenting with advanced HIV infection after moving off care are tuberculosis, cryptococcal meningitis, cerebral toxoplasmosis, pneumocystis pneumonia, and severe bacterial infections. Furthermore, funding for improving the medical management of those with severe immunodeficiency is warranted. As example, a large trial has started in South Africa to assess whether providing azithromycin to people with severe immunosuppression could reduce mortality from severe bacterial infections. If so, it could be an alternative to cotrimoxazole in those with allergy to sulfamides.

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