HIV related opportunistic infections: still relevant after 25 years of AIDS progress

Joseph Kovacs and Henry Masur

Critical Care Medicine Department. NIH Clinical Center. National Institutes of Health. Bethesda. Maryland. USA.

In 1981, health care providers were introduced to the syndrome now known as HIV/AIDS by a series of articles in Morbidity and Mortality Weekly Report and the New England Journal of Medicine[1-3]. The first decade of HIV/AIDS focused largely on trying to understand the etiology and pathogenesis of this new syndrome, and developing management strategies to improve quality and duration of life for patients with a unique constellation of infectious complications.

During the 1980s, clinicians recognized that certain pathogens such as pneumocystis, toxoplasma, and CMV presented with different manifestations in AIDS patients compared to other immunosuppressed populations. For instance, *Pneumocystis* pneumonia was a much more indolent disease in patients with AIDS compared to solid organ transplant recipients[4]. *Toxoplasma* was much more likely to cause cerebral disease rather than disseminated disease in AIDS patients compared to patients with hematologic malignancies. CMV almost never caused pneumonia, the most feared complication in transplant recipients, but did often cause retinitis, a complication rarely seen in other populations. Thus, clinical syndromes needed to be assessed and described in this unique patient population.

In addition to disease caused by previously recognized pathogens, syndromes occurred that were discovered to be caused by pathogens that had rarely, if ever, been described as causing human disease. Microsporidia, cryptosporidia, JC virus, and *Mycobacterium avium* complex were recognized and quickly became familiar to health care providers.

With the frequency of opportunistic infections came an urgency to develop new diagnostic tests and new therapies. Many clinicians in 2008 may not appreciate the epic recognition that CD4+ T cell counts were useful for predicting the occurrence of opportunistic infections[5]. Many new tests were developed including immunofluorescence for PCP, PCR for CMV, blood cultures for mycobacteria, and staining techniques for microsporidia and cryptosporidia.

These new processes needed new therapeutics. ganciclovir, foscarnet, cidofovir, clindamycin plus pyrimethamine, dapsone, liposomal amphotericin, voriconazole, and clarithromycin were discovered or adapted for therapy and prophylaxis.

As information burgeoned about clinical manifestations, diagnostic tests, new therapeutic agents, and prophylactic strategies, clinicians needed a source that could consolidate and interpret the huge data stream that was being generated. Guidelines were developed to provide clinicians access to the most up-to-date, peer validated material. Guidelines became widely used documents when published in professional society journals or Morbidity and Mortality Weekly Report[6,7]. Online versions became increasingly popular: downloads from the website for US Guidelines exceeded 2 million in 2007 for the antiretroviral guidelines, and exceeded 200,000 for the opportunistic infection prevention and treatment documents. Thus, there was clearly a need for information not being filled by textbooks and journals that these guidelines did fill.

In this issue, the GESIDA and National AIDS Plan Expert Committee have published a new guideline entitled *Treatment of Opportunistic Infections in Adolescents and Adult Patients Infected with Human Immunodeficiency Virus during the Era of Highly Active Antiretroviral Therapy*[8]. This manuscript is comprehensive and authoritative. Its authors and reviewers include some of the most highly recognized authorities in HIV-related opportunistic infections. Several of these authorities, including Drs. Podzamczer, Miro, and Cahn, were called upon to add their expertise to guideline development in other countries including the United States.

Since every geographic region potentially has different environmental issues and exposures, and different host susceptibilities, the range of pathogens may differ. In the United States, for instance, geographic fungi including *Histoplasma*, Coccidiodes, and *Blastomyces* are of concern in specific geographic areas, but these fungi are not endemic in Spain, and thus are of concern only to Spanish patients who have traveled or resided in endemic areas. Conversely, visceral leishmaniasis is not endemic in the United States in contrast to Spain, where disease is endemic in the Mediterranean basin and is occasionally transmitted by needle sharing. Tuberculosis and penicillin resistant pneumococci are more common in Spain compared to the US, requiring more awareness by health care providers in terms of implications for drug selection, drug interactions, and drug toxicities. Some populations may tolerate drugs differently due to differences in physical size, diet, or genetic polymorphisms related to drug metabolism or other issues. These latter considerations are less likely to identify relevant differences between Western Europe and the United States than differences with populations in Asia or Africa.

Region-specific guidelines also serve another important purpose: they make the information available in the language of the region. This is critical since it provides updated management information not only to health-care workers in their primary language, but also to patients

Correspondence: Dr. Henry Masur.
Critical Care Medicine Department.
NIH Clinical Center. National Institutes of Health.
Bethesda. Maryland. USA.
E-mail: hmasur@nih.gov

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who have increasingly become strong advocates for their own health care, and who today have come to expect, thanks to the internet, access to the same information as their medical care providers.

HIV-related opportunistic infections have a strong socioeconomic link in 2008. In medical practices that deal with affluent, educated, mentally stable populations, opportunistic infections rarely occur. Patients are usually recognized to have HIV infection early, before their CD4+ T cell counts fall below 350 cells/μL, patients with low CD4+ T cell counts take their prophylactic drugs as indicated, and patients present to their provider promptly if they have early signs of an infectious complication.

One has only to walk through urban medical centers to see the other face of HIV/AIDS. In that other universe, especially in countries like the United States that do not have universal health insurance, or countries with very limited resources, fulminant PCP, tuberculosis, cryptococcal meningitis, toxoplasmosis, and CMV are a few of the devastating, distressing complications that still occur[8].

In order the reduce the burden of HIV-related opportunistic infections, society must stress routine "opt out" testing, destigmatization in the community, better access to health care, and more emphasis on helping patients learn to adhere to the over two dozen antiretrovirals that we currently have to maintain or restore immunity, and prevent HIV-related opportunistic infections from occurring[9].

While we strive to prevent opportunistic infections from occurring, they inevitably continue to occur. The current guidelines will remain an authoritative and focused resource for providing our patients the most up-to-date care possible. The authors are to be commended for their efforts leading to the publication of these guidelines.

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