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Improving outcomes of cryptococcal meningitis in Sub-Saharan Africa

Cryptococcal meningitis (CM) is a leading cause of death in persons with HIV-infection worldwide and is responsible for 15% of all AIDS deaths. Despite increasing availability of antiretroviral therapy (ART) and anti-fungal therapy, CM mortality remains 50-70% and continues to kill 181,000 people per year, with most deaths occurring in sub-Saharan Africa. An important contributor to mortality in patients with CM is HIV immune reconstitution inflammatory syndrome (IRIS), a frequent and often deadly inflammatory reaction that occurs after patients with advanced AIDS initiate ART due a dysregulated inflammatory response to their infection. IRIS is associated with CM in up to 25% of cases, with manifestations that include increased intracranial pressure, blindness, deafness, cognitive dysfunction, focal neurologic deficits, or death. In patients with CM, delaying initiation of ART until after 6-8 weeks of effective anti-fungal therapy improves mortality compared to immediate initiation of ART. Delaying initiation of ART in patients with CM may prevent development of pathological inflammatory responses associated with IRIS. Biomarker studies evaluating cytokine expression and gene expression in peripheral blood or CSF have shown that the type of immune response mounted by patients with CM

can be useful to predict the development of IRIS or death. Th2 responses, characterized by production of interleukin-4, are associated with increased development of IRIS and death, whereas Th1 response, characterized by high levels of interferon-gamma, are associated with improved outcomes. Immune therapies that promote effective responses in patients with CM might could improve outcomes. A challenge to improving outcomes of CM in sub-Saharan Africa is the lack of infrastructure and resources, and further work is needed to optimize therapies in resource poor settings.

Speaker Biography

Paul R Bohjanen is Director of the Program in Infection and Immunity and Professor of Medicine, Microbiology and Immunology at the University of Minnesota, USA. He is a physician-scientist with a basic science research interest in T cell gene regulation and a clinical interest in HIV infection. He has engaged in collaborative research with the Infectious Diseases Institute at Makerere University in Kampala, Uganda for the past 16 years, with research focused on understanding the pathogenesis of HIV-associated immune reconstitution inflammatory syndrome and cryptococcal meningitis. He is currently working to improve outcomes of cryptococcal meningitis in resource-poor rural settings.

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