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Memories of John Fahey and His Contributions to the Multicenter AIDS Cohort Study (MACS)

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Abstract

John Fahey was an integral member of the small group of investigators who developed the Multicenter AIDS Cohort Study (MACS) in the early 1980s. A major research theme in the MACS was defining immune system changes in men at risk for developing AIDS. John's experience and expertise provided a solid grounding for the immunologic investigations conducted in the MACS. Additionally, he contributed enormously to the science of the MACS and pioneered the critical evaluation of serologic methods of documenting infection with HIV and T cell phenotyping. Perhaps most importantly, John recruited key new investigators to the MACS, and worked closely with the original MACS investigators to create a structure that promoted scientific innovation, openness, and the ability to quickly respond to emerging research themes.

Keywords

AIDS; immunology; natural history

PERSPECTIVES

John Fahey was an integral member of the small group of investigators who met in the fall of 1983 to plan a prospective epidemiologic investigation of the natural history of the acquired immunodeficiency syndrome (AIDS) in men who have sex with men (MSM), which subsequently became known as the Multicenter AIDS Cohort Study (MACS). With Michael Gottlieb and Roger Detels, John had already conducted seminal studies of AIDS in MSM in Los Angeles, which documented the change in CD4/CD8 ratios in men with Kaposi's sarcoma and pneumocystis pneumonia.

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The first six months of the funding period was spent developing the protocol for the visits of the participants and the scientific goals of the MACS; recruitment of participants did not begin until April of 1984. A major component of the investigation focused on the status of the immune system in these men at risk for developing AIDS. As a senior investigator, initially at the NIH and subsequently at UCLA, John's experience and expertise provided a solid grounding for the immunologic investigations to be conducted in the MACS.

John contributed enormously to the science of the MACS in the initial years of the investigation. His laboratory's critical evaluation of serologic methods of documenting infection with HIV and T cell phenotyping enabled the MACS to institute and maintain quality control at the four participating centers. He recruited the late Janis Giorgi to oversee the flow cytometry of peripheral blood mononuclear cells, which was central to the immunologic investigations in the MACS. Janis, in turn, made a number of seminal observations using results from the MACS.[1,2] John also recruited Dr. Oto Martinez-Maza, and Dr. Najib Aziz, who has continued the program assuring quality control and comparability across the four centers of the MACS, a program that was initiated by Janis.

John had quickly realized that the immunodeficiency underlying the susceptibility to opportunistic infections and neoplastic disease was accompanied by activation of the immune system. He presented a plenary talk at the second international AIDS conference in Paris in 1985, discussing dysregulation of immune function of AIDS. Publications from John's group followed these early observations[3] and led to an important series of papers from Dr. Martinez-Maza's laboratory at UCLA delineating the pathogenesis of AIDS non-Hodgkin's lymphoma.[4,5]

At the semiannual meetings of the MACS investigators to assess progress and plan further initiatives, John demanded clear thinking and had little tolerance for anything less. Although John would excoriate sloppy approaches to scientific issues, his personal interactions with colleagues whose thinking he had criticized remained cordial and friendly.

Although John focused later on international AIDS education and research programs, he maintained an interest in the MACS. A prime example of this is found in a short opinion piece[6] that he published on AIDS in 2011, after he retired from UCLA. In this note he describes the drafting of an important contribution of the MACS, which in his words "has had the widest impact"—the documentation of the importance of CD4 cell count of 200/ml or less in the natural history of infection with the human immunodeficiency virus (HIV).[7] He noted that the biostatisticians of the MACS proposed that that the cutoff level for the number of CD4 T cells should reflect a relative risk of developing an opportunistic infection of 5. The cutoff number actually was 186 but because this was an awkward number the CD4 T cell number was reset at 200/ul with no mention of 186. The recalculated relative risk was 4.9. John closes the note by citing Billingham's reflections on the importance of presentation as well as accuracy of scientific data.[8] As Alvaro Muñoz has stated, John was a scholar as well as a critical scientist and in the words of Billingham, setting the cutoff value at 200 cells/ml is an example of "mastering techniques and background knowledge pertinent to a particular problem or field of research and the art of presentation." We, and the science of the MACS, greatly benefited from interacting with John. He was a valued colleague, who

particularly in the early years of the investigation played a seminal role in the formulation and conduct of the MACS.

Acknowledgments

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ABBREVIATIONS

AIDS	acquired immune deficiency syndrome
CD	cluster of differentiation
MACS	Multicenter AIDS Cohort Study
UCLA	University of California, Los Angeles

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