

This Week's Citation Classic®

Gottlieb M S, Schroff R, Schanker H M, Weisman J D, Fan P T, Wolf R A & Saxon A. *Pneumocystis carinii* pneumonia and mucosal candidiasis in previously healthy homosexual men: evidence of a new acquired cellular immunodeficiency. *New Engl. J. Med.* 305:1425-31, 1981. [Div. Clin. Immunol./Allergy and Depts. Med. and Microbiol./Immunol., UCLA Sch. Med.; and Rheumatol. Sect., Wadsworth Med. Ctr., Los Angeles, CA]

In the fall of 1980, four previously healthy homosexual men contracted *Pneumocystis carinii* pneumonia, extensive mucosal candidiasis, and multiple viral infections. In all four, cytomegalovirus was recovered from secretions. Monoclonal-antibody analysis of peripheral-blood T-cell subpopulations revealed virtual elimination of the Leu-3+ helper/inducer subset and increased percentage of the Leu-2+ suppressor subset. [The SCⁱ® indicates that this paper has been cited in more than 1,420 publications.]

AIDS: The Discovery

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In the fall of 1980 I collected several cases of what I thought was a new syndrome. Thinking about publication, early in 1981, I phoned Arnold Relman, editor of the *New England Journal of Medicine (NEJM)*. I spoke with assistant editor Joe Elia and presented a sketch of the new syndrome to him. He quickly put Relman on the phone. I told them I had a story that would be as significant as Legionnaire's disease.

Although I was an unknown assistant professor of medicine from UCLA, Relman was both kind and responsive. He listened to my description of the patients and the T helper cell deficiency we had observed. Since it would take a minimum of three months from the time I submitted an article until it was published, he suggested that I publish a brief article in the Centers for Disease Control *Morbidity and Mortality Weekly Report (MMWR)*. *NEJM* would not view that as "prepublication" and would still consider accepting a more detailed article. He did not promise to publish my paper, but said he'd like to see it. My June 5, 1981, report in the *MMWR* allowed me to alert public health officials and practicing physicians to the new disease and to stake a claim as the "discoverer" of AIDS.

In the *NEJM* paper, I listed as coauthors people who had contributed intellectually or referred patients. In addition to describing AIDS as a new disease, I made three important observations:

(1) A few patients had a profound deficiency of CD₄ helper cells. This deficiency is now recognized as the immunologic hallmark of the

disease. CD₄ cell depletion led virologists to the hypothesis that a T-lymphotrophic virus might be involved. The CD₄ cell count is now used clinically to gauge the severity of damage to the immune system in HIV infection and specific levels are used as set points for starting antiviral drugs and primary prophylaxis against *Pneumocystis* and other opportunistic infections. And today, the Centers for Disease Control defines AIDS as a CD₄ cell count of fewer than 200/cu mm in the presence of HIV antibody.

(2) I suggested that the immune deficiency was potentially transmissible. I reached this conclusion because homosexual men were already known to have a high incidence of sexually transmissible diseases and because signs pointed to a virally mediated cell destruction.

(3) Lastly, I focused on a possible viral etiology. As a longtime student of human immune disorders, I knew that only a virus could wreak this type of damage on an adult immune system.

Because cytomegalovirus (CMV) was cultured from multiple sites, I proposed that it might be causal. This proved to be an error. CMV had been reactivated because of the immune deficiency. However, I also suggested that a previously unrecognized toxin, microbe, or virus might be the culprit.

The release of my *MMWR* article set off an explosion of interest. People began reporting cases of AIDS from New York, San Francisco, and many other cities. Publication of the *NEJM* report on December 10, 1981, changed my life,  it was one of the most heavily quoted publications in the medical literature during the first several years of the epidemic.

Since I described those early cases, I have been continuously involved with clinical research on AIDS and with the care of people in various stages of HIV infection. I authored 50 papers, mostly on clinical aspects of HIV disease, including several other first reports of phenomena associated with AIDS.^{2,3,1} I became active in AIDS causes and was willing to speak candidly with reporters at a time when there were few "experts" on the disease. Despite my record of productivity in clinical research and community service, in 1987 I was denied tenure at UCLA. While deeply disappointed at the time, I have no regrets about my role in bringing AIDS to the attention of the scientific community and the general public.

1. Gottlieb M S, Schanker H M, Fan P T, Saxon A, Weisman J D & Polzalski I. *Pneumocystis pneumonia*—Los Angeles. *Morbidity and Mortality Weekly Rep.* 30:250-2. 1981. (Cited 115 times.)

2. Holland G N, Gottlieb M S, Yee R D, Schanker H M & Pettit T H. Ocular disorders associated with a new severe acquired cellular immunodeficiency syndrome. *Amer. J. Ophthalmol.* 93:393-402, 1982. (Cited 105 times.) 3. Gottlieb M S,

3. Groopman J E, Weinstein W M, Fahey J L & Detels R. The acquired immunodeficiency syndrome. *Ann. Intern. Med.* 99:208-20, 1983. (Cited 345 times.)

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