This Week's Citation Classic®

Siegal F P, Lopez C, Hammer G S, Brown A E, Kornfeld S J, Gold J, Hassett J, Hirschman S Z, Cunningham-Rundles C, Adelsberg B R, Parham D M, Siegal M, Cunningham-Rundles S & Armstrong D. Severe acquired immunodeficiency in male homosexuals, manifested by chronic perianal ulcerative herpes simplex lesions. *N. Engl. J. Med.* 305:1439-44, 1981.

[Mt. Sinai Sch. Med., City Univ. New York; and Memorial Sloan-Kettering Cancer Ctr., New York, NY]

This report described a previously unrecognized severe acquired immunodeficiency disorder. Although unremitting herpes lesions brought these patients to us, their illnesses were in all other respects characteristic of what the world has come to know as AIDS. [The *SCI*® indicates that this paper has been cited in more than 840 publications.]

The Recognition of AIDS

Frederick P. Siegal
Long Island Jewish Medical Center
Albert Einstein College of Medicine
New Hyde Park, NY 11024

I had been working in the obscure field of adult immunodeficiencies for about 10 years by the spring of 1980, when Bernard Adelsberg consulted me about a male nurse with *Pneumocystis carinii* pneumonia (PCP). My lab investigation revealed the surprising and initially inscrutable result that the patient had almost no Leu-3a+ T cells, as measured by the then brand-new antibody of Robert Evans. I thought this unique case ought to be published, but Bernie was not so impressed. That June, I saw a young gay man whose strange perianal ulcer had correctly been recognized as chronic herpes simplex infection, which Shalom Hirschman knew to be unique to people with compromised host defenses. I set about documenting the features of his severe cellular immunodeficiency state. I mentioned this bizarre case to Donald Armstrong, who, it happened, had treated a very ill patient with virtually the same manifestations. Soon I had collected two more examples. I urged each of my immunology fellows to submit a case description. Still, no one seemed enthusiastic. We were, then, not the only people in New York encountering such curiosities; the infectious disease community was abuzz. Finally, in June, I decided to write it up myself, before everyone in the US could do so. Shortly after our manuscript's submission, Michael Gottlieb's report of PCP in gay men in California was published in *Morbidity and Mortality Weekly Report*; but complete papers by my group (*vide supra*) and others,[1,2] however, did not appear until six months later, when they were published back-to-back in the *New England Journal of Medicine*.

With the explosive growth both of worldwide cases and of AIDS literature, it is easy to see why the description of AIDS should have become a *Citation Classic*®. The epidemic heralded by these papers spawned at least five specialty journals, five to six established (and many ad hoc) NIH Study Sections, half a score of newly approved drugs, a huge and sometimes unwieldy clinical drug trials network, unprecedented disease-specific, highly vocal activist groups, and an imbroglio over credit (and patent rights) for the causative agent. Biotechnology companies have reaped incredible financial successes or speculative failures as a result of the epidemic. And this nightmare pandemic has become a political monstrosity, with social agendas too often preempting public health priorities. The world has failed to contain the spread of HIV infection, partly because of a lethal combination of disbelief, denial, delaying tactics, dogmatism, and deliberate distortion.

A combination of fascination with the immunobiology of HIV infection and horror at its human toll has kept me engaged and struggling with the clinical and research aspects of AIDS, despite a powerful impetus for burnout. AIDS suggests the existence of an alternative pathway of cellular immunity, as hypothesized in one of the literature's (undeservedly) least-cited papers.[3] Clinical observation of the associated morbidity clarified the need for newer preventative therapies.[4] The book I wrote with my wife, Marta, in 1983 became a primer for many destined to work in the area.[5] Jonas Salk, who kindly contributed its foreword, has become directly involved in the AIDS epidemic through his efforts in vaccine development.

1. **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. *N. Engl. J. Med.* 305:1425-31, 1981. (Cited 1,445 times.) [See also: **Gottlieb M S.** AIDS: the discovery. Citation Classic®. *Current Contents®/Clinical Medicine* 21(30):8, 26 July 1993.]
2. **Masur H, Michelis M A, Greene J B, Onorato I, Vande Stouwe R A, Holzman R S, Wormser G, Brettman L, Lange M, Murray H W & Cunningham-Rundles S.** An outbreak of community-acquired *Pneumocystis carinii* pneumonia: initial manifestation of cellular immune dysfunction. *N. Engl. J. Med.* 305:1431-8, 1981. (Cited 930 times.)
3. **Siegal F P, Lopez C, Fitzgerald P A, Shah K, Baron P, Leiderman I Z, Imperato D & Landesman S H.** Opportunistic infections in acquired immune deficiency syndrome result from synergistic defects of both the natural and adaptive components of cellular immunity. *J. Clin. Invest.* 78:115-23, 1986. (Cited 35 times.)
4. **Nightingale S D, Cameron W D, Gordin F M, Sullam P M, Cohn D L, Chaisson E R, Eron L J, Sparti P D, Bihari B, Kaufman D L, Stern J J, Pearce D D, Weinberg W G, LaMarca A & Siegal F P.** Two placebo controlled trials of rifabutin prophylaxis against *Mycobacterium avium* complex infection in AIDS patients. *N. Engl. J. Med.* 329(12):828-33, 16 September 1993.
5. **Siegal F P & Siegal M.** *AIDS: the medical mystery.* New York: Grove Press, 1983. 196 p.

Received November 9, 1993