This Week's Citation Classic

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This paper reviewed the current oncogenic literature on the immunodepressive effects of viruses. The spectrum of experimental data was summarized in light of current knowledge of the function of the immune system. The pathophysiology of the immunodepression was highlighted, and special emphasis was placed on the relevance of the immunodepressive effects of virus infection to the process of oncogenesis. [The SCI® indicates that this paper has been cited in over 215 publications.]

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In 1964 I joined Robert A. Good's immunology group in the Department of Pediatrics at the University of Minnesota fresh from completing two years of pediatric residency training in Toronto. I had realized that primary care pediatrics was not my calling and that immunology was a new and exciting field of subspecialization that would satisfy my academic appetite. Having been disdainfully rejected as a naive clinician by the basic biologists at the Princess Margaret Hospital at the University of Toronto, I was warmly received into Good's group as an independently funded fellow along with five other ambitious but also naive trainees.

This was the heyday of the National Institutes of Health training grants and ready availability of operating funds, and nothing seemed impossible. I was assigned to work under Raymond Peterson, a junior faculty member, career scientist, and close colleague and protege of Good. He had already been asking important questions about the relevance of immunogenesis to oncogenesis and had shown that mice destined to die of thymic leukemia as a result of neonatal injection of Gross virus were deficient in antibody production. My task was to see if cell-mediated immunity was also affected, particularly as Gross leukemia is what we now would call a T-cell neoplasm. My first experiment, which involved learning anesthe sia, plastic surgery, intensive care, and long-term follow-up in mice, was a resounding success, assuring my election to membership in the American Society for Experimental Pathology and subsequently being published in the Proceedings of the Society for Experimental Biology and Medicine.

I went on to study various other aspects of the effects of viruses on the immune system; however, none of these observations led to conceptual breakthroughs. As a final attempt to look for a meaningful focus in this field of research, and much to the chagrin of my young family, whose recreational needs took second place, I devoted a summer holiday in 1971 to the writing of this review. It turned out to be a thorough and complete analysis of all the available data on the subject. I believe it has been widely cited not because it was the first or only review of its kind on this subject, but because it contained a careful integration of the experimental data with rapidly unfolding developments in immunobiology. That it was not just a mindless and encyclopedic compilation of facts is a tribute to the truly creative environment that characterized Good's laboratory.

This review appeared some 10 years before the emergence of the quintessential immunodepressive virus, HIV. It was a state-of-the-art reference, hinting perhaps at the potential of research in the area of virus-induced immunodepression but not illuminating the future sufficiently to prevent me from leaving the field. Principles of virus-induced immunosuppression were recently reviewed by Michael B. McChesney and Michael B.A. Oldstone.1

I received no awards for this article or related work. I have, however, benefited immensely from the intellectual stimulation and personal friendships and contacts that were part of the overall experience of research in this area. I have derived great pleasure from knowing that this review has been designated a Citation Classic.