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The prevalence of autoimmune hemolytic anemia and diffuse connective tissue diseases was studied in 2,183 patients with solid tumors and malignant lymphomas and found to be significantly higher in the malignant lymphoma group. There was no evidence to suggest that one disease influenced the other. It was concluded that the same patient had an underlying susceptibility to both disorders. [The SC¹⁹ indicates that this paper has been cited in over 245 publications since 1967.]

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There were three circumstances that led to the writing of this paper. The first was the presence of two competing theories, current at that time, regarding the association of these disorders. In 1959, Macfarlane Burnet published a monograph, *The clonal selection theory of acquired immunity*.¹ In this monograph, he proposed that lymphoproliferative disorders resulted from a proliferation of "forbidden clones" of lymphocytes and that the occurrence of immune disorders was a reflection of the physiological function of the proliferating lymphocyte clone. In the same year, Dameshek and Schwartz published a paper suggesting that continual stimulation of the immune system led to lymphoproliferative disorders.² The second circumstance was the large caseload at the Lymphoma Clinic at Memorial Sloan-Kettering Cancer Center, which provided an opportunity to study these possibilities.

David Karnofsky, then chief of cancer chemotherapy, had been advocating the

study of the natural history of cancer as a more heuristic endeavor than the usual practice of staging of disease. To that end, all the members of his service, I among them, worked on a program of recording the natural history of cancer, site by site, from diagnosis to death, in a structured manner. The information so acquired provided the basis for determining the statistical significance of the association of immune disorders with various forms of neoplasia. The third circumstance that led to the writing of this article was my personal interest in immunology, stimulated at first by Ernest Witebsky at the University of Buffalo, then by Pierre Grabar at the Pasteur Institute. This interest found its expression in studies that I carried out concerning disturbances of the immune system in patients with malignant lymphomas. My ability to conduct such studies was greatly enhanced by my association with an outstanding immunologist at the Sloan-Kettering Institute, Leonhard Korngold.

I believe the publication has been so widely cited because, for the first time, it established a statistically significant basis for what had previously been an impression; i.e., that immune disturbances occur in patients with lymphoproliferative neoplasms with greater frequency than in patients with solid tumors. The other aspect of this paper, the significance of this association, has not been widely discussed in the papers in which this article has been cited. The conclusion was that immune disturbances occurred in these patients because of an underlying abnormality in the immune system that made them susceptible to both disorders. However, for me, this represented a significant turning point in my career since it led to studies of the nature of susceptibility to cancer, which research I am actively engaged in today.

For more recent work in the field, see reference 3.

1. Burnet F M. *The clonal selection theory of acquired immunity*. Nashville, TN: Vanderbilt University Press, 1959. 209 p. (Cited 1,100 times.)
2. Dameshek W & Schwartz R S. Leukemia and auto-immunization—some possible relationships. *Blood* 14:1151-8, 1959. (Cited 90 times.)
3. Chu J Y. Autoimmune hemolytic anemia in childhood Hodgkin's disease. *Amer. J. Pediat. Hematol. Oncol.* 4:125-8, 1982.