This paper was the first to relate the development of malignant lymphoma to an antecedent Sjögren's syndrome (SS). The lymphoma was either undifferentiated or associated with macroglobulinemia. We hypothesized that autoimmunity and lymphoproliferation were predisposing to malignant transformation. [The SC indicates that this paper has been cited in over 245 publications since 1964.]

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"Shortly after taking up my clinical associate position at the National Institute of Arthritis and Metabolic Diseases (NIAMRD) in the summer of 1962, I recall making rounds with the late Joseph Bunim. Bunim introduced me to a patient with Sjögren's syndrome (SS) of eight years duration who had developed malignant lymphoma diagnosed as reticulum cell sarcoma six months previously. I suggested to Bunim that the development of a lymphoid neoplasm in a patient with autoimmunity might imply a causal relationship. To my surprise, he informed me that he was following several other patients with SS who also had developed lymphoid malignancy.

"I was fascinated and began to review the charts and examine these other patients. I obtained serial serum samples and studied them by immunoelectrophoresis, a technique developed by Pierre Grabar that I had learned in France the year before. I observed that an initial hypergammaglobulinemia with high titers of autoantibodies progressively declined to hypogammaglobulinemia and loss of autoantibodies. Another patient had macroglobulinemia. Thus, we reported this series suggesting that autoimmunity predisposed to lymphoma which could take one of two forms, either undifferentiated or associated with IgM production (then called 

"I believe this publication has been highly cited because it was the first to associate two disorders of immunoregulation, autoimmunity with the subsequent development of lymphoma. Future work should help explain exactly how the underlying autoimmune process may contribute to a neoplastic transformation of cells involved in that process. The original designation of 'reticulum cell sarcoma' was a misnomer for we now know on the basis of immunohistologic studies and most recently chromosomal gene rearrangement studies that the malignant cell belongs to the B-cell lineage.

"Honors received for this paper and my subsequent studies on immune dysregulation and autoimmunity in patients and inbred strains of mice include the Hench Award (1975) and the Middleton Award (1980) presented by the US Veterans Administration."