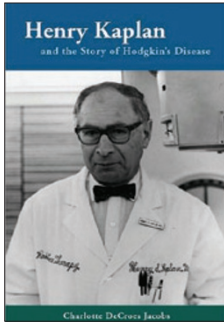


## A passion to cure cancer



### Henry Kaplan and the Story of Hodgkin's Disease

Charlotte Jacobs

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Reviewed by Anton Hagenbeek

Henry Seymour Kaplan (1918–1984) was a pioneer in the field of cancer research. This biography, written by Charlotte Jacobs, professor of Medicine in the Division of Oncology at Stanford University School of Medicine, describes his major achievements in the fight against Hodgkin's lymphoma over almost 65 years, but it also touches upon the man he was in relation to his family and peers. The fact that Hodgkin's lymphoma, a cancer arising in lymph nodes, seemed to be the first curable human malignancy makes this journey all the more exciting. Jacobs based the biography on hours of interviews and correspondence with people that worked closely with Kaplan within the US.

In 1943, Kaplan began training in diagnostic radiology in Minneapolis, spending nights and weekends learning basic skills in cancer biology and applying these to his first studies on the induction of leukemia in mice by radiation. With his first academic appointment at Yale University in 1945, he got his own laboratory and a budget of \$300 a year for his mice. At that time, it was already clear that Kaplan had a passionate desire to cure cancer. After he became a leading scientist at the US National Cancer Institute in Bethesda, Maryland, Kaplan was appointed Chairman of Radiology at Stanford University in 1948.

In the years to follow, he was responsible for moving the first linear accelerator from the lab to the clinic and started to irradiate patients in 1956, with special emphasis on patients with Hodgkin's lymphoma. Kaplan realized that he needed a team of experts to cure his patients: a pathologist to come up with the diagnosis, a surgeon to perform a so-called staging laparotomy (called by some a 'living autopsy') during which the spleen and a number of lymph nodes are removed from the abdomen, a radiologist to aid in lymph nodes visualization through lymphangiography and, later on, an oncologist to introduce chemotherapy. For this he hired Saul Rosenberg in 1961.

Kaplan initiated the first randomized clinical trial in Hodgkin's lymphoma in 1962. The trial compared radiation doses, resulting in a step-by-step increase in cure rate. Rosenberg, however, was opposed to aggressive treatments, so Kaplan openly criticized him. This soured the relationship between these two pioneering researchers.

In 1967, a study by Vincent de Vita reported that a combination

chemotherapy called MOPP could achieve a 90% complete remission rate for advanced Hodgkin's lymphoma. Because of this, Kaplan included MOPP in his next randomized trial in 1968, comparing radiation alone with radiation plus MOPP. With the combined treatment, 86% disease-free survival was achieved in patients with advanced disease. Again, Rosenberg worried about potential morbidity and late effects, but Kaplan insisted on aggressive treatment of the disease.

In the meantime, Kaplan pursued his laboratory studies focusing on detecting a virus that might cause Hodgkin's lymphoma, collaborating with Robert Gallo from the National Cancer Institute on isolating the malignant cell in Hodgkin's lymphoma and on developing monoclonal antibodies ('magic bullets') against lymphoma. However, these three programs failed.

One of the major disappointments in his professional career was that he failed to establish a Comprehensive Cancer Center at Stanford after the US National Cancer Act came into effect in 1971. This initiative was blocked by other department heads, who did not want Kaplan to be too much in control, revealing the tense relationships between Kaplan and his peers. He blamed Rosenberg for this failure, which made him very bitter, causing him to withdraw into his research lab.

In the 1970s, the formation of secondary tumors in patients previously treated with radio- and chemotherapy became apparent. Kaplan admitted this after carefully checking Stanford patients that had finished treatment. Therefore, in the early 1980s, a new chemotherapy regimen called ABVD was introduced by Gianni Bonadonna from Milano that appeared to be much less toxic than the original MOPP regimen. Even today, ABVD is recognized worldwide as the first-choice chemotherapy regimen.

During the last years of his career, Kaplan focused on reducing radiation doses and fields, to prevent late effects. Despite his achievements and recognition as one of the pioneers in developing curative treatments for Hodgkin's lymphoma, at the end he felt that he had failed to answer his major question on the cause of Hodgkin's lymphoma and to determine ways to prevent it.

A considerable part of the book is devoted to Kaplan's personal life. Although he married and had children, he was never at home. His wife called his lab his mistress, and he failed to recognize his children's needs, eventually becoming estranged from them. In the Kaplan family, achievement was presumed; no one spoke of failure. Problems were not discussed, only solutions. Among his peers, Kaplan was called a saint by some and a son of a bitch by others; he always had the last word, and he could be disrespectful to colleagues. He had few real friends. During the last weeks of his life, after he was diagnosed with lung cancer, possibly due to prolonged inhalation of radioactive radon gas in the early years, he again became close to his family.

This biography deals with an extraordinary man who was instrumental in developing curative treatment strategies for Hodgkin's lymphoma. Jacobs has provided a superb overview, although most of the stories are limited to Stanford and the US. This is a weak aspect of the book, which could have instead been situated in a more global environment. Nevertheless, I strongly recommend this biography to anyone interested in following the stormy journey of a true pioneer in medicine.

#### COMPETING FINANCIAL INTERESTS

The author declares no competing financial interests.

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