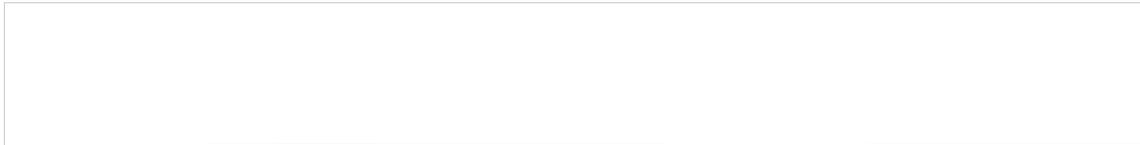


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With the Goal of Curing Cancer, Ezra M. Greenspan, MD, Helped Usher in the Modern Era of Chemotherapy

By Jo Cavallo
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Ezra M. Greenspan, MD Courtesy of Chemotherapy Foundation Symposium.

“ He was there at the real beginning of the translation of laboratory models of cancer into clinical practice. He was one of the authors in the early days of really important papers to show what kinds of drugs would shrink tumors and how they should be given.

—Larry Norton, MD

Two events in **Ezra M. Greenspan’s** early adult life convinced him to pursue a career in medicine: the death of a college friend from pneumonia when the two were students at Cornell University College of Arts and Sciences and his own bout with the disease soon after.

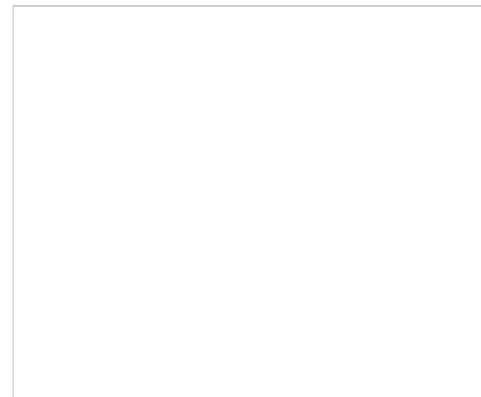
Saved by a local physician who prescribed Prontosil (sulfamidochrysoidine, the first commercially available antibacterial agent), the experience made a lasting impression of the power of drugs to cure disease and sewed the seeds of the potential of chemotherapy.

Early Career

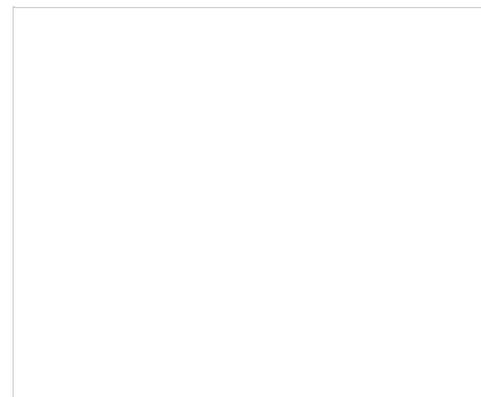
Born in Brooklyn on April 4, 1919, Dr. Greenspan did not stray far from his birthplace, spending most of his 5-decade-long medical career in New York. After graduating from New York

University School of Medicine in 1942, he was accepted into the House Training program at Mount Sinai Hospital. Under the tutelage of Isidore Snapper, MD, who was investigating the therapeutic effects of stilbamidine in multiple myeloma patients, Dr.

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Greenspan began his lifelong interest in investigating new therapies for the treatment of cancer.

A year after finishing his residency at Mount Sinai, Dr. Greenspan became Head of the Tumor Service at Walter Reed Army Hospital, where he discovered that soldiers with lymphomas and germ cell tumors could benefit from treatment with a combination of nitrogen mustard and radiation therapy. After completing his military service in 1948, Dr. Greenspan was named to head the fledgling chemotherapy unit at the National Cancer Institute (NCI).

It was there that Dr. Greenspan and his colleagues used mouse models to demonstrate the effectiveness of combination chemotherapy in the treatment of cancer. He also discovered that the lack of certain enzymes in the mice increased their susceptibility to drug toxicity and found that giving them folic acid before chemotherapy reduced their toxicity levels. Several of his other early laboratory efforts at the NCI led to the development of pharmacogenetics—the use of genetic information to identify the right drug for each patient—and cancer tumor markers.

No Magic Bullet

After leaving the NCI in 1952, Dr. Greenspan returned to Mount Sinai Hospital as an attending physician and continued his research in serum biomarkers to guide chemotherapy treatment. He also investigated the effectiveness of combining chemotherapies to treat solid tumor cancers and developed the combination of thiotepa and methotrexate in the treatment of breast and ovarian cancers.

But not all of Dr. Greenspan's colleagues applauded his efforts, fearing that the toxic mix of chemicals would not be good for patients. According to the book *This House of Noble Deeds: The Mount Sinai Hospital, 1852-2002*, Dr. Greenspan's contribution to cancer care "was in showing that there was no one magic bullet but that, by using combinations of drugs, clinicians could make significant gains in the treatment of cancer.... The premise of using combinations of potentially toxic chemicals to treat cancer was not greeted enthusiastically by the medical community...."

Undeterred, Dr. Greenspan persisted in his research, publishing his studies of thiotepa and methotrexate to treat advanced ovarian cancer and advanced breast cancer in the *Journal of the Mount Sinai Hospital* in the early 1960s.

According to *This House of Noble Deeds*, traditional medical journals would not accept Dr. Greenspan's research for publication. "He was fortunate.... Mount Sinai allowed him to continue his efforts, even though, early on, few understood the value of his work or the science behind it," wrote the authors.

Dr. Greenspan's long-time administrative assistant Jaclyn Silverman concurs. "He would turn in his research studies to the *Annals of Internal Medicine* and get back comments like 'He's not treating cancer,' or 'This treatment is much too difficult for patients,'" said Ms. Silverman, now the Chemotherapy Foundation Symposium Management Director at Mount Sinai Medical Center. "He was always a controversial figure because of his theories about combination chemotherapy."

Chemotherapy Foundation

In 1968, when medical oncology was still a developing specialty, Dr. Greenspan launched the Chemotherapy Foundation to fund innovative cancer research and served as its Chairman and Medical Director for over 3 decades. Four years later, Dr.

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Greenspan founded the Chemotherapy Foundation Symposium, the educational arm of the Chemotherapy Foundation, to provide a forum for clinical investigators to present studies of new chemotherapy agents proving effective in the treatment of cancer. That first symposium attracted 100 oncologists who were introduced to the emerging field of cancer immunotherapy. Today, the conference attracts nearly 2,000 oncologists and other oncology professionals from around the world and the mission is the same: to advance cancer care to improve patient outcomes.

After retiring as Clinical Professor of Medicine at Mount Sinai School of Medicine in 2001, Dr. Greenspan continued his work at the Chemotherapy Foundation until his death on September 3, 2004, at the age of 85. Although he suffered from crippling osteoporosis, Dr. Greenspan attended the Chemotherapy Foundation's 21st Annual Symposium in 2003 and was honored for his lifelong achievements during a breast cancer session titled "Adjuvant Therapy: Trailblazers and Milestones."

The following year, just 2 months after his death, Dr. Greenspan's friends and colleagues, including Larry Norton, MD, Deputy Physician-in-Chief for Breast Cancer Programs and Medical Director of the Evelyn H. Lauder Breast Center at Memorial Sloan-Kettering Cancer Center, New York, paid tribute to Dr. Greenspan's career in a video, *Talking About Ezra*, shown at the 2004 Symposium.

"He was there at the real beginning of the translation of laboratory models of cancer into clinical practice. He was one of the authors in the early days of really important papers to show what kinds of drugs would shrink tumors and how they should be given.... Scheduling was very important to him, dosing was very important to him. And the idea of combining drugs properly in combinations so you don't reduce the dosages of the various components was very important to him. And this just didn't come as a vision. This came because he had the laboratory expertise in the early days to motivate him ... to prove to himself that these things would work. And he translated those ideas to the clinic," said Dr. Norton.

Lasting Legacy

To acknowledge Dr. Greenspan's achievements, in 1982, the Mount Sinai Alumni presented Dr. Greenspan with its most coveted award, the Jacobi Medallion, for extraordinary service to the alumni. In 1997, Mount Sinai established the Ezra M. Greenspan Chair in Clinical Cancer Therapeutics in his honor.

Dr. Greenspan was an early supporter of ASCO after its founding in 1964 and a member of the American Association for Cancer Research and the New York Cancer Society.

He and his first wife, Ann, had three children—Karen, Ellen, and David. ■

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