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Part III: Clinical Departments and Divisions --- Chapter 16: Division of Medical Oncology (pages 362-368)

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CHAPTER SIXTEEN

Division of Medical Oncology

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"While there are several chronic diseases more destructive to life than cancer, none is more feared."

—CHARLES H. MAYO (1865–1939)

ALTHOUGH medical oncology was first officially recognized as a medical subspecialty by the American Board of Internal Medicine in 1972, a formal Division of Medical Oncology in the Department of Medicine at Jefferson had been established since 1961. The first Director (1961–1970) was Arthur Weiss, M.D. (Figure 16-1), and the second (1970–1980) was Chester Southam, M.D. (Figure 16-2). Acting Directors were William E. Delaney, M.D. (Jefferson, 1953; 1980–1981), and J. Frederick Laucius, M.D. (Jefferson, 1967; 1981–1984). The third Director is Michael J. Mastrangelo, M.D., appointed in 1984.

The major activities of the Division since its inception have been patient care, teaching, research, and the training of medical oncology Fellows. Among the latter, the first Fellows were Laird Jackson, M.D., who was the first National Institutes of Health Postdoctoral Fellow (1961–1962), and Harvey Brodovsky, M.D. (1961–1963). Several additional Fellows have served in the Division since that time, most notably Carla Goepf, M.D. (Figure 16-3), (1965–1967), who became Associate Dean of Student Affairs and Director of the Office of Student Counseling and Career Planning, and Michael J. Mastrangelo, M.D. (1968–1970). Significant accomplishments in cancer care, research, and teaching at Jefferson occurred in the years before the establishment of the Division.

The Tumor Clinic and Elizabeth Storck Kraemer Foundation

The Tumor Clinic was informally begun in 1928 and has continued since that date as the major institutional follow-up mechanism for cancer patients. Formal establishment began in the fall of 1929 when, through the auspices of William H. Kraemer, M.D. (Figure 16-4, Jefferson, 1906),
Associate Professor of Surgery, a grant received from Mr. Pierre S. DuPont, consisting initially of $35,000 plus $10,000 annually for five years, was augmented by an initial grant of $15,000 for one year from Mr. Lammot DuPont. Through an additional 30 years (1934–1964), Pierre DuPont provided the sole support of Jefferson’s Tumor Clinic through annual grants from the Longwood foundation to the Elizabeth Storck Kraemer Foundation.

All of the Department Chairmen have served as Attending Physicians or Surgeons in the Tumor Clinic. Outstanding contributors to the activity of the Tumor Clinic over the years have been Drs. James M. Surver (Assistant Professor of Surgery), Harry J. Knowles (Assistant Professor of Surgery), and Gerald J. Marks (Professor of Surgery), who directed the day-to-day activities of the staff.

The Tumor Registry began as an offshoot of the Tumor Clinic in June, 1959. From that time through December 1983, as many as 28,593 patients have been accessioned, and 19,139 patients are known to have died. By June 1984, as many as 9,973 patients were under active follow-up, a rate of 92.3 percent. This Registry is the resource for all professionals interested in follow-up data over the years for Jefferson’s oncology activities. Its overall direction is through the Cancer Committee of the Hospital.

The other major activity of the Elizabeth Storck Kraemer Foundation was to provide an investigative arm for the development of new cancer treatment drugs that had been isolated or synthesized by chemists of the DuPont Company. Dr. Kraemer died in March, 1962, and on December 31, 1964, the Foundation was dissolved. For nearly 35 years it had actively supported not only the Tumor Clinic and weekly Tumor Clinic conferences but also chemical research at the DuPont experimental station in Wilmington.
Delaware, and biological research conducted by the Department of Pathology under the supervision of Dr. Peter A. Herbut. Dr. Herbut was Director of the Biological Division of the Foundation, incorporated from September, 1946, to December 31, 1964, on a stipend of $200 a month payable by the Tumor Clinic. Dr. Kraemer was Director of Research from 1929 until his death. The funding after 1964 came through the Hospital budget.

The first publication from the Foundation appeared in 1931 and was a preliminary report on colloidal lead phosphate with manganese as an anticarcinogenic agent. In subsequent years the Foundation was responsible for 22 publications in experimental cancer by Dr. Herbut, 14 of which were coauthored with Dr. Kraemer. In a 1955 article, Herbut and Kraemer stated that the Walker Rat Mammary Carcinoma 256 had been carried in their laboratory since 1936. Dr. Kraemer’s cancer research was recognized formally by his Jefferson alma mater in the award of an Honorary Degree of Doctor of Science at graduation on June 16, 1961.

William H. Kraemer (born 1879) came to the United States as a boy from Germany. The family settled in West Virginia where he learned frugality and a proper set of values. He was trained as a pharmacist, and his application to Jefferson was accepted on the basis of his pharmacy credits. He worked at pharmacies during medical school and graduated in 1906. While working as a physician with the DuPont Company, he began to experiment on cancer in his garage using rats he caught there.

In 1926 Dr. Kraemer attracted the attention of Pierre S. DuPont, who requested his treatment for a leg ulcer that DuPont attributed to a kick by John J. Raskob intended to keep him awake during a General Motors Corporation board meeting. Dr. Kraemer had x-rays taken of DuPont’s teeth out of desperation because he had

Fig. 16-3. Carla Goepp, M.D.

Fig. 16-4. William H. Kraemer, M.D.
found nothing systemically to account for the poor healing. The film revealed two abscessed wisdom teeth on each side, which Kraemer believed to have contributed to DuPont's somnolence. He immediately brought his patient to Jefferson, and taking a hospital room next to DuPont for himself, began to take care of all his health needs, including extraction of the teeth. Although the mandible was fractured in the extraction of the teeth, rendering DuPont speechless for a time, DuPont was grateful because his somnolence completely disappeared. While recuperating, DuPont communicated with Dr. Kraemer by written notes. In one of them he asked: "What is this I hear about your experimenting with cancer in the garage?" Dr. Kraemer told him about it and suggested that DuPont Company's vast chemical expertise be used to develop cancer chemotherapy.

In addition to personal physician, Dr. Kraemer became a friend and confidant. He played golf with DuPont, went on trips with him, and with Mrs. Kraemer moved to the DuPont area. Mr DuPont put him on a lifetime retainer of $6,000 per year and gave Mrs. Kraemer $5,000 per year for life. He also set up the Elizabeth Storck Kraemer Memorial Foundation in honor of Dr. Kraemer's second wife, who died of cancer.

In the early years, the biological aspect was carried out in New York's Memorial Hospital for Cancer, through Dr. James Ewing and later at New York University by Dr. Robert Chambers. In the mid-1940s, following Dr. Chamber's death, biological studies were centered at Jefferson. The chemical division of the Elizabeth Storck Kraemer Memorial Foundation was headquartered in the experimental station in Wilmington, Delaware. By December 3, 1959, the Foundation had completed its thirty-first year of activity, and during that time 4,000 chemicals had been screened for antitumor activity and 1,000 cancer patients had received chemotherapy. After the 1964 termination of the research support, the Trustees of the Foundation granted $24,650 to Jefferson Medical College for research at Dr. Herbut's discretion. As an outgrowth of the research activities that had been supported by the Kraemer Foundation, a National Institutes of Health grant award to Dr. Herbut was renewed for three years in 1965.

The Interdepartmental Endocrine and Cancer Research Group

The relationship between Drs. Abraham Cantarow (Biochemistry), Karl E. Paschkis (Medicine) (Figure 16-5), and Abraham E. Rakoff (Obstetrics and Gynecology) led to their formation of an informal endocrine and cancer research group in 1940. In 1945, at the close of World War II, they began to contribute significantly to the literature, and by 1959 they had realized more than 300 publications. The Board of Trustees in 1948 formally organized the Endocrine and Cancer Research Group with Dr. Paschkis as the first and only Director. He was the unique catalyst who was involved in all activities of the group. It received partial funding by the American Cancer Society on the recommendation of the Committee on Growth of the National Research Council and by the National Cancer Institute.

In the field of steroid hormone metabolism they originated the concept of the biliary excretion and enterohepatic circulation of estrogens and androgens. They first showed that androgens accelerated the development of malignant hepatomas when the carcinogen 2-acetylaminofluorine (AAF) was fed to rats and that thiouracil given with this chemical protected the liver exposed to testosterone; in addition, they first demonstrated the enhancement of the carcinogenic action of progesterone on the breasts of rats treated with AAF. Their work on pyrimidine metabolism as related to normal growth of malignant tumors led to the synthesis by Charles
Heidelberg, Ph.D., at the University of Wisconsin, of 5-fluorouracil, a drug widely used in many cancer chemotherapy programs. Their research further indicated that in the presence of regenerating liver, not only tumor growth but also a large variety of nonmalignant growth processes were stimulated; similar effects could be obtained by injection of certain liver fractions. Another basic investigation was the transmission of tumor by subcellular units. Thus, injection of isolated tumor chromatin induced tumor growth in recipient animals. The effect was noted to be specific in that chromatin from malignant lymphoma cells induced malignant lymphoma after subcutaneous injection and chromatin from hepatoma cells induced hepatomas after intrahepatic injection.

Dr. Paschkis faced his own terminal illness from bronchogenic carcinoma with composed heroism. With his death of January 27, 1961, at age 65, the Endocrine and Cancer Research Group ceased to function as a unit and was dissolved.

Cooperative Cancer Therapy Groups

Among the earliest investigators cooperating with other institutions in the evaluation of new drugs for the management of cancer, Arthur Weiss, M.D., Assistant Professor of Medicine, was the leader at Jefferson since 1958, when he established the Jefferson branch of the Clinical Drug Evaluation Program of the Cancer Chemotherapy National Service Center, a subsidiary of the National Cancer Institute. In 1960, Dr. Weiss also led Jefferson into the Central Oncology Group as a cochairman of that body. In addition, in 1960, Farid Haurani, M.D., became the representative at Jefferson of the Cancer and Acute Leukemia Group B in an association that lasted through 1981. Eastern Cooperative Oncology Group participation has been continuous since 1968 at Jefferson under the direction of Harvey Brodovsky, M.D. He has been a coauthor of 17 papers published on ECOG trials and was a grant recipient of ECOG funding for many years until 1981.

A significant contribution to the use of adriamycin in chemotherapy occurred when the Cooperative Group, with Arthur Weiss, M.D., as the senior author and R. William Manthei, Ph.D., Professor of Pharmacology, as coauthor, reported the decrease in cardiac toxicity of low-dose infusions at frequent intervals as compared to the significant cardiac toxicity of high-dose bolus therapy with this drug. This modified the approach to the use of this excellent chemotherapeutic agent and has extended its useful application in all fields of cancer chemotherapy.

Applied Research and Clinical Oncology

Shortly after exfoliative cytology was developed in the early 1940s by Dr. George Papanicolaou, its
application to the detection and eradication of gynecologic tumors was led by such men at Jefferson as Lewis C. Scheffey (Jefferson, 1920), Professor of Gynecology, and Abraham E. Rakoff (Jefferson, 1937), Professor of Gynecologic and Obstetrical Endocrinology.

The bronchoscopic diagnosis in lung cancer by cytology studies of aspirated secretions won for Louis H. Clerf (Jefferson, 1912), Chairman of the Department of Otolaryngology, and Peter A. Herbut, Chairman of the Department of Pathology, the Gold Medal of the American Medical Association in 1951.

Early research into naturally occurring stimulators and inhibitors of granulocytic and lymphocytic proliferation in human leukemia was the special interest of Franklin Miller, M.D., Assistant Professor of Medicine, who was one of the early associate members of the Cardeza Foundation for Hematologic Research.

In the management of human breast cancer in the 1950s, when endocrine manipulation of the tumor was the major therapeutic modality, Ralph A. Carabasi (Jefferson, 1946) was a pioneer. Early immunologic studies in cancer were conducted by Irwin L. Stoloff (Jefferson, 1951), in addition to those performed by Chester Southam, M.D.

Lymphangiography was originally described as a unilateral procedure for the analysis of lymph flow in 1955. In 1960, Dr. Phillip Hodes, Professor and Chairman of Radiology, and Dr. Simon Kramer, Head of Radiation Therapy, realized that this technique might be adaptable to the evaluation of lymph node involvement by cancer. They encouraged Sidney Wallace, M.D., Assistant Professor of Radiology, and Laird Jackson, M.D., who was then a medical resident, to develop the procedure. Drs. Wallace and Jackson performed the first bilateral simultaneous injection of intralymphatic contrast materials in humans in 1960. This was a tedious procedure in the beginning, requiring prolonged hand-delivered injections by two people, until Dr. Jackson invented a motor-driven pump that became universally used for lymphangiography. By 1985 the information gained by lymphangiography was largely replaced by noninvasive methods.

Laird G. Jackson, M.D., Professor of Pediatrics, Director of the Division of Genetics, Professor of Medicine and Professor of Obstetrics and Gynecology, performed all of his early work in chromosomes and on the genetics of cancer while assigned to the Division of Medical Oncology of the Department of Medicine. This began in 1961 when he was a medical oncology Fellow and investigated chromosomes in leukemia. He expanded this work after he took the Bar Harbor course in medical genetics given by Victor McCusick, M.D., in 1962.

With the return of Michael J. Mastrangelo, M.D. (Figure 16-6) to Jefferson in 1984 to renew an association he had begun as a medical intern in 1964, Jefferson entered a new era of research and therapy of malignant melanomas. Dr. Mastrangelo’s interest has been in the immunologic aspects of cancers in general and of malignant melanoma in particular since he took postdoctoral training in the laboratory of Richmond T. Prehn, M.D., in the Institute for Cancer Research of Philadelphia (1971–1972). Mastrangelo was an early member of the Malignant Melanoma Clinical Cooperative Group (1973–1977) and a member of the Committee on Tumor Immunotherapy of the Division of Cancer Biology and Diagnosis of the National Cancer Institute.

FIG. 16-6. Michael J. Mastrangelo, M.D.; Director, Division of Oncology (1984–).
Institute (1975–1979). Since 1980 he has been a member of the Experimental Therapeutic Study Section of the National Institutes of Health, serving from 1982 to 1984 as its Chairman. He continues an active program in immunologic aspects of cancer and of malignant melanoma in particular.

Medical science is still at the frontier in understanding the complex mechanisms that lead to cancer, its better palliation, and the ultimate goal of total prevention and cure. The progress thus far engendered by interdepartmental cooperation has been significant, but more intense focus on the possible role of viruses not yet isolated, genetic investigation, and study of neoplasms at the molecular level will increase Jefferson's stature in this field.

References