

The  
*Clinical Cancer Program*  
at YALE

BY DAVID S. FISCHER, MD



STERLING HALL OF MEDICINE  
ON 200<sup>TH</sup> ANNIVERSARY OF  
YALE SCHOOL OF MEDICINE



SMILOW CANCER HOSPITAL AT  
YALE NEW HAVEN

NOTICE: Every effort has been made to ensure that the facts in this publication are correct, but since some of this is oral history, errors will occur in spite of attempts to verify the facts in published accounts. In a few instances, published accounts were apparently in error according to reports of multiple individuals who had contemporary personal knowledge of the events. The interpretation of events is subjective and individuals may view them differently. The opinions and interpretations herein are the responsibility of the author and not of the individuals consulted or those who reviewed all or portions of the manuscript.

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A HISTORY OF THE CLINICAL CANCER PROGRAM  
AT YALE-NEW HAVEN HOSPITAL AND YALE  
COMPREHENSIVE CARE CENTER: ONE MAN'S VIEW  
AND A PERSONAL MEMOIR

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In 2010-2011, the Yale School of Medicine (YSM) will celebrate 200 years since it was chartered by the Connecticut Legislature as the Medical Institution of Yale College, and thereby became the sixth medical school in the United States. It was preceded by the Medical Department of the University of Pennsylvania in 1765, the College of Physicians and Surgeons in New York in 1807 (originally in 1768 as King's College), and the Medical Departments of Harvard in 1783, Dartmouth in 1797 and the University of Maryland in 1807. To celebrate this occasion, a well illustrated series of chronologic vignettes has been compiled (Falvey, KL, *Medicine at Yale: the First 200 Years*, Yale University Press, 2010) and published. Several departments have been asked to write histories of their department and some that had written histories in the past were asked to bring them up-to-date. So far, the only one that I have seen is the excellent review on Pediatrics by Dr. Howard Pearson. I am aware that Dr. John Fenn is doing one on Surgery for which I have provided him with some information on the first use of cancer chemotherapy at Yale for which he has done much additional research.

Some colleagues have asked me to review the clinical cancer program at Yale since I have been involved in it for more than 48 years. This is an attempt to do that based on what I have read of the early years and what I know from personal experience. The first five years of that experience was in the department of pharmacology where I observed and participated in both basic science and clinical studies. The remaining experience has been in the clinical practice of oncology and hematology, most of it in the community but interacting with the full-time faculty, and since 1993 as a volunteer, consultant and as an administrator with an office (starting in 1995) in the Yale Cancer Center (YCC). I have limited knowledge of the extensive and impressive basic science studies done here, which are documented in the thousands of publications available in the literature but I will refer to them when they interact with the story that I know from some personal experience. It is therefore both a history and (after 1962) a personal memoir, subject to my bias and an overemphasis on events in which I participated and to the neglect of important events of which I have no personal knowledge. In the course of writing what I had originally hoped would be a brief history, many interesting events came to my attention that I thought might be of interest to readers. This includes some observations on the founding of the Collegiate School that later became Yale University. It also includes some observations on how economic problems impacted its development and almost resulted in the dissolution of the medical school in the 1910-1913 period, after World War I and again after World War II, and the near loss of the National Cancer Institute (NCI) designation as a NCI affiliated Comprehensive Cancer Center (CCC) around the turn of the 21<sup>st</sup> century. This is one man's view and a personal memoir.

The history prior to 1962 (the year that I came to Yale) is gleaned from published reports (Gerard N. Burrow, *A History of Yale's School of Medicine*, Yale University Press, 2002; Brooks Mather Kelley, *Yale: A History*, Yale University Press, 1974; George Wilson Pierson, *The Founding of Yale: The Legend of the Forty Folios*, Yale University Press, 1988; Howard H. Spiro and Priscilla Waters Norton, *Dean Milton C. Winternitz at Yale*, *Perspectives Biol & Med*, 46:403-412, 2003; Dan Oren, *Joining the Club: A History of Jews at Yale*, Yale University Press, 1974; Toby Appel, Lilli Sentz, *Medicine at Yale, 1901-1951*, accessed at <http://info.med.yale.edu/library/exhibits/yalemed2/1901-1911.html>), and 1951-2001 at same URL but /yalemed3/1951-2001, and unpublished documents made available to me. The Historical Register of Yale University Online (HRO) 1701-1968 was a great help in checking dates, but after 1968, there are only some spotty additions to individual records up to the early 1980s and then none – a great historical loss. I have been unable to find much published material on the cancer program at YSM and Yale-New Haven Hospital (YNHH) prior to 1962 except for scattered reports. Some valuable faculty information for the period after the HRO discontinued adding new faculty data was provided by Julia Buchanan of the Faculty Affairs Office. I can fill in some information from that time forward with my own records, observations and information (memory permitting, because I had to discard many records in 1993 when I moved to a smaller office with less storage space). Some information was given to me by participants who will be cited when appropriate.

I had intended to make this report brief, but many colleagues were generous with their time and made information and records available to me that helped to give a better picture of events and the people involved. In many cases I have quoted or paraphrased the information. I will also attempt to tell the stories of some of the remarkable people who trained here and became faculty here and their contributions to the Yale Cancer Program and occasionally their contributions to the greater national and international society when they left Yale, but of necessity, will omit many. While much emphasis will be placed on the leaders, as in most histories, I plan to include many who worked here and are less well known so that they not “pass and be forgotten like the rest.” I will try to be as accurate as the data and memory allow and include the successes and the failures, the good and the bad decisions and results as I noted them. Others may have seen or interpreted the events somewhat differently. We all make mistakes and often only time will judge what decisions were correct. In my years at Yale, I have not personally encountered any member of the staff who acted out of malevolence. There was a single such event to which I will refer based on accounts by several trusted members of the faculty, but since I have no personal knowledge of the individual, I omitted his name. I will go into less detail about most individuals in the last decade because that is more like current events than history and is better known to current members of the staff than the earlier history. There will be large amounts of other significant information omitted because I just don't know about it and where I do have personal knowledge or have been provided with information, I have presented it, and sometimes much more than some readers want to know. That is particularly true when it is events in which I participated, but that is what I know best and I present it for what it is worth, although many readers will choose to skip it because it includes too much about me. I apologize for that in advance.

To understand the history of the Yale Cancer Program, one must have some understanding of the groups that comprise it: Yale College (later University), the Community (Physicians and Patients), the Yale School of Medicine, and Yale New Haven Hospital, and how they interact, and how they have all changed over the years. Some information on the other area hospitals will augment that understanding.

Yale College was founded in November 1701 by the General Court of Connecticut (General Assembly), meeting for the first time in New Haven (the town had just become the co-capital of the colony with

Hartford). That is a well documented fact. There has been some controversy over the legend of whether Yale was actually founded a few months or a year earlier by a group of Puritan clergymen and that the General Assembly simply put its stamp of approval on a completed action. Whichever formulation is accepted, Yale became the third college in the colonies after Harvard College (1636) and the College of William and Mary (1693). When the Assembly passed “An Act for Liberty TO ERECT (sic) a Collegiate School” (not incorporate because only the King could create a corporation) it also granted the ten “reverend undertakers, trustees or partners and their successors,” what was for the time, a generous amount, “the full & just sum of one hundred and twenty pounds in Country Pay to be paid Annually.” The new school’s primary mission was to instruct youth to fit them “for Publick employment both in Church & Civil State.” Not quite a month later, led by Rev. James Pierpont of New Haven, seven of the ten met to elect Rev. Samuel Russell of Bramford (today Branford) as an 11<sup>th</sup> trustee and to organize, regulate and staff the institution with 40 books. It is alleged that each clergyman stated, “I give these books for the founding of a College in this Colony.” One or more of the 40 books or folios was probably donated by each of the seven clergymen, but most of them were donated by Rev. Pierpont [from the Eaton-Davenport collection], Rev. Abraham Pierson [from his father’s large collection] and Rev. Israel Chauncey of Stratford [who was the son of Charles Chauncey (or Chauncy) the second president of Harvard College and had inherited a substantial library from his father]. They voted to open the Collegiate School in Saybrook, Connecticut with Rev. Abraham Pierson of Killingworth (originally Kenilworth but referred to in the 1701 Act as Kennelworth and today split into Killingworth in the north and Clinton in the south and Pierson’s parsonage was in today’s Clinton) as “regent” or “rector”, but his congregation would not let him leave and therefore classes were conducted in his home until his death in 1707. Then the Seniors (sic) were sent to the Rev. Samuel Andrews of Milford (one of the original ten trustees who was then elected rector pro tempore), and the rest were moved to Saybrook under a tutor. Although that small community was welcoming, it was an inconvenient location; the winters were bleak and severe, and the students were ravaged by sickness over the ensuing nine years and wanted to relocate.

The school was moved to New Haven in 1716 where a new building was constructed on what is now the corner of Chapel and College Streets, which was completed in 1718 (but that building is no longer in existence). After a generous donation by the London merchant Elihu Yale, who sent a ship with 400 books, a portrait of King George I, and cloth goods that sold for 562 pounds, the school named the building Yale College (in the tradition of the English universities of Cambridge and Oxford, and not Yale Hall) in 1718 to encourage further financial support from this “foreigner.” Actually, Elihu Yale was not a “foreigner.” He was born in Boston, Massachusetts in 1649 to David Yale and Ursula Knight, and was the grandson of Anne Lloyd Yale, who after the death of her first husband, Thomas Yale, married Theophilus Eaton while in England and came with him and her three Yale children (Anne, David and Thomas) to Boston Colony and later to New Haven Colony, of which Eaton was a co-founder with the Puritan minister, Reverend John Davenport in 1638. Davenport had a dream from 1647-1668 of starting a collegiate school in New Haven to prepare young men for the Puritan clergy. Why not? He noted that Boston was settled in 1630 and only six years later, the Great and General Court of the Massachusetts Bay Colony authorized the founding in 1636 of New College in Newtowne which was later named Cambridge, but no buildings were built or students enrolled until 1639 when John Harvard’s will endowed the college with books, land and money. Its name was changed to Harvard College.

The trip to Harvard College was long and arduous and Davenport, as a devout Puritan, was also concerned about some theological deviance at that institution and in 1656 he convinced Eaton (who was rich) to buy 20 pounds worth of books for the proposed collegiate school. When New Haven was incorporated

into Connecticut in 1665, Davenport's dream died and in 1668 he went to Boston and left the books to the town of New Haven. These books were purchased by Rev. James Pierpont in 1689. In the Spring of 1701, a document was received by Rev. Pierpont and several other Connecticut ministers entitled, "Proposals for Erecting an UNIVERSITY (sic) in the Renowned Colony of Connecticut: Humbly Offered by an Hearty (tho' unknown) Well-wisher to the Welfare of that Religious Colony." Franklin Bowditch Dexter, author of *The Founding of Yale College: A Selection from the Miscellaneous Historical Papers of Fifty Years*, New Haven, 1918, and *Documentary History of Yale University under the Original Charter of the Collegiate School of Connecticut*, New Haven, 1916, believes it was written by Rev. Cotton Mather of Boston. The letter reinvigorated the Connecticut ministers, most of whom were graduates of Harvard College, to revive Davenport's dream of a college founded and directed by Puritan clergymen in New Haven. Eaton became Governor of the New Haven Colony in 1639 and was reelected each year until his death in 1658. After he died, Anne Lloyd Yale Eaton returned to England with her family and lived with her son David Yale and his children. Elihu was then about eight years old and strongly attached to his grandmother Eaton. After the family moved back to England they never returned to North America but had cousins in New Haven.

Who influenced Elihu Yale to become a benefactor of the Collegiate School in New Haven? We do not know for certain. It may have been his New Haven cousins, or his grandmother Eaton. But we do know that on January 14, 1718 the Boston clergyman, Cotton Mather, who was disillusioned with Harvard College for several reasons, including the fact that his father, the Rev. Increase Mather, had been denied the presidency of that institution, sent a letter to his friend, Elihu Yale, then 69 years old and urged him to make a substantial gift to the struggling New Haven school. He even suggested that the new building under construction might be named in honor of its major benefactor. The London representative of the colony, Jeremiah Dummer, approached Yale in March 1718 in support of Cotton Mather's plea for a donation to the school. Yale, a good Church of England man, was doubtful about supporting a school of dissenters (Puritans), but Dummer, as he wrote to Governor Saltonstall, convinced Yale "that the business of good men is to spread religion and learning among mankind without being too fondly attached to particular Tenets, about which the World never was, nor ever will be agreed." The building was named Yale College in gratitude. (Some people began to call the entire institution Yale College in 1718/1719, but it was not until 1745 that the entire institution was officially named Yale College. It is interesting to note in passing that Cotton Mather wrote what some regard as the first medical treatise in New England, *Angel of Bethesda*. Collaborating with the physician Zabdiel Boylston, Mather was one of the earliest advocates of variolation [inoculation with a weak strain of smallpox for immunization] before its public introduction in England).

**REV. THOMAS CLAP**, the fifth "Rector" (or Regent), 1740-1745) and first "President" of Yale College (1745-1766) was a Congregational minister. Although the school's major mission was to prepare students for the clergy and Clap was very dogmatic about his Calvinist theology, he was interested in science and inclined to provide a broader education for the students. In 1742, he clashed with some of the local ministers and with the students and closed the college and sent the students home. The General Assembly supported him and some of the more ardent dissenting students transferred to other institutions. Yale reopened in 1743, the year after Clap catalogued the library and the year he proposed a new charter. In 1745, the General Assembly granted the new charter with the corporate name of the institution as "The President and Fellows of Yale College in New Haven." Clap was sworn in as President and the name of the Collegiate School was formally changed to Yale College. As enrollment increased, Yale needed another building and did not have enough money to build it. In 1747 Clap requested the General Assembly



to allow Yale to raise the money through a lottery. This was approved and Yale became the first active American college to raise money by this relatively new method. Only 500 pounds was raised which was insufficient to build the new hall, so the General Assembly voted to give Yale the proceeds of the sale of a French boat recently captured by the colony's frigate (the King George's War had just ended). With this additional money, construction was started on Connecticut Hall in 1750 and completed in 1753 and it is the oldest remaining building on the Yale campus.

In 1766, Clap wrote the *Annals or History of Yale* to prove that Yale was a private institution to beat off attempts by the General Assembly to interfere in Yale's governance. In his earliest draft, he wrote that in 1702, ten ministers assembled in the parsonage of Rev. Samuel Russell in Branford, and brought 40 books or folios for a library for the Collegiate School. The General Assembly had authorized the trustees to "ERECT" (not found or incorporate) the Collegiate School in October 1701, so he changed his date to early 1701 (and some have claimed it occurred in Summer 1700) to prove that the school was established before its legislative authorization and therefore was a private institution and not answerable to the General Assembly. The "Legend of the 40 Folios" caught on and is memorialized in a stone statue in Branford, a carving in Sterling Memorial Library (SML), the naming of Branford College and the doors to the Russell parsonage were installed in the "1742 Room" in SML with those original books and folios that could be found. Dexter and Kelley in their histories suggest that Clap was somewhat inventive and doubt that the event occurred as he described it, and G.W. Pierson thinks that it is possible but unlikely to have happened as described by Clap, but that some books and folios were promised to the school shortly before its authorization by the General Assembly. Clap was successful in establishing Yale's freedom from government, but the General Assembly discontinued the annual grants to the college.

Clap did a lot of good, but made many enemies who, together with the students, drove him from the presidency in 1766. He was succeeded by Rev. Naphtali Daggett (1766-1777), who is recorded as president pro tempore. There was considerable controversy over the mission of the school at that time and hence over the choice of the new leadership. Rev. Ezra Stiles, pastor of the Second Congregationalist Church of Newport, R.I. had studied Hebrew with Reverend Isaac Touro and with Rabbi Haim Isaac Carigal of the Touro Synagogue of Newport in the 1670s before Stiles moved to a congregation in Portsmouth, New Hampshire. When, after a few years there, he was called to be the next president on a divided vote, he was hesitant about accepting the position without making it clear what his intentions were. Accordingly, in November 1777, before becoming president, he sketched out "A Plan." As described by Kelly, "he decided that Yale should have a professor of physic (since the state needed doctors), a professor of law (to train men for government service), and also professors of ecclesiastical history, civil history, Hebrew and oriental languages, and oratory and belles-lettres. These were to be in addition to the two existing professorships in divinity and mathematics and natural philosophy." Over the next 30 years, about 10% of Yale College graduates became physicians, some as physicians and clergymen. It should be noted that these foundational stories are related to the names of some of Yale's colleges, including Branford, Davenport, Timothy Dwight, Pierson, Saybrook, Ezra Stiles, and as we will soon see, Silliman.

**THE COMMUNITY:** In colonial times, anyone could call himself a physician, and many people with no training did so. To establish camaraderie, disseminate educational information, and bring some order to medical practice (regulate charlatans), the Litchfield County Medical Association was formed in 1767 as the first medical society in the colonies (the United States had not yet been established). Eneas Munson and Leverett Hubbard, brothers-in-law of Ezra Stiles, founded (with others), the New Haven County Medical Society (NHCMS) in 1783. The NHCMS published *Cases and Observations by the Medi-*

cal Society of New Haven County in the State of Connecticut, the first volume of medical transactions published in the United States. The Connecticut State Medical Society (CSMS) was formed from the amalgamation of several county medical societies and was chartered by the legislature in 1792 and directed, among other things, to confer medical degrees as well as act as an examining and licensing board to control the chaos created by the lack of criteria for claiming the title of physician. The regulations of the society stated that the M.D. degree was honorary, and was only awarded to distinguished physicians who had been in practice for a long time. By 1800, physicians in Connecticut could be licensed after serving a satisfactory apprenticeship of three to five years under an established physician who was recognized by the CSMS. A fair idea of what it entailed is described in the Spring 2010 issue of *Yale Medicine*, in an article entitled "The Physician's Apprentice," adapted from *Medicine At Yale: The First 200 Years* by Kerry L. Falvey, cited above. (The book was published in November, 2010, when this review was 90% completed, and although it is a beautiful and well illustrated book covering the 200 years, it has relatively little about the cancer program).

The New Haven Medical Association (NHMA) was organized in 1803 and developed a constitution and by-laws by 1835 and in 1860 hosted the annual meeting of the American Medical Association, which itself had been established in 1845. The NHMA soon became the central meeting place of the small cadre of city physicians and was incorporated in 1869. For many years the meetings were held every two weeks at one of the physicians' homes. They were social and educational and discussed medical advances and economic problems of medicine. They invited noted physicians, often from other areas, to give lectures, including Sir William Osler from Johns Hopkins Medical School and Hospital and Dr. Frank Lahey, founder of the Lahey Clinic. As the number of physicians increased and some YSM faculty members joined, the NHMA needed a larger site for their meetings and met either at a hotel, restaurant, or the lecture hall of the Yale Law School until they purchased for their headquarters an old home on Whitney Avenue with a dining room and a lecture hall. Meetings were then held monthly during the academic year. I had the privilege of serving as secretary for more than a decade and as president in 1990-1991. As more and more medical educational opportunities became available at the YSM, attendance at NHMA lectures progressively decreased and more discussions of economic and political issues and their impact on medical care were held.

**THE YALE SCHOOL OF MEDICINE:** In 1806, when Yale College began negotiations with CSMS to establish a medical institution, Ezra Stile's successor, Timothy Dwight, IV, was president, and no medical, law or divinity school had been established yet. (The medical school was established in 1810; the divinity school (arguably) in 1822; the law school in 1824; and the graduate school of arts and sciences was established in 1847 and granted the first PhD in the United States in 1861). There were many medical schools of questionable quality throughout New England and they vied with each other for paying students. The students paid to hear lectures about the theory and practice of physic (the art of medicine) but had no supervised clinical experience unless they became apprentices. Although the charter for the Medical Institution of Yale College was granted in 1810, it did not open until November 1813. It had 37 students, including 17 from Connecticut, eight of whom came from the New Haven area. Medical students were required to be high school graduates, and they could attend lectures of their choice so long as they paid for a ticket. The founding members of the faculty were:

Dr. Nathan Smith, professor of the theory and practice of physic, surgery and obstetrics; Dr. Eneas Munson, professor of materia medica and botany; Dr. Eli Ives, adjunct professor of materia medica and botany, and a pediatrician; Dr. Jonathan Knight, a surgeon, who also taught anatomy and obstetrics;

Professor Benjamin Silliman, professor of chemistry and pharmacy.

Although not a physician, Silliman played a major role in the development of the medical school. The instructors and the school derived their income from the fees paid by the students. Yale tried to upgrade by introducing a graded three year course in 1879, which meant that students had to take lectures in a sequence deemed by their faculty to be best designed to build their knowledge progressively, not haphazardly. This interfered with the need for some students to be home and available for planting and harvesting in a primarily agricultural society. It also meant that they had to have enough funds to get through three consecutive years. As a result, enrollment decreased drastically and so did the income of the school. However, Yale retained the advantage of being state chartered and hence the only institution in the state able to award the M.D. degree to its graduates.

The Medical Department of Yale College was the name chosen in 1884 when the CSMS and Yale amicably agreed to sever their joint management of the school, and the name change suggested that it was more a part of Yale rather than an appendage. To further improve the quality of the students, it required a matriculation examination for students lacking a college degree. Yale and Harvard were the only medical schools in the northeast to set such high standards and as a result, enrollment fell another 50%. Although Yale's medical department emphasized science and was better than the legion of horrific medical schools in the region, it was not very good, and its own faculty said as much in an 1871 document submitted to the Yale Corporation. On the other hand, in 1869, the Massachusetts Medical College of Harvard University had been described as "a money-making institution, not much better than a diploma mill" (Henry Beecher and Mark Altschule, *Medicine at Harvard: The First 300 Years*, University Press of New England, 1977). In 1869, the chemist, Charles W. Eliot became president of Harvard University and integrated the medical school into the university and laboratory sciences were emphasized in an attempt to make medicine more science based. At that time the Yale Corporation felt that it was unable to afford laboratories for its medical department so the professors, who were science oriented, pledged a portion of their income to provide some laboratory facilities. As pointed out by former Yale Medical School Dean Gerard N. Burrow, MD in his 2002 book, *A History of Yale's School of Medicine*, (to which I am hugely in debt and from which I have garnered much of the information in the early part of this review, sometimes copying a sentence or two without quotation marks), the scientific ethos of Yale College strongly influenced the medical institution. He suggested: "partly as a result of this basic emphasis on science, clinical medicine has never assumed the importance at Yale that it did at other medical schools."

The physical plant of the YSM had been marginal since its founding. The first building was on Grove Street at the corner of Prospect Street and opposite the Grove Street Cemetery. It was originally designed as a hotel but was rented from James Hillhouse until it was purchased in 1814 for \$20,000 with a grant from the Connecticut State Legislature. It was three stories and had space for a lecture hall, a dining room, an anatomy laboratory in the basement and student rooms scattered about. In 1858, it was sold to Joseph Sheffield for \$165,000 for a new location for the Yale Scientific School which was soon renamed the Sheffield Scientific School in his honor. The Medical Institution used the proceeds to build a new three story building at 150 York Street which it occupied from 1860 until 1925 when the Sterling Hall of Medicine was built on Cedar Street. Until then, some classes in anatomy were held in two other buildings on York Street while some classes in physiology and public health were held in a building on Park Street in the remodeled former Elm City Hospital. Chemical physiology had space in the Sheffield mansion on Hillhouse Avenue, pharmacology was divided between the York Street building and the Brady Laboratory; applied and physical physiology as well as public health were located in a converted brick house a

quarter mile from the hospital. A pair of wood frame buildings on Cedar Street was used for chemistry and for obstetrics and gynecology until 1920. Most of the “basic science” courses were taken at Yale College or at the Sheffield Scientific School. After World War I, an Army barracks near the corner of Cedar Street and Congress Avenue that had been used during the war was converted to provide an additional site for teaching and a nearby two story brick building near the Brady Memorial Laboratory was used for a student laboratory. Students saw patients in the New Haven Dispensary and increasingly in the New Haven Hospital, but it can be appreciated that the facilities were scattered all over town until the 1920s.

The New Haven Dispensary opened in 1872 to deliver outpatient care to the underprivileged of New Haven and welcomed the medical students who were barely tolerated in the hospital, but more about the hospital later. The school improved slowly, but was hampered by lack of clinical facilities. By 1906, there were more than 200 medical schools in the U.S. In that year, Yale invited the famous Johns Hopkins neurosurgeon, Harvey Cushing (Yale BA 1895) to become Chief of Surgery at Yale. In a stinging rebuke to the administration, he declined and explained that it was because of the lack of a year-round clinical teaching program in a university hospital or at the least in an affiliated-hospital as well as the immaturity of the medical students as potential doctors. Yale tried to improve the maturity of students by raising its entrance requirements to a minimum of two years of college to even be eligible to take a matriculation examination. This caused a further drop in enrollment and hence in tuition income. In 1913, with only nine graduates and a large deficit, the Yale Corporation looked at the Medical Department and entertained a motion to “kill or cure” the medical school. It was fortunate that the 1910 report, *Medical Education in the United States and Canada* by Abraham Flexner for the Carnegie Foundation for the Advancement of Teaching was published and drew wide attention. It concluded that of the 147 American medical schools and seven Canadian surveyed, most of them were so inferior that only 31 should survive. Flexner’s report suggested that in New England, only the medical schools of Harvard and Yale should survive, and that Yale was deficient in having an inadequate connection to a teaching hospital and needed more adequate laboratory facilities. Armed with this report, the supporters of the medical school prevailed by a single vote and the Corporation voted to retain the medical school and provide it with some funds. Professor George Wilson Pierson, Chairman of History (1956-1962) and Director Division of Humanities (1964-1970) was also an official Historian of the University. When he was a patient in YNHH, I attended him as a consultant in hematology. During one of our discussions about the history of YSM, he told me the story of the crucial vote and that his recollection was that the deciding vote to retain the YSM and improve it, was cast by William Howard Taft, then a member of the Corporation. (Taft was well respected and had been Yale class 1878, second in class rank, Phi Beta Kappa, President of U.S. 1909-1913, and later served as 10<sup>th</sup> Chief Justice of U.S. Supreme Court, 1921-1930).

George Blumer, MD became the first full-time Chief of Medicine in 1906 (although the official history of the Department of Internal Medicine suggests that John Slade Ely was the first chief, but the HRO does not list either of them as chair or chief, only as Professors of Medicine). In 1910, Blumer also became the first full-time Dean and recruited full-time chiefs of surgery and of obstetrics/gynecology. In 1910, Flexner had found that the provisions for pathology and bacteriology were unsatisfactory at YSM. The heirs of Anthony N. Brady, in 1914 provided \$625,000 for the construction and the equipping of a pathology laboratory (Brady Memorial Laboratory on the corner of Cedar Street and Congress Avenue) for the New Haven Hospital (NHH) to be run by YSM. William Henry Welch, MD, a Professor of Pathology at Johns Hopkins School of Medicine (JHSM) and a Yale A.B. 1870, recommended that his best disciple, an associate professor of pathology at JHSM, Milton C. Winternitz, MD should come to Yale as Professor of Pathology in 1917. Welch was a consultant to the Yale Corporation; he was the Dean of JHSM and its first

Professor of Pathology; he had introduced European pathology and educational methods to the U.S. and his advice was widely sought. He, along with his student Simon Flexner, MD (founding Director of the Rockefeller Institute for Medical Research [RIMR], and brother of Abraham Flexner), all members of the General Education Board (GEB) of the Rockefeller Foundation, recommended that the YSM make provisions for enhanced facilities and leadership in pathology and bacteriology and remain a four year school. In 1913, Blumer, acting on behalf of Yale, made an agreement with the NHH, facilitated by Flexner (and with \$500,000 from his employer, the Carnegie Foundation) to improve its clinical laboratories and allow its general patients to be used for teaching throughout the year. The official name, Yale School of Medicine (YSM), was adopted in 1918. However, World War I stressed the budgets and enrollments of most schools. In 1914, YSM graduated only 8 physicians; in 1915, only 7; in 1916, there were 6; in 1917 it increased to 10, but by 1918 it was down to 8. Although there were 12 graduates in 1919, the lack of funds became so severe that by 1920, Dean Blumer and two of the senior faculty resigned and one signaled his intention to do so. Of the seven remaining faculty members, two were primarily affiliated with other schools in the University.

At this nadir of the YSM, there were only 65 applicants for 50 positions. The University had to periodically give some money to YSM to keep it solvent. President Arthur Twining Hadley, an economist and the first non-clergyman to serve as a President of Yale University, had to do something drastic or the YSM would either be discontinued or turned into a two year school with students sent to New York City for their clinical rotations. What should Hadley do? Who could he turn to? Should he take a chance at this difficult time and make it a two year school or shut it down entirely? Milton C. Winternitz, MD did such an incredibly good job as chief of pathology that when Blumer resigned, Hadley knew that he had his man and in 1920 elevated Winternitz to Dean of the medical school. This presented an immediate problem because the President met with his Deans at the Graduate Club and that organization would not extend membership to Winternitz because he was Jewish. (If he had not been Jewish, it is likely that he would have succeeded Welch as Professor of Pathology at JHSM). After considerable pressure by President Hadley, membership was extended to Winternitz.

Abraham Flexner became assistant secretary of the GEB of the Rockefeller Foundation in 1914. At that time he was also urging other medical schools like Washington University, Rochester, University of Chicago and Vanderbilt University to adopt a full-time faculty system similar to that of the JHSM. (It should be noted that the Hopkins model allowed some faculty, like Osler, Halsted, Kelley, Cushing, etc. to have a limited private practice, and when William Welch was advising Yale, he advocated retaining some private practice for faculty, but Flexner did not). Having been a medical student, house officer and faculty member at Hopkins, Winternitz, was eager to cooperate and expand the YSM faculty with more full-time members. After meeting with Winternitz and before going to the GEB to get money for YSM, Flexner felt that courtesy demanded that he get the approval of President Hadley. In his autobiography, *I Remember*, (Simon and Schuster, N.Y., 1940) Flexner recalls that episode.

“Quickly upon the heels of this action (giving money to Washington University), came a similar application from the medical school of Yale University. Yale possessed one of the oldest medical schools in the country, but its facilities were absolutely outgrown; its endowment was small, its personnel in most departments quite inadequate. In 1917, however at the suggestion of Dr. Welch, himself a Yale graduate, Dr. Milton C. Winternitz, who had been associate professor of pathology in Baltimore, had become professor of pathology and subsequently dean of the medical school. Winternitz was one of the most energetic, keen, and able administrators that I encountered in the whole course of my dealings with medi-

cal schools. He had the sympathy and co-operation of Dr. Anson Phelps Stokes, secretary of Yale and a member of the General Education Board. The phenomenal rise of the Yale Medical School is an interesting story. No sooner was full-time teaching introduced into the Johns Hopkins than Winternitz posted down to New York to see me. It was obvious that the school had simultaneously to raise endowment, to find a building fund, and to reorganize its faculty. At the request of Winternitz, I went to New Haven and visited the Medical School and the New Haven Hospital with him. The shortcomings were enough to daunt anyone but Winternitz himself. As a matter of courtesy, of course, I first called on President Hadley, who was skeptical as to the possibility of raising funds or making the necessary changes in personnel without creating too great a furor. I recall very distinctly this interview with President Hadley in his room in Woodbridge Hall. In his nervous way he paced up and down, explaining to me that before I went into details with Winternitz, he wished to call to my attention a few points which he thought would have to be borne in mind."

"The Yale Medical School," he said, "is not only practically without funds but relies upon the facilities and courtesies of the New Haven Hospital, which we have hitherto enjoyed free of all cost. Now," he went on to say, "the head of the Board of the New Haven Hospital is Colonel Isaac Ullman, and it is in reference to Colonel Ullman that I particularly want to speak to you. In the first place," said Mr. Hadley, "Colonel Ullman is not a Yale graduate."

"Well," I replied, "inasmuch as I am not a Yale graduate myself, I do not think we are likely to encounter difficulties on that score."

"In the second place," he said, "Colonel Ullman's closest friend is a Roman Catholic (William Verdi, MD, a surgeon who had graduated YSM and was the leader of the group that had founded the Hospital of St. Raphael; note that Hadley did not mention that Ullman's second closest friend was President William Howard Taft, a Protestant) while he himself is a Jew and we are anxious to avoid anything that might be attributed to racial and religious prejudice."

I answered, "As I am a Jew myself and have been for years making my way among Christians and working with them, I think the situation can be handled tactfully, so that prejudice need not be stirred."

"Finally," said Mr. Hadley, "there is a third point, namely, Colonel Ullman's business. He is a corset manufacturer."

"Oh well," I said, "now I feel perfectly certain that he and I will get on famously."

Colonel Isaac M. Ullman was not simply a "corset manufacturer," he was the director and part owner of the largest employer in New Haven at that time. He was a business leader, politician and philanthropist. He served as President of the Chamber of Commerce of New Haven for nine years and his influence in civic affairs was very important. Thus, when "town-gown" relations were at a nadir in 1910, he counseled the local community (as quoted by Judith A. Schiff, *Colonel Isaac Ullman: Philanthropist, Politician, and Patriot, Jews in New Haven*, Jewish Historical Society of New Haven, 1979; 2:32-40) that, "The interests of the city and those of the university are in a measure inseparable. Each is useful and necessary to the other. As one grows and expands so is the other benefited. The university brings fame to our city and income to our people. And, upon the other hand, the city gives to the university freedom from taxes and protection to its property. By working together in harmony, the interests of each can be enhanced, and from such cooperation there is bound to grow results which will be of mutual benefit." Ullman demonstrated that in his personal life when he served, among other activities, as Chairman of the Executive Committee and President of the Board of the NHH from 1919 until his death in 1930. (Unfortunately, the schism between "town and gown," reasserted itself in later years and has continued to the present).

Winternitz, Ullman, and Flexner then worked out a cooperative program to make the NHH more of a University Hospital and a teaching and clinical research facility for the YSM with full-time Yale faculty as chiefs of surgery, medicine, pediatrics, and obstetrics/gynecology. Colonel Ullman volunteered to raise money for the New Haven Hospital to be able to build and equip laboratories and upgrade the hospital's facilities. He was as good as his word and with a little help from his friend William Howard Taft, by then past-President of the U.S., Ullman raised nearly \$300,000 in New Haven and its neighboring towns thereby saving NHH from default and its improved credit rating allowed it to borrow \$1,000,000 for laboratories.

Having established such an amicable arrangement, Flexner then had to get the approval of the GEB. He says, "Meanwhile, I had reported to Dr. Buttrick (then Secretary of the GEB) and Mr. Gates (then Chairman of the GEB) what I had been doing. Dr. Buttrick approved. Mr. Gates, though his own sons were Yale graduates, was opposed."

"You cannot," he said, "develop a medical school successfully in a small town so close to New York."

"I called his attention to excellent German medical schools which were situated in small towns---Giesen, Marburg, Tubingen, and others---and to the fact that the Mayo Clinic had developed at Rochester, Minnesota, an almost inaccessible spot. I argued that patients would go wherever first-rate medical care could be procured and that it would in the end prove an advantage if the town were not too large and the out-patient departments not too numerously frequented. When the matter came before the General Education Board for action, Mr. Gates' opposition was still strong, but he did not insist upon having his way, and after a long discussion the Board finally overruled its chairman. After Winternitz proceeded relentlessly from one branch to another, expanding section after section of the New Haven Hospital, securing a contract which gave the medical school unhampered facilities in the hospital and the right to appoint its entire clinical staff, and finally obtaining from the Sterling Trustees funds to construct and equip the laboratories which constitute the Sterling Hall of Medicine, Mr. Gates saw that he had been mistaken. Characteristically he came into my room at the General Education Board one day, sat down at my desk, and said:

"You remember I fought you on the Yale Medical School?"

"Yes," I said, "I recall the incident."

"Well," he replied, "I was wrong."

Flexner was then able to get the GEB to give Yale \$1,000,000 (the first of several gifts) on condition that it raise another \$2,000,000 for the medical school – which it did.

Winternitz was able to reorganize the Dispensary. It had originally been opened in 1872 at 31 Crown Street through the efforts of Stephen Henry Bronson, MD and others and was for a long time, the main clinical teaching facility of the medical school. It was estimated that the average senior student spent five hours a week at the dispensary (which was only open three hours a day for the free care of the indigent) and spent one hour a week at the New Haven Hospital. At the students' request, the Dispensary was moved to a site adjacent to the medical school on York Street in 1878 and finally moved to Cedar Street--the Hope Building (which was built from a gift of Mrs. Thomas G. Bennett as a memorial to her mother, Jane Ellen Hope, wife of Oliver Fisher Winchester). The Dispensary and NHH had separate Boards of Directors and medical staffs until Winternitz brought them together with a single Board and Staff. In a relatively short time he was able to have the Sterling Hall of Medicine (SHM, still the main teaching facility of YSM) built on Cedar Street immediately across the street from the NHH. Later, SHM was expanded with the construction of the Institute of Human Relations (IHR, to develop a program of social medicine in cooperation with the law and divinity schools), establish a Department of Psychiatry, organize

and build a School of Nursing, and introduce the “Yale System of Medical Education” (which emphasizes critical thinking in a non-graded, noncompetitive environment and requires students to write a thesis based on original research). He founded the Yale Journal of Biology and Medicine (YJBM, to provide a vehicle to publish student research, along with other worthwhile, peer-reviewed material – it is the only internationally recognized medical journal edited and published by students and listed in the Index Medicus). He also brought the neurosurgeon, Dr. Harvey Cushing to Yale in 1932 from Harvard. Cushing brought his brain collection and his historical book collection (which with the collections of Drs. John Fulton and Arnold Klebs form the center-piece of the Yale Historical Library).

Winternitz’s other innovations included the establishment of the Atypical Growth Study Unit in conjunction with Samuel Clark Harvey and George W. Smith. In 1921, Winternitz brought the Physiological Chemistry Research Group from Yale College to YSM and moved it into the SHM on its opening. Lafayette B. Mendel, PhD. who headed the group, was recognized as a world authority on nutrition. He was highly regarded for his pioneer work on the vitamins, particularly vitamin A. He also made notable contributions to the studies on the physiological chemistry of digestion, protein metabolism, the physiology of growth and accessory food factors. In addition to training medical students, he trained 124 PhDs at Yale of whom 48 were women. For this expansion of basic science to the medical school and the efforts to add a training program for primary care physicians and to have the Institute of Human Relations include law, divinity, sociology and psychology, Winternitz was accused of trying to build a competing university on Cedar Street. Still, Yale President James Rowland Angell, a psychologist, called Winternitz “a steam engine in pants” and supported most of his innovations. When Dean Wilbur of Stanford made uncomplimentary remarks about YSM, Flexner wrote to him, “As a matter of fact, no medical school in the United States or in any other country, with which I am familiar, has within so brief a period – about six years – made anything like the progress which has been made in New Haven.” A supposed blemish was the accusation that Winternitz, a Jew by birth, was anti-Semitic in his admission policy and actively discriminated against Jewish students and potential Jewish faculty. Some contemporaries suggest that he made most of his selection of students based on merit, but was aware of Yale’s restrictive policies. In fact, during the 10 years when Winternitz is said to have interviewed every applicant, Jews represented 17% of graduates whereas in the preceding 20 years they were only 12% of the graduating class, and in the 16 graduating classes after his intervention, they comprised only 8.9% (Fischer, DS, Jews in New Haven, Jewish Historical Society, 2009, p. 121). As far as faculty was concerned, Yale was generally weak in the sciences at that time because it had inadequate laboratory facilities. In addition, it was well known that Yale rarely hired Jews. Kelley noted that when talented Jews were fleeing Hitler’s Germany, that discrimination persisted. “Where this attitude was not present – as at Princeton and Columbia – science blossomed. At Yale, unfortunately, it prevented the university from seizing a great opportunity.” Winternitz did hire Eugen Kahn, a Jew, from Munich to establish a department of psychiatry and mental hygiene, but he was otherwise constrained in similar hiring by the university-wide practice.

When Winternitz stepped down as Dean in 1935 (he was actually pushed out by his faculty; Harvey Cushing commented that “purely personal animosities and grudges were really the moving causes”) he continued as professor of pathology until 1950 and served on most of the important YSM committees. When Winternitz became Dean, there were 65 applicants for the 50 places in the incoming class and when he retired, more than 500 qualified applications were received for the 50 places in the incoming class. By 1935, the amount of floor space available for all activities had increased from 78,000 square feet to over 423,000. Endowment went from under \$2 million to over \$8 million and the budget rose from \$253,000 in 1919-1920 to over \$900,000 in 1933-34. Full-time faculty increased from 45 to 150. During his dean-



ship, the New Haven Hospital was partially rebuilt with the addition of a private pavilion, two new wards, and a clinic building. The quality of the student body improved as the pool of applicants increased and Winternitz stressed the importance of preventive medicine and the consideration of “the patient..., not only [as] an individual with a mind as well as a body, but [as] an individual living, and acted upon by a social environment.” He was revered by some and hated by others, but Winternitz had transformed a third rate medical school into a first rate one, worthy of its parent institution.

The Deans of Yale School of Medicine were:

Prior to 1845, there was no dean. Nathan Smith, followed by Jonathan Knight, provided leadership in the early years.

Charles Hooker	1845-1863
Charles Augustus Lindsley	1863-1885
Herbert Eugene Smith	1885-1910
George Blumer	1910-1920
Milton Charles Winternitz	1920-1935
Stanhope Bayne-Jones	1935-1940
Frances Gilman Blake	1940-1947
C.N. Hugh Long	1947-1952
Vernon William Lippard	1952-1967
Fredrick Carl Redlich	1967-1972
Lewis Thomas	1972-1973
Robert Williams Berliner	1973-1984
Leon E. Rosenberg	1984-1991
Robert M. Donaldson	1991-1992 (acting)
Gerard Noel Burrow	1992-1997
David Aaron Kessler	1997-2003
Dennis Spencer	2003-2004 (acting)
Robert Alpern	2004-

The Medical Institution of Yale College and later of Yale University was almost always financially marginal and from time to time had to receive support from its parent. The New Haven Hospital was also frequently unable to pay its bills, and once Yale University made an agreement with the hospital to use its patients for some of the teaching of medical students, the University helped subsidize some of the losses of the hospital. Hence, the University played a prominent role in the fortunes of both the YSM and the NHH, and some of its presidents strongly influenced or directed key decisions. This was particularly true during the tenure of Winternitz, and, we will see, in some later events.

The Rectors of the Collegiate School were:

Rev. Abraham Pierson	1701-1707
Rev. Samuel Andrew	1707-1719 (pro tempore)
Rev. Timothy Cutler	1719-1726
Rev. Elisha William	1726-1739
Rev. Thomas Clap	1740-1745

The Presidents of Yale College (renamed University in 1887) were:

Rev. Thomas Clap	1745-1766
Rev. Naphtali Daggett	1766-1777 (pro tempore)
Rev. Ezra Stiles	1778-1795
Timothy Dwight IV	1795-1817
Jeremiah Day	1817-1846
Theodore Dwight Woolsey	1846-1871
Noah Porter III	1871-1886
Timothy Dwight V	1886-1899
Arthur Twining Hadley	1899-1921
James Rowland Angell	1921-1937
Charles Seymour	1937-1951
Alfred Whitney Griswold	1951-1963
Kingman Brewster, Jr.	1963-1977
Hanna Holborn Gray	1977-1977 (acting)
A. Bartlett Giamatti	1977-1986
Benno C. Schmidt, Jr.	1986-1992
Howard R. Lamar	1992-1993 (acting)
Richard C. Levin	1993-

Harvey Cushing, MD, became aware in 1937 of the desire of his Yale classmate, Starling W. Childs and his wife Alice C. Coffin to establish a fund for cancer research in memory of their daughter, Jane Coffin Childs who died of cancer. In its first three years, the Jane Coffin Childs Memorial Fund made grants for cancer research totaling \$138,000 to build on the work of the Atypical Growth Study Unit. Bayne-Jones was the first chairman of the Scientific Advisory Board, but after he left the deanship, Winternitz became chairman. One of its beneficiaries was Joseph Fruton, PhD, who later became the distinguished chairman of biochemistry at YSM. Today the Fund continues to award fellowships for cancer research to recent MDs and PhDs.

With the outbreak of World War II, the military was concerned about the potential use of poison gas by the Germans, who had used it in World War I. Winternitz, among other Yale faculty, had been a consultant to the Chemical Warfare Service then. In 1942, he was asked to serve in a similar capacity. Due to his efforts, a contract was signed between Yale University and the Office of Scientific Research and Development to investigate chemical warfare agents. It was assigned to the pharmacologists, Louis S. Goodman, MD, PhD, and Alfred Gilman, PhD. Working with Frederick S. Philips, Roberta Allen, Thomas Dougherty, Jean Dougherty and C.C. Hunt, they found that the drug, nitrogen mustard, would dramatically shrink the Gardner mouse tumor (developed by William Gardner at Yale), as well as other tumors. When Gustaf E. Lindskog, MD, then an assistant professor of surgery, had a patient with lymphoma who had responded to surgery and later to radiation but was now refractory to both and was apparently dying, he contacted Goodman and Gilman and told them about the problem. On August 25, 1942, J.D. a 47 year old man who worked in a ball bearing factory was admitted in the terminal stages of a lymphosarcoma that was resistant to radiation therapy. With no other useful therapy available, they agreed that he was a suitable subject for the experimental drug. The patient had tumor masses involving the tonsils, neck, axilla, mediastinum and submental region with a resulting cyanosis, venous dilatation and edema of the face

and the upper chest, anisocoria and paresis of the right facial nerve. With the patient's informed consent to the experiment, a dose of 0.1 mg/kg/day of nitrogen mustard was administered IV for 10 days.

The patient had a dramatic response and all the tumors regressed. They later recurred and he died on December 1, 1942; but the proof of principle had been established, a chemical agent could cause the regression of large lymphosarcomas. The age of cancer chemotherapy had begun. Six additional patients were treated at Yale. Investigators at other institutions who were cleared for this classified information were notified and several treated patients at their own institutions. Wartime security prevented this information from becoming publically available until 1946 (Goodman LS, Wintrobe MM, Dameshek W, Goodman MJ, Gilman A, McLennan MT. Nitrogen Mustard Therapy, JAMA 132:126, 1946). By July 1943, Goodman and Gilman had been passed over for promotion and left Yale, (Goodman went to the University of Vermont where he established a department of pharmacology, and later to the University of Utah's new medical school in Salt Lake City and Gilman went to work at the Chemical Warfare Service at the Edgewood Arsenal, but not before they produced their classic, first edition of *The Pharmacological Basis of Therapeutics*, published in 1941, and used by generations of medical students and now in its eleventh edition under several subsequent editorships). Lindskog entered military service and after the war returned to Yale and later became chair of surgery.

Further studies of nitrogen mustard were performed from 1944-1947 in the Yale Tumor Clinic and 16 cases were reported by Max Taffel, MD, from the Department of Surgery (Yale J Biol Med 1947; 19(6):971-977. I presented this story in more detail to the Beaumont Medical Club at YSM on March 18, 2005 as part of a lecture entitled, *A Brief History of Cancer Chemotherapy with Special Reference to Yale Medical School*. The portion of the lecture relative to the original use of nitrogen mustard at YSM was summarized by John Curtis in the Summer 2005 issue of *Yale Medicine*. I have presented this story in detail because Burrow does not mention it in his history of YSM, Falvey mentions it briefly with a few details and the *Medicine at Yale, 1901-1951* article mentions the work of Gilman, Goodman and Lindskog briefly and it correctly concludes, "This has been considered to be the beginning of cancer chemotherapy." We might add that this demonstration of the potential of chemical (drug) therapy to cause cancers to decrease in size was the psychological stimulus that led to people thinking seriously about treating and curing cancer by modalities other than surgery or radiation or a combination of the two. (NOTE: After this article was written, but before it was proof-read and vetted by colleagues, John E. Fenn, MD, on behalf of himself and Robert Udelsman, MD, decided to track down the original record of J.D. and learn more about him and the original first trial of cancer chemotherapy. I regret that I did not have the good sense to do that, but I did not. John contacted me and I suggested that he check the records of the Department of Pathology for 1941-42 and that we also check the Yale Tumor Registry for those years. Michael Kashgarian, MD, found the patient's name and unit number in pathology records and John Fenn notified me of that find about three hours before Teresita Vega, CTR, called to tell me she found them in the tumor registry. This fascinating detective story throws new light on this historic event and rectifies the record. We learned that J.D. was not a silversmith (as originally reported) and that his disease involved the tonsils extensively, and we learn the details of his laboratory studies. He was verbally advised of and consented to the experimental drug and unprecedented procedure. His nitrogen mustard therapy began on August 27 and he had a remarkable response to a state where there was no clinical evidence of disease; but then he had a recurrence and he died on December 1, 1942. It is a story worth reading (Fenn, JE, Udelsman, R, J Am Coll Surg 2011; 212:3:413-417).

An interesting but tragic side story is worth noting. To be prepared for retaliation in case the Germans used war gases, the United States had sent a Liberty Ship, the John E. Harvey, with mustard gas to the port of Bari, Italy where it was sunk by a Luftwaffe raid on December 2, 1943 (a year after J.D. was treated and died in New Haven). The resulting release of mustard gas caused hundreds of deaths and thousands of casualties. The sailors rescued from the water frequently died from thrombocytopenia and bleeding or severe leukopenia and overwhelming infection. When the histopathologic specimens of their organs were sent to scientists at Yale, it became clear that the changes in the bone marrow and spleen were due to the effects of the mustard. Clearly, Hodgkin's disease, other lymphomas and perhaps leukemia would respond to this agent. Again the information was disseminated to several investigators interested in cancer therapy who took notice and studies with nitrogen mustard and congeners became more common. In his 1971 book, *Disaster at Bari*, Glenn B. Infield suggests that the information derived from the studies of that tragic episode led to widespread investigations of chemical therapy for cancer. While he clearly states that the studies done at Yale were December 1942 (actually August to December 1942) and the events at Bari were December 1943, some authors (Gerald Reminick in 2001 in his book, *Nightmare in Bari*), and others, failed to note the chronology and suggested that the information from Bari led to the pioneering studies at Yale. The time sequence indicates that they did not. However, the studies of the histopathology of the large number of cases from Bari sent to YSM, stimulated further studies by Clarence P. Rhoads, Maxwell Wintrobe and many others.

During World War II, Yale's contribution to the war effort was outstanding. As war broke out in Europe, the YSM affiliated with the army's 39<sup>th</sup> General Hospital which later served in the South Pacific area. Yale established several training programs including: ROTC, NROTC, V-1, V-5, V-7, EV-G, quartermaster corps of the army, navy supply, navy cryptography, and civilian pilot training. After America's active engagement in the war, Yale became heavily involved. First, the Army Air Force Technical Training School (AAFTS) was established on campus; then came the Army Specialized Training Program (ASTP) and the navy's V-12 (similar to ASTP), V-1 (intelligence), and V-7 (engineers). The military dominated the campus with more than 8,000 personnel in various stages of military training, including the 418<sup>th</sup> Army Air Corp Technical Training Command Band under the direction of Glenn Miller.

When the war ended, Yale had "a perfect storm" of severe financial problems that impacted the medical school, and potentially its cancer program. Yale had to readmit those college and graduate students who left to join the military. It also felt an obligation to the secondary schools (prep schools and public high schools) that had sent it students over the years to admit the approximate number of candidates it had in the past. In addition, non-Yale veterans who would not have been able to afford Yale were clamoring for admission under the G.I. Bill of Rights with federal tuition support. In 1948, tuition was \$550 per year at Yale, Harvard and Williams (which I attended) colleges. The tuition at Harvard Medical School (HMS) in 1951 was \$800/year and went up to \$1,000/year in 1954. Dean Reginald Fitz at HMS told me that it cost Harvard \$5,000/year for each student, so I would guess that it cost Yale something in the same range but YSM's costs may have been somewhat higher. The difference was that Harvard was affiliated with at least seven major hospitals in Boston where their clinical full-time faculty practiced and the hospitals paid the bulk of their salaries. They also had a large cadre of well-trained part-time faculty, (some nationally known, like Drs. Paul Dudley White and Samuel Levine, among others) who attended at the hospitals, did extensive teaching, and received no remuneration from Harvard. A similar situation obtained at Cornell Medical School and its hospitals. Both of those institutions also had more robust endowments than YSM and had balanced budgets. YSM was affiliated only with NHH and its clinical faculty received little or no remuneration from the hospital, its part-time faculty was of high caliber but was generally not welcomed and it had a moderate cadre of PhD candidates whose tuition covered only a fraction of their cost.

Yale had an active alumni association that made substantial contributions during the 1920s and 1930s but the university did not pay enough attention to the alumni in the 1940s and did not derive the same level of financial support. In addition, the university Treasurer and his staff had decided that the safest way to guard the endowment in the turbulent post-war financial market was to invest 65% in bonds and 35% in equities, and when the equity value rose, to sell some and rebalance to the desired 65/35 formula. This was a period in which equity values grew substantially and some universities increased their endowments rapidly, while Yale's grew slowly. At the conclusion of the war, most of the Yale buildings were in disrepair and needed repairs and temporary housing had to be built for the large influx of new students (many of them married). During the war, science played an important role, but Yale had fewer scientific assets than most of the better Eastern colleges. The most recent scientific laboratory had been put up in 1923 and the physics building had been put up in 1912. Clearly, there was a need for more laboratory space but the period was notable for a brisk inflation which made construction very expensive. Meanwhile YSM had grown but its income had not grown commensurate with its needs for many reasons including those already mentioned, but its expenses had increased dramatically, as had debt in other medical schools. In 1946-1947, YSM had a deficit of \$700,000, a large sum for that period, and the university was subsidizing it. It had very limited laboratory space for research. In addition, NHH was not meeting its expenses and had to be subsidized by the university.

In December 1946, President Charles Seymour informed the Medical Board of YSM, "The question as to whether the university can actually afford a four-year medical school must be frankly faced. Any increase in contributions to the Medical School budget from general University funds is out of the question." Yale College and many of the other schools on the main campus felt that YSM was draining university funds that should have gone to their support. Kelley notes, "The situation at the Medical School was, in fact, destroying that institution." In 1946, George B. Darling, a public health specialist and President of the Kellogg Foundation and a former Executive Director of the National Academy of Sciences, was appointed Director of the Division of Medical Affairs of the University. He reported that on taking office, "relations between the Medical School and the rest of the University were poor. A large segment of the University and an important fraction of the Corporation questioned the advisability or, indeed, even the possibility of continuing a four-year medical school. While the reasons for this were clearly related to the heavy financial burden of the Medical School, this was further aggravated both by a general lack of appreciation of the real contributions of the School and, as far as alumni and colleges were concerned, by awkward handling of School admissions. The School's own inadvertently poor relations with the medical profession in the community of New Haven and of Connecticut reflected a lack of understanding of the need for an integrated community program, particularly of post-graduate education, but also in intra-hospital relations. The morale of the School was at low ebb." According to Darling, "there was little professional cooperation. Departments, and even individuals, at times, acted as completely isolated units. Personal animosities, both suppressed and expressed, reached extraordinary potentials. This was true not only within the School but between units of the School and other sections of the University."

As Dean Burrow has noted in his history (from which I have garnered much of this information), while YSM was having its problems, there was still a shortage of physicians, and many Connecticut citizens felt that it was very difficult for Connecticut applicants to get into YSM, the only medical school in the state. At the time, there were 1,500 applicants and the entering class was only 65. Accordingly, there was a widespread public feeling, particularly in Hartford, that there was a need for a second medical school in Connecticut. Yale opposed the idea of a new medical school, dropped any idea of abandoning or downsizing YSM and agreed to increase the size of its admitting class, just about the time there were Fed-

eral stimulus funds to increase the size of medical school classes across the country. However, politicians jumped on the idea of building a new medical school and hospital near Hartford. The legislature appointed a study group and soon \$12 million was appropriated to start it and in 1961, after the appropriation of considerably more millions, the University of Connecticut Health Center (medical school and hospital) was opened in Farmington, just west of Hartford.

In spite of the financial crisis, Darling felt that a solution for YSM was imminent. In his 1949 Alumni Day address, President Seymour committed the University to the support of the medical school. "Alumni of a generation ago not infrequently raised the question as to whether Yale could afford a medical school. Today, I am here to say that the school, in its prestige and its service is an essential and vital part of Yale. We cannot afford to omit any effort that would increase such prestige and heighten such service." When A. Whitney Griswold became President of Yale in 1950, he told a meeting of the Board of Permanent Officers in November 1950 that the administration was attempting to achieve economies in operations and trying to increase the endowment. Soon thereafter, the Corporation authorized an increase of 15 students in the YSM entering class. Still, rumors of the medical school's demise persisted and in a July 1951, Walter Winchell essentially said as much in a radio broadcast. Darling sent him a telegram that said, "It is reported you said Yale School of Medicine would close after next semester...Contrary to your report, entering class in the fall will be enlarged from sixty-five to eighty and the school will definitely not close now nor in the future."

Dr. Howard Spiro told me that President Griswold, in a personal conversation with him, claimed that he (Griswold) had prevented the demise of the medical school. While there is much truth in that claim, a number of things converged to rescue the medical school. The clinical faculty agreed to see more private patients and assign the money raised to the Clinical Research and Teaching Fund, some of which found its way into departmental budgets. The University was able to help NHH collect more of what was owed to it by patients and governments and thereby was able to reduce its subsidy to the hospital and give more to the medical school. Meanwhile the National Science Foundation (NSF) was established by Congress in 1950 as an independent federal agency "to promote the progress of science; to advance the national health, prosperity, and welfare; to secure the national defense." Grants were made to universities and research institutions and that helped Yale, although it received less than it had hoped because both the University and YSM had very limited laboratory space in which to conduct the research, but it served as a stimulus to improve its laboratory facilities and its scientific faculty. In 1930 the U.S. Public Health Service (USPHS) created a division which later became the National Institute of Health (NIH) and by the 1960s was giving universities and research institutes grants for medical and health research and that became a major support for Yale, especially a little later when overhead allowances were increased. Dean C.N. Hugh Long thought that the national policy of spending increasingly larger amounts of money in the hope of finding cures for diseases like cancer was not sound. He was also concerned that "The present emphasis on research as the sole criterion for academic advancement is not encouraging to those who believe that a teacher should teach and a clinician be at the service of the sick." The Korean War (or as some preferred to call it, "Conflict") started in 1950. Although the need for physicians increased, the medical schools did not accelerate their programs because they felt that the accelerated program in WW II had caused a lowering of standards, but, as previously noted the Federal government did provide financial incentives to increase the size of medical school classes.

In 1952, Griswold appointed Vernon W. Lippard, MD, an YSM 1929 graduate, who specialized in pediatrics but had served as dean of the medical school of Louisiana State University and then the University

of Virginia School of Medicine. He was the first full-time dean at YSM, and was also appointed as Professor of Pediatrics. He insisted that the position of Darling as director of medical affairs be folded into his position as dean. He appointed Arthur Ebbert, MD, as a deputy dean and retained Thomas R. Forbes, PhD, as dean of admissions. Lippard's most significant appointments (in relation to the cancer program) were of Paul B. Beeson, MD, as chair of internal medicine in 1952 and of Arnold D. Welch, MD, PhD, as chair of pharmacology in 1953. In 1953, the West Haven Veteran's Administration Hospital (WHVAH) opened and provided a great many teaching beds for YSM students at no cost to the medical school and in fact provided a significant number of faculty salaries to physician-educators working at the WHVAH. With the building of the Memorial Unit of GNHCH in 1953 and its coordination with the New Haven Dispensary, additional clinical teaching opportunities became available. With better lines of communication between the faculty, department chairs, the dean's office and the University, and with 15 additional students, financial problems were overcome and the school began to prosper. Thus, the YSM resurrection by Winternitz that was almost lost because of the post-WW II problems, was overcome by the University, a new dean, new chairs and the national commitment to scientific and medical research, in which Yale learned to excel. (According to Dean Alpern, YSM now is fifth in NIH grants and second in grants per full-time faculty member, brings in 40% of the revenue of Yale University, occupies 20% of its space and represents 60% of the faculty and derives only 2% of its income from student tuitions).

It may be useful at this point to interrupt our history of the YSM and look at its partner hospital and other hospitals in New Haven.

Yale-New Haven Hospital (YNHH) is the lineal descendant of the General Hospital Society of Connecticut which was chartered in 1826 to establish a hospital and "as an auxiliary to the Medical Institution," but it did not open its doors until 1833. It was the fourth voluntary hospital in the U.S., having been preceded by the Pennsylvania Hospital in 1751, the New York Hospital in 1771 and the Massachusetts General Hospital in 1810. (Most of the information is derived from General Hospital Society of Connecticut: Centenary, 1926; Murphy W, A Leader of Substance: Yale-New Haven Hospital at 175 Years, 2001; The Hospital of St. Raphael: Answering the call to care for more than 100 years, 2008; and Toby Appel, Shari Laistand & Allison Carbonari, New Haven's Hospitals, Exhibit at the Cushing/Whitney Medical Library in 2000, accessed: <<http://info.med.yale.edu/library/exhibits/hospitals/beginnings.html>>, and from where I have borrowed information, sometimes verbatim text; and additional material made available to me by Susan Dee, YNHH Archivist and Katherine Krauss Murphy, Associate Director of Marketing and Communications), and for its more recent history, my own personal experience and knowledge as a member of the staff.

It took several years to raise enough money for a hospital in a port town with a population of less than 10,000. Of the ten founding members of the General Hospital Society of Connecticut, five were Yale faculty. The four Yale medical faculty members, Thomas Hubbard, a rural practitioner, obstetrician and surgeon; Eli Ives, a pediatrician; Jonathan Knight, a surgeon; and Nathan Smith, a physician and surgeon and the acknowledged leader of the group, each pledged ten percent of their annual income or a minimum of \$100 a year for five years, a considerable sum for that period; (the other founding faculty member, Benjamin Silliman, was a chemist [Professor of Chemistry and Natural History] and not a physician). The physicians also agreed to treat all hospitalized patients at no charge. (Nathan Smith died in 1829 before the hospital actually opened its doors for patient care in 1833). The Connecticut Medical Society donated the examination fees it collected from medical graduates. The U.S. government agreed to allow the hospital to receive the port fees paid by sailors in New Haven in return for free medical care and infec-

tious disease treatment. Citizens of New Haven and surrounding towns made contributions and the State of Connecticut donated \$5,000, so the hospital was sometimes called State Hospital. On a seven acre plot a building was constructed for \$13,000 capable of accommodating 75 patients. Indigent patients were treated at no charge and the hospital filled slowly. In 1862, during the Civil War, the U.S. military leased the hospital, renamed it Knight Hospital, in honor of Dr. Jonathan Knight, one of the founders who was still active, and built temporary quarters that accommodated 1,500 patients.

After the war, the hospital resumed its former quarters and name, but in 1872 had to expand and add 126 beds to meet the needs of its patients and a dormitory for the Connecticut Training School for Nurses. In deference to common usage, in 1884 the hospital officially became the New Haven Hospital (NHH). Although the hospital admitted community physicians to their staffs who were not affiliated with the Yale Medical Institution, it restricted the number of Jews, Catholics (especially Italian Catholics) and allowed no women or African-American physicians. This may be one of the reasons that no African-Americans graduated from YSM between 1903 and 1948 (although two were in the class of 1911, they did not graduate) while nine African-Americans had graduated with an MD in the previous century, the first being Cortlandt Van Rensselaer Creed, MD, in 1857 (see Daryl Keith Daniels, African-Americans at the Yale University School of Medicine: 1810-1960, YSM thesis). The first female MD candidate, Louise Farnam, was admitted to YSM in 1916. The first African-American to graduate from YSM in the 20<sup>th</sup> century was a female, Beatrix McCleary, MD, in 1948. It should be remembered that Yale and New Haven were relatively tolerant of African-Americans, Catholics and Jews immediately after the Civil War, but the United States became increasingly intolerant after about 1900 and severely discriminatory after World War I and well into the 1930s until the U.S. was drawn into World War II in December 1941. Attitudes started to change then, although African-Americans were still segregated in the military until President Truman integrated the armed services after World War II.

The Chief Executive Officers (Presidents) of Yale New Haven Hospital were:

Albert W. Snoke, MD	1946-1967
Charles B. Womer	1967-1976
C. Thomas Smith	1977-1991
Joseph A. Zaccagnino	1991-2005
Marna P. Borgstrom	2005-

It should be noted that after Dr. Snoke, none of the presidents of YNHH were physicians. Accordingly, the responsibility for the quality of care on the University Service was delegated to the Chief Medical Officer (CMO) more commonly called the Chief of Staff (COS). Originally there was a COS only for the Grace-New Haven Community Hospital (GNHCH) General Service because Dr. Snoke was the CMO of the University Service. Later, after the affiliation agreement when it became YNHH, the single COS was also the bridge between the community physicians (part-time YSM faculty) and the full-time YSM faculty and it was his job to moderate the sometimes stormy relationship when resources did not meet the needs of both groups, such as operating room availability, operating times, and intermittently, a moratorium on appointments in a particular specialty or subspecialty. The position requires great judgment and considerable tact to keep the staff and hospital relations as smooth as possible.



The Chiefs of Staff of Yale New Haven Hospital were:

Luther K. Musselman (General Service)	1949-1959
Courtney C. Bishop	1960-1973
Lawrence K. Pickett	1973-1981
John E. Fenn	1982-1993
Edwin C. Cadman	1994-1999
Peter N. Herbert	2000-

We will return to the NHH later and watch its evolution to Yale New Haven Hospital (YNHH) and the major institution it is today, listed in the top 20 in the U.S.

### **OTHER HOSPITALS:**

Grace Hospital (GH) was organized as a response to the exclusiveness of the NHH in excluding women, most Jews and Catholics (especially Italian Catholics) from its staff. It was chartered in 1889 and all its incorporators were members of the Connecticut Homeopathic Medical Society and/or the Connecticut Eclectic Medical Society. Among them were two women. It was organized as a charitable hospital and invited all licensed physicians to join the staff and admit patients. In 1895, it established a training school for nurses. Homeopathy was very popular at the time in many cities and the large Hahnemann Hospital in Philadelphia was named for the German founder of the idea. The Yale physicians would not participate because they regarded homeopathy as an unscientific cult, bordering on quackery. Nonetheless, the hospital grew to 100 beds by 1906, while the NHH had 190 beds by then. Later, we will learn about its merger with the New Haven Hospital to form the Grace New Haven Community Hospital (GNHCH).

The Hospital of St. Raphael (HSR) had its origin in New Haven in 1907 largely through the leadership of Dr. William F. Verdi (a graduate of Yale Medical School in 1894, an assistant in obstetrics, gynecology and surgery from 1896 to 1906). According to a note on page 16 of the published history of HSR at 100 years (cited above), “unfortunately, as an Italian-American and a Catholic, Verdi was not accepted at New Haven’s existing hospitals, particularly New Haven Hospital. Anti-Catholic discrimination was not just common, but rabid at the time.”

Verdi led a group of 14 physicians who invited the Sisters of Charity of St. Elizabeth in New Jersey to open a hospital in New Haven “to receive and care for all patients who might apply for admission without regard to creed or race,” and “to extend charity to the sick poor and to offer the institution to those of the medical profession who wish to care for their own patients.” They named their new hospital after St. Raphael, the archangel who was the second in the biblical hierarchy of angels and who was sent to restore Tobit’s sight and to free Sarah from the dominance of the evil spirit and thereby became the symbol of health. In the Bible, God is the great healer (“Rofeh” in Hebrew). El was the high God of the Canaanites and his name became the generic name for God in the area. So, Rofeh plus El became Raphael, which roughly means, God heals. The concept of the three professions derives from the religious obligation to serve God and mankind. Thus, professionals have to put the welfare of those they served, above their own welfare: clergy for their followers, lawyers for their clients and physicians for their patients. Hospitals derive from Hospices which were lodgings for travelers who were ill and the institutions were generally maintained by a religious order. Hospice now refers to a residence for end-of-life care. (We will discuss a New Haven hospice later). By 1921, the HSR had 180 beds, GH had 150 beds and NHH had 250

beds. Yale would not affiliate with HSR because it was church controlled. The Yale affiliation had to be with the NHH. In 1972, YSM and HSR worked out a formal affiliation that allowed Yale house staff and fellows to rotate through some of the services at HSR whose chiefs were selected by a search committee which included YSM senior faculty.

The success of HSR had an important influence on the NHH. It forced it to open its staff to all qualified physicians regardless of creed but not yet color. The 1913 agreement of YSM with NHH opened the hospital wards in 1914 to white medical students, but not to African-American medical students, physicians, nursing students or nurses. It was not until YSM admitted its first 20<sup>th</sup> century African-American student who actually graduated (Beatrix McCleary, YSM 1948) that the color line for professionals was ended. However, the presence of HSR in 1907 had at least opened an avenue for qualified physicians to take their patients to HSR if the full-time faculty at NHH dominated the available time in the operative suites, or in admissions during the winter months when infectious diseases tended to keep bed occupancy to near maximal levels, or when NHH had a periodic moratorium on appointments in a particular specialty. Interestingly, Dr. Verdi is listed in the annual reports of NHH from 1907 to 1918 as an attending physician, and from 1911-1957 as a member of the board. He is listed by YSM as a Clinical Professor of Surgery from 1919 to 1942 and Emeritus in Surgery 1942 until his death in 1957.

The West Haven Veterans Administration Hospital (WHVAH) was formed after World War II as an outgrowth of the "Dean's Committee Hospital System" for select VA hospitals that were near and could affiliate with medical schools. As described by Yesner (Yesner R, Yale J Biol Med 1998; 71:397-408), "The medical school would be responsible for the medical aspects, and the VA for the administration. The Newington (Connecticut) VA Hospital, built in 1925, thirty-five miles from Yale, was accepted by Dean Francis Blake as an affiliated hospital until a new VA Hospital could be constructed adjacent to the medical school. However, it became clear that parking would be a problem with this plan, so the Yale-owned Winchester property in West Haven, Connecticut, was sold to the Veterans' Administration as the site for the new hospital. That sale, together with other gifts, provided the money that Yale needed for its own post-war construction program. The new WHVAH was designed to be a 500-bed general hospital and a 400-bed tuberculosis hospital." It opened in 1953. Cancer therapy was surgical if possible, but some patients with tumors treatable with radiation therapy were sent to Yale. In 1965, Rose Papac, MD, was appointed as the first chief of hematology/medical oncology at WHVAH. She initiated the use of chemotherapy there. Hematology and oncology fellows rotated through the service which was a highly prized rotation because of the excellent teaching. As clinical trials became available, VA patients who fit the criteria and were willing to participate were entered on Yale protocols. In 1991, Papac returned to the YSM main campus and John C. Marsh, MD, became Acting Chief of Medical Oncology/Hematology and Director of the WHVAH Cancer Center from 1991 to 1993, when he returned to the main YSM campus. Edward Chu, MD, became the new chief when he came to YSM in July 1996. Under his direction WHVAH continued to participate in YSM clinical trials, but began to initiate some of its own that seemed more attuned to the particular distribution of diseases encountered at that institution. He also initiated the participation of WHVAH in the American College of Surgeons (ACoS) Committee on Cancer (CoC) Program and he asked me to be a consultant to that program. It has been a gratifying association which I continue to the present. In 2004, Chu was appointed Chief of Medical Oncology at the main campus and Michal Rose, MD, became the third chief of the Cancer Program at the WHVAH. Under her direction and with outstanding leadership by the Tumor Registrar, Donna Connelly, CTR, the program was credentialed in 2005 with a commendation, and in 2008, was awarded an Outstanding Achievement Award (OAA) for having earned a commendation in each of the eight areas in which it was offered. The

OAA is designed to recognize cancer programs that strive for excellence in providing quality care to cancer patients. A total of three hospitals in the U.S. received the award for 2008 and only one the previous year. Only one other hospital in Connecticut has ever been honored with the award. As of the end of 2008, the hematology/oncology staff at WHVAH consisted of Michal Rose, Herta Chao, Lisa Rome, Manuel Rosado and Stephen Wrzesinski.

While the HSR and NHH continued to grow and develop dedicated medical staffs, GH, which had changed its name to Grace Community Hospital (GCH) did not. Its leadership contemplated affiliation with NHH in 1925, but its staff refused to do so. In 1945, faced with deteriorating facilities and a growing debt, the GCH medical staff agreed to merge with NHH to form Grace-New Haven Community Hospital (GNHCH). As a result of the merger, there were parallel staffs, the University Service and the General Service. In 1951, the chiefs of the University Service included: Francis G. Blake in Medicine; Gustaf E. Lindskog in Surgery; Milton J.E. Senn in Pediatrics; Fredrick C. Redlich in Psychiatry; Herbert Thoms in Obstetrics and Gynecology; Arnold H. Janzen in Radiology and Averill A. Liebow (a protégé of Winternitz) in Pathology. On the General Service, the chiefs were: Theodore S. Evans in Medicine; Lewis C. Foster in Surgery; William R. Wilson in Pediatrics; Luther K. Musselman in Obstetrics and Gynecology and Robert M. Lowman in Radiology. The Grace School of Nursing became the Grace-New Haven School of Nursing. It continued until 1975, when it was closed because of a growing preference for a baccalaureate program rather than a diploma program.

The New Haven Dispensary formally merged with GNHCH in 1951. In 1953, an eight story 442 bed Memorial Unit (MU) was opened as the centerpiece of GNHCH and Yale University signed a Joint Declaration of Policy with the hospital. This linked the two institutions, and although they retained separate governing boards, it set the stage for an academic medical center. YSM would appoint the chiefs of all GNHCH clinical services from its full-time staff and the community staff would elect its own chief of each of the clinical services it staffed, who would be community physicians with a Yale part-time faculty appointment and GNHCH admitting privileges. In 1965, a new affiliation agreement between Yale and GNHCH resulted in a name change to Yale-New Haven Hospital (YNHH) and the consolidation of hospital and medical school clinical departments of medicine, surgery, obstetrics/gynecology and pediatrics. Each department would be headed by a single chief who was also a full-time clinical chairman, and the assistant or associate chief would be a community physician acceptable to the chairman. Yale University was granted the privilege of nominating up to one-third of the members of the hospital's Board of Directors. The agreement recognized the community service and patient service responsibilities of the university teaching hospital and the preservation of the role and responsibility of the community physicians. The hospital medical board includes the chairs of all services and associate chiefs and a group of community physicians at large who are periodically elected to the medical board, and the chair of that board rotates between a full-time and a part-time faculty member.

As the hospital census grew and beds in the old New Haven Unit were closed, a new South Pavilion was opened in 1982 attached to the Memorial Unit (East Pavilion). When additional beds were needed and the pediatric service increased in size, the Yale-New Haven Children's Hospital (West Pavilion) was opened in 1993. In 2009, the fourth pavilion, the Smilow Cancer Hospital (North Pavilion) opened and almost all inpatient and some outpatient cancer care will be concentrated in that facility.

The Cancer Program at Yale dates back to 1896 when Arthur Wright, a physicist at Yale's Sloane Physical Laboratory produced the first X-ray in the United States and 1901 when Ross Harrison, MD,

PhD, professor of anatomy and biology, developed the first methods for growing tumor cells in flasks on nutrient media that led to an understanding of how tumors develop and grow. He also produced work on the explanation of the neurons for which he was voted a Nobel Prize in Physiology or Medicine, but it was never awarded because of the outbreak of World War I. In 1922, Francisco Duran-Reynals, MD, succeeded in producing different types of sarcomas in animal models by overcoming the species barriers of certain oncogenic viruses. William U. Gardner, PhD, did studies on steroid hormones and their role in experimental carcinogenesis that led to the production of mouse tumors, including the lymphomas used by Goodman, Gilman and Dougherty to study nitrogen mustard in 1942. In 1973, George Palade, MD, came to Yale where he became the chairman of the new Department of Cell Biology. His wife, Marilyn Farquhar, PhD, also an outstanding scientist, came with him to work in cell biology and she was given a secondary appointment in pathology. In 1974, Palade shared the Nobel Prize in Physiology or Medicine with Albert Claude and Christian de Duve. The awards committee said that the three had been “largely responsible for the creation of modern cell biology.” Here, Palade continued the pioneering studies he developed at Rockefeller University using electron microscopy and relating it to biochemistry to discover tiny structures within cells and to discern their functions. He discovered the ribosome, the cell’s protein-making factory, and helped explain the way proteins are transported out of the cell, as when a pancreatic cell secretes insulin. Such discoveries later proved useful in understanding diseases and in the protein production that is the basis of the biotechnology industry, which has produced powerful tools to treat a variety of cancers.

The Cancer Committee (CC) at YNHH was established in 1931 to oversee the developing cancer program. In 1930, the American College of Surgeons (ACoS) Committee on Cancer (CoC) first released its standards and in 1931 the first CoC accreditations were released. According to Asa Carter of the ACoS, YNHH (then NHH) is listed as accredited in 1932, although she points out that there was a delay in confirming accreditation decisions by the Committee and the NHH may have been part of the first group that was accredited in 1931. It has been accredited at all renewals since then. Mss. Paula Omara, Stephanie Hudson and Laura Sims-Olson as CC coordinators were of great help to the committee and to me and bore much of the burden of compiling the annual Cancer Program Reports for the ACoS-CoC. In 2004, commendations were introduced and YNHH received accreditation with commendation in 2004, 2007 and 2010 (although it was my intention to end this story with December 2008, it has taken so long to gather, verify and write this that I am taking the liberty of mentioning the fact that in 2010 YNHH and its CC received six commendations of a possible 10). The CC was usually under the chairmanship of a surgeon from the 1930s until the 1970s. In those days, cancer was considered primarily a surgical disease and the main business of the CC was its oversight of the tumor registry. The first medical oncologist (of whom I can find a record) to chair the CC was John Marsh, MD, who was chair 1977-80 and remained a member of the committee until his retirement in 1998. In the 80s, the section of medical oncology grew and some members began to stake out areas of special interest and expertise, especially in breast and gastrointestinal cancer, and wanted to coordinate with experts in other disciplines. This was the beginning of interdisciplinary tumor boards and the CC began its role in the support and regulation of the tumor boards.

The Cancer Program of YNHH underwent a major change in 1993. With the departure of the oncologic surgeon and CC Chairman, Dr. T. Ravikumar, YNHH administration asked Dr. Vincent DeVita, the newly appointed Director of the Yale Comprehensive Cancer Center (YCCC) to assume the role of Chair (note that I use the abbreviations YCCC and YCC for Yale Cancer Center interchangeably, because it has been so used in public statements). Several meetings of the committee were devoted to the organizational

status of the committee and a broadened role in both the affairs of the Hospital and the Cancer Center mission. Since the ACoS bylaws allow for, and even encourage institutions designated by the National Cancer Institute (NCI) as Comprehensive Cancer Centers (CCC), to integrate the functions of the cancer committees with the Executive Committee of the Cancer Center, permission was requested of the ACoS and YNHH to do this and was granted. The bylaws of YNHH were amended to specify the charge of the CC. Since then, each new Director of the YCC has been chair of the committee.

The newly enhanced Cancer Committee had a large infusion of new people in 1993, including: Drs. Samuel Bobrow, community medical oncologist; Darryl Carter, pathologist; John Concato, medical oncologist; William Crede, general internist and part-time Director of Quality Assurance; Vincent T. Devita, Jr., Director YCCC and chair of the committee; David S. Fischer, former community medical oncologist, now volunteering part-time at YCCC; Gary Friedlaender, orthopedic surgeon; Morton Glickman, diagnostic radiologist; Nina Horowitz, community general surgeon; Clarence Sasaki, otolaryngologist; Barbara Ward, surgical oncologist and Mr. Brian Condon, Senior Vice President of YNHH;. This new group joined those who remained on the previous CC and included: Mr. Stephen Bencivengo, diagnostic radiology administrator at YNHH; Ms. Constance Donovan, oncology nurse specialist; the husband and wife team of Drs. Diana Fischer, tumor registrar and James Fischer, therapeutic radiologist, respectively; C. Friedman, otolaryngologist; Bruce Haffty, therapeutic radiologist; Ms. Bonnie Indeck, social worker; Drs. Diane Komp, pediatric hematologist; John Marsh, medical oncologist; Charles McKhann, surgical oncologist; Ms. Marion Morra, YCCC administrator; Drs. Joseph Piepmeier, neurosurgeon; Ronald Salem, surgical oncologist, Peter Schwartz, gynecologic oncologist. This group was quite effective because most of the members were fairly senior in their specialties and could make decisions and commitments. It was very helpful to have Mr. Brian Condon, an YNHH senior V.P. because he could usually speak for the institution without having to go back for instructions, and CC decisions could become institutional decisions.

The role of the Cancer Committee is to have the institution's clinical program consistent with the standards for a cancer program as promulgated by the CoC of the ACoS and to help the administration and staff improve cancer patient care. Unlike the Joint Commission on Accreditation of Healthcare Organizations (JCAHO), recently renamed The Joint Commission (TJC), whose stamp of approval is used by most states as a condition for licensure and by Medicare and Medicaid as an approved institution for federal funds, the accreditation by ACoS-CoC is simply an endorsement of the quality of the hospital's cancer program, but one that is voluntarily and eagerly sought as proof of quality. Accordingly, the CC supervises the hospital's tumor boards (YNHH now has 11) to make sure that their patients' care is examined by an interdisciplinary group of board certified cancer specialists (usually including surgeons, medical oncologists, radiation oncologists, pathologists and diagnostic imaging specialists). The role of this interdisciplinary group is to determine the stage of the patients' cancer according to the latest edition of the American Joint Committee on Cancer (AJCC) Cancer Staging Manual which has been coordinated since the 1980s with the classification of the International Union for Cancer Control (UICC). The primary job of the tumor board is to make sure that appropriate tests are done to develop a clinical stage and then to recommend a therapeutic program largely (but not entirely) based on that stage of the disease so that the patient will not be treated based on which specialist was first encountered. The CC serves a secondary role as an educational forum using the case system for teaching house staff, fellows, nurses, faculty, etc and 75% of the cases presented must be prospective. Additional activities of the CC include improvement of the quality of cancer care and assurance of the quality of that care; educational outreach to the community with lectures, symposia; patient and family support groups, etc.; and supervision of the

tumor registry and assurance of its quality.

By 1997 the activity of the committee had become such that it was becoming a burden to the Director who was busy with a multitude of other problems including plans for a consolidated Cancer Center building. Accordingly, Dr. DeVita asked Dr. David Fischer to become the vice-chairman and oversee its day-to-day commitments. This was unanimously approved by the full CC. To have better coordination of the CC with YSM, Dr. Lawrence Cohen, special advisor to the dean, was invited to join the committee (and when he had to leave, Sally Rockwell, PhD, associate dean became the liaison). In 1999, Arthur Lemay, RPh (formerly director of the pharmacy), was appointed to the CC from YNHH administration and in 2000, Ms. Teresita Vega, our first Certified Tumor Registrar (CTR), joined the CC from the tumor registry. When Dr. Richard Edelson became Director of YCC in 2003, he became chair of the CC and asked Dr. Fischer to remain as vice-chair. When Dr. Frank Detterbeck was recruited in 2005 as Chief of Thoracic Surgery and Associate Director of Clinical Affairs, he was also appointed as a co-vice-chair. In 2004 Mr. Condon retired and Mr. Lemay became the main representative of YNHH and Dr. Diana Fischer retired and Ms. Vega became the Tumor Registry Manager.

The members of the Cancer Committee in 2008 were:

Baehring, Joachim	Neurosurgery
Beaulieu, Nancy	Outpatient Pharmacy, Y-NHH Oncology Service
Bobrow, Samuel	Medical Oncology (community physician)
Carafeno, Tracy	Y-NHH Chemotherapy Use Committee
Cheng, David	Diagnostic Radiology
Chu, Edward	Medical Oncology
Crede, William	Quality Assurance
Detterbeck, Frank	Thoracic Surgical Program, vice chair
Edelson, Richard	Yale Cancer Center Director, chair
Fiore, Denise	Y-NHH Radiology and Laboratory Medicine
Fischer, David S.	Medical Oncology, vice chair
Flatow, Fred	Connecticut Hospice
Ford-Flanel, Debbie	Y-NHH Clinical Nutritional Services
Friedman, Louis	Rehabilitation Services
Glazer, Peter	Therapeutic Radiology
Gomes, Maria	ACS Observer
Grasso, Judith	Oncology Nursing
Goszewski, Susan	Rehabilitation Services
Indeck, Bonnie	Social Work
Kupfer, Gary	Pediatric Hematology/Oncology
Lannin, Donald	Surgical Oncology, Breast Service
Lemay, Arthur	Y-NHH Administration
Lewis, Margaret	Y-NHH Religious Ministries
Lindskog, Dieter	Orthopedics and Rehabilitation
Lopman, Abe	Y-NHH VP, Executive Dir. Smilow Cancer Hospital
Mande, Jerold	Cancer Center Policy
Mani, Sheida	Therapeutic Radiology
Miller, Kenneth	Pain Control/Palliative Care, Oncology Services
Roth, Norman	Y-NHH Sr. VP Hospital Administration

Salem, Ronald	Surgical Oncology
Sanchez, Tahiry	Patient Services, Nursing
Schwartz, Peter	Gynecologic Oncology
Silber, Andrea	Medical Oncology (community physician)
Sinard, John	Pathology
Snyder, Edward	Y-NHH Blood Bank
Starick, Kathleen	Oncology Nursing
Tavassoli, Tanya	Pathology
Vega, Terri	Tumor Registry

Therapy of cancer with drugs began to increase in some institutions after W.W. II. The earliest such demonstration (not counting that by G.T. Beatson in the *Lancet* 2:104-107, 162, 1896 who demonstrated that bilateral oophorectomy could lead to remissions of advanced breast cancer) was in 1939 when Charles Huggins at the University of Chicago treated men with prostate cancer with hormones and/or castration and showed responses. The big breakthrough was the treatment with chemicals of lymphoma with nitrogen mustard by Goodman, Gilman and Lindskog here in 1942-43. The next exciting use of chemicals was the demonstration by Sidney Farber at Harvard's Children's Hospital in 1947-48 of the benefit in childhood leukemia of the folate antagonist, aminopterin (and later, a less toxic antifolate, methotrexate). In 1955, Min C.Li, Roy Hertz and D.B. Spencer at the NCI, showed that methotrexate was capable of actually curing most early cases of choriocarcinoma (a trophoblastic tumor), not merely shrinking them. In 1957, at the University of Wisconsin Charles Heidelberger synthesized 5-fluorouracil and Anthony Curreri (a surgeon) and Fred Ansfield (an internist), showed the activity of this drug in colorectal cancer. However, there was no significant change in survival from clinical cancer therapy until Ezra Greenspan et al., at the Mt. Sinai Hospital in New York in 1963 reported that a combination of two drugs used to treat breast cancer led to a dramatic increase in response rates. Frei and Freireich et al. the NCI, Holland et al. at Roswell Park with the Acute Leukemia Group B and Pinkel, et al. at St. Jude's Children's Cancer Hospital used combination chemotherapy to obtain complete remissions (potentially "cures") in childhood lymphocytic leukemia. When Vincent DeVita, et al. at NCI showed in 1970 that a 4- drug combination with the acronym MOPP could produce complete remissions in up to 50% of patients (potential "cures") with Hodgkin's Disease, this was another proof in principle that at least two cancers could be "cured" with drugs and accelerated the rapid growth of combination chemotherapy.

A history of the Yale cancer program would be incomplete without at least briefly mentioning a little more about the Department of Pharmacology at Yale that led to its worldwide reputation. As described by Arnold Welch, the chairman: over the years, many of the group received various honors and special appointments, e.g. Career Development Awards, Scholars in Cancer Research awards, Markle and Burroughs-Wellcome scholarships as well as career professorships. The department grew rapidly, in part because of the early financial help that came in the form of no-strings attached grants from either the Squibb Institute for Medical Research or the Upjohn Company where Welch had been a consultant for eight years. With the initial success from early financing, Welch said that additional funds were relatively easy to obtain, especially since, in addition to outstanding research the department gained a deserved reputation for good teaching of medical students (often in small discussion groups). Many medical students chose to do their senior thesis with a member of the department. A major emphasis of the department was the training of graduate students, while offering an excellent atmosphere for post-doctoral training in excellent facilities. I remember the \$500,000 grant from Burroughs-Wellcome (pharmaceutical company) to renovate the pharmacology laboratories because it made the newspapers. I have no idea how much

money was received from other commercial donors.

The chairmen of Pharmacology were:

William T. Salter	1941-1952
Arnold D. Welch	1953-1967
Nicholas Giarman	1967-1968 (acting)
William H. Prusoff	1968 (acting)
Murdock Ritchie	1968-1974
Robert Handschumacher	1974-1977
Alan C. Sartorelli	1977-1984
John Perkins	1984-1989
Leonard K. Kaczmarek	1989-1998
Alan C. Sartorelli	1998-2000
Joseph Schlessinger	2000-

Arnold Welch, MD, PhD, came to Yale in 1953 to become the second chairman of the Department of Pharmacology at YSM after William T. Salter died during his term of office. Welch had studied folate metabolism and antifolates as anticancer agents at Western Reserve University in Cleveland and brought with him William Prusoff and Charles Carter, two outstanding researchers. He soon hired a remarkable group of additional investigators, including, Alan Sartorelli, Robert Handschumacher, Glenn Fischer, M.Y. Chu, Van Canellakis, S.-H Chu, Nicholas Giarman, Jack Cooper, John Vane (who later received a Nobel Prize), Henry Mautner, Julian Jaffe, Charles Nichol, Jack Green, Paul Hagen, David Ludlum, Norman Gillis, David Johns and others. Joseph Bertino soon joined that illustrious group. As the first department of biochemical pharmacology, in contrast to physiological pharmacology, it soon gained world-wide recognition.

The contributions by Welch's team were most impressive and I can only mention a few and even then I do them an injustice in summarizing them so briefly.. William H. Prusoff, PhD, synthesized 5-iodo-deoxyuridine (IUDR) in 1958 and studied it extensively. It proved to be a better antiviral than an anticancer drug, and it is used to treat herpes simplex of the eye. Prusoff is generally acknowledged as the father of antiviral chemotherapy. More recently, with the late Tai-Shun Lin, he developed the reverse transcriptase inhibitor, stavudine, licensed to and marketed by Bristol-Myer-Squibb under the trade name, Zerit, for treatment of AIDs infections. It generated substantial royalties for Yale and partially financed the Anlyan research building. Humanitarian that he is, Prusoff was instrumental in arranging for the drug to be made available in Africa at a little above cost while still on patent to help control the AIDs epidemic there. Prusoff was always very generous with his help and mentoring of a great many young people, including me. He has been on many journal editorial boards and honored by learned societies around the world. He has received the Peter Parker award, YU's highest, and the YSM lifetime award and the William Prusoff Professorship was set up in 2000.

Robert Handschumacher, PhD, did outstanding work on a variety of purines and pyrimidines, but his most celebrated work was on the pyrimidine, 6-azacytidine. He also worked on molecular approaches to immunopharmacology and studies of mechanisms involved in the modulation of cancer chemotherapy. He studied the family of receptors for the immunosuppressive drug cyclosporine. He was Director of the Division of Biological Sciences of Yale University and later was awarded a Career American Cancer Society



Professorship. He was chairman of the Pharmacology Department from 1974 to 1977. When the Yale Corporation was considering the appointment of a new president, they considered the fact that a basic scientist had never been president and they narrowed down the choice to three candidates, one of whom was Handschumacher. In the final vote, they decided against a scientist and elected A. Bart Giamatti, PhD, a classicist, who turned out to be a good president, supported science and cancer research, but after many years, he left to become more widely known as the Commissioner of Baseball.

Alan C. Sartorelli, PhD, came to Yale from the McArdle Laboratory at Wisconsin and did pioneer work in combination chemotherapy in animals. He elucidated the concept of bioreductive activation of pro-drugs by oxygen-deficient (hypoxic) tumor cells. He synthesized and evaluated potential anticancer agents, contributed to our understanding of tumor cell metabolism and how it could be deranged by anticancer drug action, worked on the induction of terminal differentiation by anticancer drugs, and characterized the molecular mechanism for some tumor cell resistance to anticancer drugs among many other significant contributions too numerous to detail. He was a co-founder of the Vion Pharmaceutical Company in New Haven and was a major leader in the development of several of their drugs. Sartorelli and David Johns edited a two-volume monograph on anti-neoplastic and immunosuppressive agents that remains a classic in these fields. He was chairman of the department from 1977 to 1984 and 1998-2000. From 1982 to 1984, he was Deputy Director of the YCC and from 1984 to 1993 he was Director of the YCC. In 1984 he was one of the two finalists for appointment as Dean of YSM. He was also American editor of *Biochemical Pharmacology* and executive editor of *Pharmacology and Therapeutics*. He served on the editorial boards of many scientific journals, on many NIH committees and mentored more than 100 graduate students and PhD candidates.

Joseph Bertino, MD, was recruited to Yale in 1961 as an assistant professor of pharmacology from Seattle (where we met as hematology fellows in the laboratory of Clement Finch). Joe spent most of his three years as a U.S. Public Health Service (USPHS) Research Fellow working in biochemistry with Frank Huennekens, studying folate metabolism. He did seminal studies of the mechanisms of resistance to folates and fluoropyrimidines here at Yale. He was promoted to associate professor of pharmacology and medicine in 1964 and to full professor in 1969. He did so many things that only a few can be mentioned here. He pioneered the use of leucovorin rescue following high-dose methotrexate. He developed trimetrexate to an FDA approved drug. He mentored 12 PhD students, one MD-PhD student and over 50 post-doctoral candidates. He was founding editor of the *Journal of Clinical Oncology* and was president of ASCO, 1975-76, among a plethora of other editorships and honors. He was the first Director of the Yale Cancer Center, 1974-1975, but more of that anon.

Joseph (Yossi) Schlessinger, PhD became the William H. Prusoff Professor and Chairman of the Department of Pharmacology after Sartorelli's second stint as chairman. He was born in Croatia and educated at the Hebrew University and the Weizmann Institute of Science in Israel. He took postgraduate training in chemistry and applied physics at Cornell and in immunology at NCI. He was a member of the Weizmann Institute 1978-1991 and then was Chairman, Department of Pharmacology at New York University until he was recruited to Yale by Dean Kessler. He has done outstanding research in the area of signaling through tyrosine phosphorylation, which is important in areas of cellular regulation, especially growth control. His studies have led to an understanding of the mechanism of trans-membrane signaling by receptor tyrosine kinases and how the resulting signals are transmitted within the cell to control cell growth and differentiation. These and other studies of his laboratory have led to drugs to inhibit cancer. In 1991, he co-founded the biotechnology company, SUGEN which developed the drug, Sutent (Suni-

tinib) which was approved by the FDA for treating gastrointestinal stromal tumors and renal cell carcinoma. In 2001, he co-founded Plexxikon which uses a pioneering structural biology-based platform for drug discovery. Plexxikon's experimental compound PLX4032 is in development with Roche and shows great promise in early-stage clinical trials for the treatment of melanoma and is now in phase III trials for melanoma and phase I trials for colorectal cancer. Under his chairmanship, the department has grown in size and stature, and especially in the field of cancer.

The recent cancer program history will be described from documents including the Cancer Center Support Grant [CCSG] Renewal Application for April 1, 2007 to March 31, 2012); medical oncology fellowship records compiled by Savannah Woods and adult hematology fellowship records compiled by Savannah Woods, Richard Carr and Dr. Bernard Forget; YSM archival material in the Historical Library made available by Toby Appel, head librarian; more recent faculty data supplied by Julie Buchanan of the Office of Faculty Affairs; YNHH archival material supplied by Susan Dee and Katie K. Murphy, personal observations and background information from colleagues who were participants or close observers, including, but not limited to, Drs. Alan Sartorelli, William Prusoff, Joseph Bertino, John Marsh, Vincent T. DeVita, Jr, Edward Chu, Ronald DeConti, Malcolm Mitchell, Ronald Salem, Stephen Ariyan, Peter Schwartz, Tish Knobf, Ruth McCorkle, Howard Pearson, Bernard Forget, Robert J. Levine, Richard Edelson, Mss. Marion Morra, and Paula Wilson. Earlier drafts of this article were reviewed by many people who offered corrections and additional information and I am in debt to them, including Drs. Howard Spiro, Howard Pearson, John Fenn, Richard Edelson, Edward Chu, Alan Sartorelli, Joseph Bertino, John Marsh, Michael Kashgarian, Vincent T. DeVita, Jr., William Prusoff, Tish Knobf, Robert J. Levine, Bernard Forget, Gerard Burrow, Thomas Duffy, Mss. Toby Appel, Teresita Vega, Marion Morra, Katie Kraus Murphy, Paula Wilson, Laura Sims-Olson and Sandra Dee. None of these individuals is responsible for any errors of fact or interpretation; I alone am responsible for all such errors. In the nature of a narrative based on personal observation, I will naturally spend more time discussing those events that I know first-hand as a participant or close observer, particularly when I think that they illustrate a more general point, and I do so at the risk of being self-serving and narcissistic, overemphasizing my personal role. I will omit much important information of which I have little or no reliable information, particularly basic science research outside of pharmacology. Dean Burrow's history of YSM ends in 1973, the Yale Historical Library exhibit goes up to 2001, and Falvey's book, of necessity, mentions relatively little about the cancer program as it reviews the first 200 years of YSM. This history will end with 2008 with the exception of a few comments about the Smilow Cancer Hospital at Yale-New Haven and YCCC recruiting. Section II A of the Cancer Program 2008 Annual Report makes some reference to the projected plans and goals for the future. The new Cancer Center Director, Thomas Lynch, MD, outlined his plans and goals for the Smilow Cancer Hospital and YCC in the 2009 Cancer Program Annual Report and will continue to do so in many other forums.

How and why I came to Yale. After graduating from Harvard Medical School in 1955, I became interested in hematology during my internship at the Kings County Hospital (the teaching hospital of the State University of New York School of Medicine in Brooklyn) with mentoring by Herbert Lichtman, MD. He arranged for me to study with Maxwell M. Wintrobe, MD, PhD, (author of Clinical Hematology) at the University of Utah in Salt Lake City while fulfilling part of my residency. There I was first exposed to the use of chemotherapy drugs for the treatment of cancer. (It should be recalled that the original clinical paper describing the first human treatment of lymphoma with nitrogen mustard included seven patients from New Haven and 34 from Salt Lake City; and although the Yale studies using chemotherapy agents ceased in 1943 [except for the cases reported by Taffel as previously mentioned], cancer chemother-

apy studies had continued uninterrupted at the University of Utah). While I was in Utah working with Dr. Wintrobe, I had the opportunity to meet Dr. Goodman, who had become chair of pharmacology there after he had left Yale and then Vermont. Then I spent another year as a medical resident at Montefiore Hospital, an affiliate of the Albert Einstein College of Medicine, where I coauthored my first paper with Jim Javid and Theodore Spaet which appeared in *Blood* in 1959. The Director of the Pathology Service who I first met there was Dr. Harry Zimmerman, of whom more anon. Later, I had a fellowship in hematology with Dr. Clement Finch at the University of Washington in Seattle where I met Dr. Joseph Bertino. I spent a year doing clinical hematology, learning to use radioactive isotopes, primarily of iron, started a study of synthetic chelating agents in iron metabolism (which was finished by another fellow) and I also set up the University of Washington coagulation section in Dr. Finch's laboratory and then I left for two years of Army service. (That interlude gave me an opportunity to sharpen my clinical skills and publish three papers based on unusual cases. A paper on hereditary acropachy included an extensive review of the literature).

Bertino chose to spend his three year USPHS fellowship in the biochemistry laboratory of Frank Huennekens, PhD, where he did outstanding work in the field of folate metabolism. After completing my Army service, I took a clinical position with an HMO in Nassau County, N.Y. which allowed me a day off a week to work at nearby Brookhaven National Laboratory in the laboratory of Eugene P. Cronkite, MD on two independent research projects involving iron metabolism which led to publications with me as senior author and David Price, MD as a co-author (Dr. Cronkite graciously chose not to be a co-author since he had not participated in the actual research). As a result of recent and rapid progress in genetics and DNA research, I felt the need for more basic science training and had discussed doing that at Johns Hopkins Medical School with Dr. Victor McKusick. However, Dr. Bertino, who was then at Yale doing further work on folate metabolism in the department of pharmacology, convinced me to come to YSM as a fellow in the Department of Pharmacology because of its strong biochemically oriented research program of targeted anti-cancer drugs based on inhibitors of DNA and RNA.

Paul B. Beeson, MD, Chairman of the Department of Medicine and Chief of the Medical Service at YNHH, impressed me as a great clinician and investigator and a role model. He was in my humble opinion, second only to Winternitz in making YSM one of the most outstanding medical schools in the U.S. His father, John, was a general practitioner and surgeon for a railroad in Anchorage, Alaska. Paul attended the University of Washington for his undergraduate studies and after three years was accepted to McGill University Medical School, from which his older brother, Harold, and he graduated. He had an internship at the University of Pennsylvania and then joined his father and brother in practice in Ohio. After a short time, he left to do research at the Rockefeller Institute and Hospital in the laboratory of Dr. Oswald Avery, who discovered that DNA is the substance of genetic material. In 1939, Beeson left New York to become chief resident to Soma Weiss, MD at the Peter Bent Brigham Hospital. Weiss was legendary for his research, his brilliance, and for his dedication to his students, and for his concern for his patients as people and this had a profound influence on Beeson as a physician and teacher. Beeson volunteered to work at the Harvard-Red Cross Field Hospital in Salisbury, England during World War II and met Barbara Neal, RN there and they were subsequently married.

Beeson was recruited to Emory University in Atlanta, Georgia in 1942 by Eugene Stead, Jr., MD. There in 1943, he was the first to report that hepatitis could be transmitted by blood transfusion. He studied fever and infection and became the authority in those areas. When Stead became Chairman of Internal Medicine at Duke University in 1946, Beeson became chairman at Emory and served from 1947 to 1952.

While there he met Philip K. Bondy, who became his chief resident and an eminent endocrinologist. In 1952, when Beeson came to YSM, he brought Bondy with him (and Bondy later succeeded him as chairman). Beeson took over a relatively small department of internal medicine populated primarily by generalists, but with a few young specialists who would later develop into distinguished leaders in their fields, including Gerald Klatskin (liver disease), Franklin Epstein (nephrology), Allan Goodyer (cardiology), Frank D. Gray, Jr., (pulmonary disease) and Louis G. Welt (who went on to become Chief of Medicine at University of North Carolina in Chapel Hill and returned to serve as Chief of Medicine at Yale 1972-1974 and literally died in his office). John Plunkett Peters was already renowned for his national leadership in metabolic diseases and he retired in 1955. Before Beeson arrived, practitioners in the area usually referred most of their problem patients to New York or Boston hospitals.

Beeson was a generalist at heart but recognized the necessity of further building up the specialized skills of his staff and in recruiting young physicians with newly acquired specialty training so that problem patients could be referred to YSM. In a relatively short time Beeson recruited Gilbert Glaser (neurology), Howard Spiro (gastroenterology), David Seligson (laboratory medicine), Aaron Lerner (dermatology) Stuart Finch (hematology), William Hollingsworth (a hematologist who Beeson encouraged to become a rheumatologist) and sometime later, Fred Kantor, an allergist and immunologist (who 20 years later became the Paul B. Beeson Professor of Medicine). In a relatively brief time period, Beeson had created one of the premiere departments of internal medicine in the U.S. In his 13 years as chairman, Beeson tripled the number of full-time faculty to almost 70. When the Veterans Administration Hospital opened in West Haven in 1953, he made sure that Yale and the VAH would be closely linked and this partnership provided access to facilities and teaching opportunities that strengthened research and medical education at Yale. House staff began working at the VAH during Beeson's tenure and this raised the quality of care for the veterans and increased the size of most of the disease sections as they integrated with Yale. His sections of dermatology, neurology and laboratory medicine became so large and distinguished that they were later spun off as independent departments. Beeson's personal research was brilliant. He was the first to identify proteins in white blood cells now known as cytokines, particularly IL-1. His interest in and studies of fever and infection were so productive that that they were widely quoted and became frequently cited models of research and many of his trainees and colleagues made that area of study a major part of their distinguished careers, including Robert Petersdorf, , Elisha Atkins, and Phyllis Tuck Bodel. However, there was no section devoted to the study or treatment of cancer (medical oncology).

What distinguished Paul Beeson was not that he was an editor of the first two editions of Harrison's Textbook of Internal Medicine or that with Walsh McDermott, MD, he co-edited five editions of the Cecil-Loeb Textbook of Medicine, but that he was a real doctor. He set a standard as a caring physician and a bedside teacher who by example conveyed to his students and his staff the importance of the patient as a person, as his mentor, Soma Weiss had done. On Tuesday and Thursday mornings, after morning report, Beeson made rounds for two hours with the interns, residents and the students assigned to his service. Except for vacations or out of town medical meetings, he made ward rounds all year long. It was the highlight of a student or a house staff rotation. Beeson would sit down to talk to a patient (so that they would be on the same eye level) and say, "Tell me your story." Or he would sit with the patient to listen as the history, physical examination and relevant laboratory studies were recounted and a differential diagnosis was proposed. He always made sure that the patient was not traumatized by this encounter with the medical staff and that the patient was fully respected, whether at that time, or in a private discussion away from the patient. He was a gentleman and wanted his staff to be good and caring and polite physicians.

Robert J. Levine, MD told me about Beeson's high regard for members of the clinical faculty (part-time teachers) whose primary professional concern was patient care. During Levine's year as chief resident at the West Haven Veterans Administration Hospital, he became aware of two incidents in which Beeson demonstrated his respect for them in very practical terms. Beeson was approached, on two separate occasions, by physicians who had arrived recently in New Haven, one a resident and the other a clinical fellow (as Levine recalls), for advice on which physician they should contact to care for an ailing relative. They were surprised that Beeson recommended they contact a member of the clinical faculty explaining that such physicians, who met the high standards necessary to be appointed part-time faculty and were part-time teachers, devoted most of their professional effort to patient care and were generally more attentive to the needs of the patient than members of the full-time faculty, whose other activities such as research and teaching competed for most of their attention.

Beeson was concerned about the welfare of his students, house staff and faculty above and beyond their education. Somehow, his secretary, Betsy Winters, managed to find a way for the legion of people who wanted to talk to Beeson privately to do so. I remember one day when I asked to see him after he had just returned from Boston and Betsy cautioned me to keep it brief because "he is way behind in his work and he seems depressed." Before I had a chance to state my business, he said, "If there is something you want me to do, today is not a good time to ask. My mind is still in Boston." I respectfully asked if he wanted to talk about it, and he agreed that talking might help. He explained that he had been in Boston as an examiner for the American Board of Internal Medicine (ABIM) and the days seemed long and he had examined quite a few candidates. At the end of the day, he realized that "those that I examined in the afternoon were just as smart and as well prepared as those that I examined in the morning, but I flunked all the afternoon candidates and passed all the morning candidates. They did not really fail the examination, I failed them. I told the chief examiner to change my grades and pass all the afternoon candidates, but he said it was too late and those that I failed would have to repeat the examination at a future time." I suggested to him that I had heard many candidates mention the fact that there was a well known disproportionate failure rate among those examined in the afternoon. That seemed to energize him as he realized that it was a widespread phenomenon and not just his personal failure. He said that he was going to contact the president of the ABIM and get the figures on the rates of failure in the morning and afternoon, but he thought the oral examination was meaningless anyway and should be abolished. It was not fair for young physicians to be put through a totally uncontrolled and unscientific exercise that would do no good and was evidently doing much harm. (Note: The oral examination was discontinued a few years later). He got up, thanked me for listening and told Ms. Winters to reschedule me for a visit later in the week. It was just another example of Beeson caring not only about patients as people, but doctors as people, even doctors he had never seen before and would probably never see again. He was willing to back up his concern with action. Like William Osler and Soma Weiss, Paul Beeson was a role model and the embodiment of the good physician. He left Yale in 1965 to become Nuffield Professor of Medicine at Oxford, one of the most prestigious endowed chairs in the world.

Paul Calabresi, MD, was recruited to Yale in 1959 as a research fellow by Beeson. Calabresi had graduated from Yale College and medical school, had an internship on the Harvard Service at the Boston City Hospital and served as a Public Health Service field investigator and as a project associate in the Department of Medicine at the University of Wisconsin. There he worked with Fred Ansfield (internist) and Anthony Curreri (chair of surgery) in studies of the new drug synthesized by Charles Heidelberger at Wisconsin's McArdle Laboratory, 5-fluorouracil (5-FU), in the treatment of colon cancer. With his background in the use of the pyrimidine, 5-FU, Calabresi soon began to work with that part of Welch's

group in pharmacology that was studying purines and pyrimidines as potential targeted anticancer drugs by interfering with DNA synthesis or action. He worked with several pharmacologists, including Robert Handschumacher, William Creasy, a multitalented biochemist, Alan Sartorelli, Joseph Bertino and with William Prusoff. Calabresi also studied the effects of 5-FUdR on viruses, and its effects on tumors. With Pasquale Perilli and Stuart Finch (then chief of hematology), he studied the use of 5-FU in a variety of cancers. His understanding of the pharmacology and metabolism of cancer chemotherapeutic agents and their toxicity led to his writing a number of review articles explaining this to non-specialists in the profession. He ran clinical trials on new drugs, clarified the superiority of 5-FU by prolonged infusion compared to bolus 5-FU, and developed the drug azarabine (triacyl-6-azauridine) with the dermatologist, Charles MacDonald, for psoriasis, in collaboration with others, but it was recalled from the market because of an increased incidence of thrombotic episodes in a few susceptible individuals with a deficiency of pyridoxal phosphate. Calabresi was also an early supporter of combination chemotherapy in solid tumors as well as combined modality therapy, combining surgery or radiation therapy (notably with Morton Kligerman, the first chairman of radiation therapy at Yale) or with both chemotherapy and radiation therapy when appropriate, in a relatively safe and effective fashion. He was also appointed assistant director of the NCI sponsored Yale Clinical Research Center (CRC). He was certified in 1964 by the American Board of Internal Medicine (ABIM).

Rose Papac, MD, was recruited by Beeson in 1963 to increase the expertise in clinical cancer therapy. She had graduated from St. Louis University Medical School, taken a residency at Stanford University and then went to London to become the first American to take an oncology fellowship position at the prestigious Chester-Beatty Institute where she worked with David Galton, a pioneer in cancer chemotherapy. Returning to the U.S., she went to Memorial Sloan-Kettering Cancer Center to continue her medical oncology fellowship training under David Karnofsky, another one of the pioneers in cancer drug development especially with nitrogen mustard. She was an outstanding clinician, teacher and human being and much beloved by her students and patients. She was a general oncologist with broad knowledge of the literature in many areas of medical oncology, and developed clinical trials in breast cancer, head and neck cancer and lung cancer. She was the first female Professor of Medicine at Yale (Dorothy M. Horstmann, MD became Professor of Epidemiology and Pediatrics in 1961, and was the first female to receive tenure in YSM).

With this strength in cancer chemotherapy and pharmacology, Welch and Beeson established a joint section of Clinical Pharmacology and Chemotherapy in late 1963 with Calabresi as chief, to develop and test new drug treatments for cancer. The section was so respected that Calabresi and Welch were asked to write the first chapter on cancer chemotherapy agents for Goodman and Gilman's Pharmacological Basis of Therapeutics. The CP&C section attracted many young physicians as fellows; the first, was Ronald DeConti, who stayed on as a faculty member and the second was Estelle Lefkowitz, who eventually went into primary care practice because there were no junior faculty positions in oncology available then at Yale and there were, as yet, no opportunities for oncologists outside of academia. Papac later went to the West Haven Veteran's Hospital to head the Yale oncology/hematology program there and continued her work in lung and head and neck cancer and as an excellent teacher, clinician and role model. Calabresi's CP&C section was actually the first section of Medical Oncology in the U.S. although it was not re-named Medical Oncology until 1973. In late 1965, as previously noted, Beeson left to become Nuffield Professor at Oxford. In early 1966, Calabresi was promoted to Associate Professor of Medicine and Pharmacology and coordinator for cancer training in internal medicine at Yale. Later that year he went to the University of Lausanne in Switzerland as a Visiting Scientist. While he was there, Henry Williams, MD, who had

trained at MSKCC with David Karnofsky and Joseph H. Burchenal, and was the first trained medical oncologist in private practice in Connecticut, came down to Yale three times a week from his practice in Hartford, to supervise the section of CP&C, and its three fellows, Ronald DeConti, Malcolm Mitchell and Stephen Kaplan. That was when I first met Williams, of which more anon.

Two of Calabresi's grants were frozen while he was in Switzerland. Philip K. Bondy, MD, then Chairman of Medicine (a renowned endocrinologist and co-author of a standard textbook of endocrinology), was in the Netherlands at the time. According to Dr. Bondy, he was called by the acting chair who had met with the department of medicine executive committee to discuss this sudden turn of events which would create a shortfall in funds to support the section of CP&C and its fellows. The acting chief told Bondy that he had consulted Welch and Handschumacher. Under the circumstances, they suggested that Bondy approach Bertino, who had been an associate professor of pharmacology and medicine for several years, and ask him if he would consider becoming chief of CP&C. Bertino was well-funded and well-known as a productive basic scientist and it was likely that he would be successful if he applied for further grant support for the section. Yale (and perhaps other universities) frequently appointed basic scientists as chairs of clinical departments or chiefs of clinical sections. Bertino agreed to accept the position of co-section chief of CP&C (the section was originally set up to bring together basic science and clinical medicine and Calabresi headed both the section that involved cancer and the non-oncologic studies which involved fewer studies at the time). Although Bertino loved bench research and had been so successful at it that he had done no patient care for seven years and had not even taken the ABIM examination for certification (which made him ineligible for later certification in medical oncology), he was also excited about doing translational research with methotrexate and other anti-cancer drugs because he was a physician. Bondy says that he reluctantly acceded to the suggestion of his departmental executive committee when he was assured of Welch's concurrence in view of Calabresi's close association with Welch. Bondy then traveled to Lausanne to personally explain to Calabresi what had transpired in New Haven and asked Calabresi to remain in the section and to continue as assistant chief of the CRC which paid part of his salary and to continue his oncology research as a member of the department. The leadership of CP&P was then split as it was terminated as a discrete entity. Bertino became chief of a section called Cancer Chemotherapy (which a few years later was called Medical Oncology) which was for oncologic studies and Robert J. Levine became chief of a section called Clinical Pharmacology for non-oncologic studies, which were then becoming more common. When Bertino became section chief of Cancer Chemotherapy, he began to attend in the medical oncology clinic and to serve as an attending on the medical oncology inpatient unit. He tried to assure Calabresi that he wanted him to stay and continue his work and teaching in the section.

In 1967, Welch left Yale to become V.P. at the Squibb Institute for Medical Research. Calabresi returned as a newly appointed associate professor and he remained in the section for a year and one half and then in 1968 he accepted an appointment as Chairman of Medicine at the Roger Williams Hospital and Professor of Medicine in the newly formed Brown University School of Medicine. In 1969 he was elected president of the American Society of Clinical Oncology (ASCO), its sixth president. Calabresi went on to an illustrious career as a leader in medical oncology and was on the committee that wrote the first examination for the ABIM subspecialty in medical oncology which was given in 1973 – accordingly he never took the subspecialty examination. He was appointed chairman of the National Cancer Advisory Board by President H.W. Bush in 1991 and then he was appointed to the President's Cancer Panel by President William J. Clinton in 1995. George W. Bush appointed him to serve on the National Dialogue on Cancer. He served on many boards, committees and advisory panels of many organizations, but the two he seemed to like the best were ASCO and the New England Cancer Society (NECS) and he served both as

president in separate years. At his suggestion I became an ASCO member in 1967 and took the ABIM test in internal medicine successfully that year and was certified in medical oncology in 1973 (the first year it was offered), and in hematology in 1974 (the second year that it was offered). He convinced me to join the NECS in 1980 and we went together on a NECS tour of cancer centers in Italy in 1992 with our wives and other medical and surgical oncologists.

Some people have wondered about the change of leadership in CP&C and why someone with such a distinguished career before the change and such a distinguished career afterward had been asked to step down. That is why, in writing this history, I asked Dr. Bondy for his recollections of the episode, which were very clear in his mind. I checked with four other faculty members, Bertino, Handschumacher, Sartorelli and Prusoff who were involved at the time and they had similar recollections. Concurring in the decision was difficult, but particularly painful for Welch and Handschumacher who were close friends of Calabresi. A different interpretation of the events was described by Vincent T. DeVita, Jr. and Edward Chu in *Cancer Research* 2009;68:8643: “the chemotherapist Paul Calabresi, a distinguished professor and founding father in the field, was forced to leave because he was involved in too much early testing of new anticancer drugs, an exercise as unpopular with the faculty and house staff at Yale as it was at Columbia” (where Dr. Alfred Gellhorn, Director of the Delafield Hospital division and mentor to some of the most outstanding early leaders of cancer chemotherapy were trained, was also asked to step down). There is some truth in the DeVita-Chu observation of the unpopularity of cancer chemotherapy at YNH and YSM in that period which both Bertino and I were to learn personally in succeeding years. When Calabresi left Yale to become the Chief of Medicine at the Roger Williams Hospital, Glenn Fischer (no relation) also went to Brown to become professor of biochemical pharmacology there, and Ming Chu joined him there with her husband, S-H Chu, also a biochemist who had worked with Henry Mautner at Yale. In 1974, Calabresi became first Chairman of Internal Medicine at the new Brown University Medical School. We remained friends and he often referred patients to me who lived closer to New Haven. He went on to be senior editor of the well received textbook, *Medical Oncology: Basic Principles and Clinical Management of Cancer* and invited me to write the chapter on *The Office Practice of Oncology* for his second edition in 1993.

The Section of Clinical Pharmacology and Chemotherapy continued with Bertino as section chief. He asked Ronald DeConti, MD who had been Calabresi's fellow from 1964-66 to remain as an assistant professor and John Marsh, who had trained with Wintrobe in Salt Lake City was hired in 1967 as an assistant professor to round out the section. Malcolm Mitchell, who had become a fellow with Calabresi in 1966, stayed on and became a faculty member in 1968. DeConti remained here and published in a variety of areas of oncology until 1973 and then went to Springfield, MA, then Albany Medical School and in 1993 became Professor of Medicine at the University of Southern Florida and a Senior Member of the H. Lee Moffit Cancer Center in Tampa, FL with a major interest in melanoma. Malcolm S. Mitchell, MD remained here and published in cancer chemotherapy but his main interest was immunology. After leaving Yale in 1978, he became Director of the University of Southern California Cancer Center where he continued his immunologic studies started at Yale and developed Melacine, a melanoma vaccine which was effective in several studies but not all and was never approved by the FDA. He did additional work at the Karamanos Cancer Center until his retirement. Stephen Kaplan, MD left Yale to go to Brown's new medical school with Calabresi and it is my understanding that Kaplan became a rheumatologist.



John C. Marsh, MD was the proverbial “triple threat;” he was a good researcher, a fine teacher and a good and a compassionate physician and the “go-to-guy” for difficult clinical problem. He graduated from YSM, was a clinical associate at NCI and took a clinical and then a research fellowship with Maxwell M. Wintrobe, MD, PhD at the University of Utah. Wintrobe considered him one of the best hematologists in the country. Marsh had done work with Dane Boggs on hematopoietic stem cells while in Utah and he came to YSM in 1967 and remained here until his retirement as Professor of Medicine in 1998. His research here included a demonstration of a neutrophil releasing activity in neutropenic patients and the first growth of CFU-C (colony forming units-culture) from the bone marrow of dogs. His was one of the first clinical studies of the effects of BCNU and his review of the effects of cancer therapeutic agents on normal hematopoietic stem cells was an important contribution. He was the Yale Principal Investigator (PI) for both the Eastern Cooperative Oncology Group (ECOG) and for a time, the Gastro-Intestinal Tumor Study Group (GITSG) {Elliot M. Livstone was PI of GITSG for a time}. Marsh contributed patients to their protocols and a number of protocols internally generated. In 1980, he joined me as co-sponsor of a series of lectures to oncologists at hospitals all across Connecticut. We collected the text of the lectures to distribute to those who were unable to attend the lectures. The material came to the attention of G.K. Hall Medical Publishers of Boston. They felt that there was a need for a new intermediate size textbook of medical oncology. Accordingly, John and I wrote 31 additional chapters of the total 69 chapters in the book and we published it as Fischer, DS and Marsh, JC, Cancer Therapy in 1982. It was cited by Weiss and Vanderpool, in their article, Ethics in Oncology Textbooks, *J Clin Oncol* 1985; 3:1432-1435 as the only oncology textbook published to have a chapter on ethics (Ethical and Social Dilemmas in Cancer Care). It was also special for that time in having chapters on The Oncology Nurse, Follow-up of Cancer Patients, Unproved Methods; there was a listing of common toxicities of individual drugs to be copied and given to patients, and it had the first textbook notice of the association of Kaposi’s Sarcoma in presumably healthy young homosexual men with pneumocystis carinii and we speculated whether this was caused by infection or severe immuno-suppression. The book was well received and very favorably reviewed in the *JAMA*, but it was soon displaced by the publication of the much larger, more comprehensive and superior text by DeVita, Hellman and Rosenberg, *Cancer: Principles and Practice of Oncology*.

Roland T. Skeel, MD, in 1971, became an assistant professor and in 1972, Robert L. Capizzi, MD did also. Both did significant clinic and laboratory studies. Skeel left YSM in 1976 to become Chief of Hematology and Oncology at the Medical College of Ohio in Toledo and edited the Handbook of Cancer Chemotherapy. Capizzi left YSM in 1977 to become chief of medical oncology at the University of North Carolina School of Medicine at Chapel Hill. His distinguished career included later service as Director of the Wake Forest Cancer Center in North Carolina and then he was Chairman of Medicine at Jefferson Medical College. He is well known for the “Capizzi Regimen,” using methotrexate followed by L-asparaginase, developed while he was at Yale. Meanwhile, the section had been granted a reconditioned 6-bed area on the 5<sup>th</sup> floor of the Farnum Building for inpatient studies on cancer patients and began to do some good clinical work albeit with limited funds.

Charles C. Carter, PhD, a brilliant biochemist, directed the laboratory where I was fortunate to work. There I did studies of the inhibition of reticulocyte ribosomal protein synthesis by chloramphenicol in cell free systems. Carter insisted that I publish that work as sole author although the work was his idea and was done in his laboratory. He explained that his name was on many papers and one more would not influence his career and if his name was on my paper, some might refer to it as Carter’s work because I was an unknown in the field. While there, I also developed an interest in immunology and in viruses as one of the causes of some cancers. That gave me an opportunity to make antibodies and in collaboration

with Sartorelli (J Immunol 1966; 96:676-682), developed a technique of making relatively large quantities of antibodies in mouse hyperimmune ascites tumors. Some of these antibodies were used by Wilbur Downs, MD, Professor at the School of Public Health in the Rockefeller Arbor Virus Unit (and one of the co-isolators of the Lhassa Virus) to identify viruses immunologically. I also made high titer rabbit antibodies to dihydrofolate reductase for a study with Bertino and Perkins (Mol Pharmacol 1969; 5:213-218).

At the time, Yale was an excellent place for cross departmental collaboration. I was able to collaborate with Stuart Finch, MD (then section chief of hematology) on a combined basic science-clinical study of autoerythrocyte purpura; and with Richard Gershon, MD (a brilliant immunopathologist) on studies of the immune response and immunosuppression in the hamster which was different from that in the mouse and explained in part the increased susceptibility of hamsters to oncogenic viruses. My interest in viruses as a cause of cancer led to an invited article on a brief survey of the research relating cancer and viruses for the November 1964 issue of the Yale Scientific Magazine. I also worked with Albert Jonas, DVM, a veterinarian and director of the animal facility. We collaborated on a study of cerebellar hypoplasia resulting from cytosine arabinoside (CA) treatment in the neonatal hamster. CA studies were a major area of investigation in our pharmacology department. (When CA was approved and marketed by the Upjohn Company, one of its most significant toxicities in high dosage was cerebellar toxicity manifested by lethargy, confusion, ataxia, nystagmus and occasional slurred speech). I also worked with Robert Galambos, MD (chairman of psychology) and Elias Manuelidis, MD (chief of neuropathology) on a study of anti-brain antibodies and had an appointment as a research associate in psychology.

Carter left Yale in 1964 to become chairman of the Department of Pharmacology at Western Reserve School of Medicine. Then Welch asked me to stay on as an assistant professor and work independently in his laboratory supported by a two year grant from the NCI. In his laboratory, I was able to complete the study that I had initiated in Carter's laboratory with the virologist, Frank Black, PhD on the formation of tumors (primarily renal) by an oncogenic polyoma virus in neonatal hamsters. If we treated the animals with the halogenated deoxyribonucleoside, 5-iododeoxyuridine (IUDR), their survival was prolonged. This suggested that the agent either suppressed virus multiplication (as Prusoff had demonstrated with herpes simplex virus) or that the agents suppressed the growth of the tumor cells, or acted in both capacities. The paper was published as Fischer, Black and Welch since the later studies were done in Welch's laboratory and he submitted the paper for publication. The study was later expanded when a medical student, Eugene Cassidy (doing his senior thesis with me as his mentor) asked me to repeat the study using IUDR but also testing 5-iododeoxycytidine (ICDR) in our system. The ICDR worked as well as the IUDR and the four of us published the results.

Eugene Cassidy also worked with me on studies of immunosuppression by the pyrimidine nucleoside analogs fluorodeoxyuridine (FUDR), bromodeoxyuridine (BUDR), IUDR, ICDR, and cytosine arabinoside (CA) as compared to 6-mercaptourine (6-MP), azathioprine and methotrexate, agents already in use as immunosuppressives. CA proved to be the most potent of the drugs we tested. This pleased Dr. Welch because he was a consultant to the Upjohn Company and we were among a small group of institutions studying the Upjohn drug, then known by the code name U 92,200 and later marketed as Cytosar® (generic-cytarabine). In fact, much of the early work on the drug was done in our department by two excellent biochemists, Glenn Fischer, PhD and Ming Chu, PhD, who also did other fine work. As we learned more about CA, I suggested that we test it as an anti-leukemic drug in animals, preferably a well known mouse leukemia that we already had. Welch wanted it tested in vitro against mouse lung cancer and melanoma. It failed to show any activity against those tumors. Later, studies elsewhere showed it to be one of the most effective drugs in the treatment of human leukemia.

In 1964, Dr. Paul Beeson appointed me an assistant professor in internal medicine. Welch was delighted. He said that it added prestige to the department, just as Bertino's appointment had. Welch was also pleased that I joined a Yale faculty group interested in immunology and transplantation. It was led by William Glenn, MD, a thoracic surgeon and Fred Kantor, MD, an immunologist (who kindly allowed his technician to teach me some of the newer immunology laboratory techniques). Kantor asked me to give a lecture to the group that I expanded into an article. Beeson heard about it, read the draft, and asked me to have it published in the Yale Journal of Biology and Medicine (circulation at that time, 900), and I did so. The article, Theories of Antibody Formation, Yale J Biol Med 37:1-30, 1964, was well received nationally, (4,000 reprint requests) but it upset Welch who had asked me to submit it to Biochemical Pharmacology of which he was a co-editor. However, he had asked me after Beeson, and having given my word to Beeson, I felt I had to stand by my agreement. Then Beeson asked me to devote a month to the public ward as the on-service Attending Physician. The only month available was July, when the interns were last week's students, and the residents were last week's interns. I served as attending on a Fitkin ward and spent a good part of each day with the house staff because they were so inexperienced.

Welch was displeased with the amount of time I was spending out of the laboratory to teach and support the House Staff. In a half hour discussion that changed my career, he told me that I was doing good work; that I had published frequently, although not always biochemical pharmacology, and that I had a promising future, but I was not to waste time teaching the interns and residents. He pointed out that Bertino, with an appointment as an associate professor in pharmacology and medicine, had never done ward rounds. That was a luxury that had to wait until one had a solid base of good research publications and NCI grants. He told me that I should stick to "bench research" if I wanted to be promoted in pharmacology because at Yale, "you either publish or perish," and must obtain grant support, preferably NIH support. There is little reward for clinical teaching or service on committees, he said. I told him that I wanted to continue to do some "bench research," but that I enjoyed taking care of patients. I had spent 10 years becoming a physician and did not want to give that up to work exclusively with mice and hamsters. He indicated that there was no room at Yale for such a career for me because Calabresi was ahead of me chronologically and in publications and grants. However, he had discussed the Clinical Pharmacology and Chemotherapy program at a national pharmacology meeting with Frederick Shideman, PhD, the chairman of pharmacology at the University of Minnesota (and one of the outstanding U.S. pharmacologists) who wanted to establish a similar program there. I was invited to give a lecture there and was then interviewed in Minneapolis and offered the job. However, my wife protested that we had moved five times in our eight years of marriage; we had just had our third child, and we were struggling on my \$12,000 salary; and things would not be much better on the \$18,000 salary in Minnesota, far from both of our families in New York.

Philip K. Bondy, MD succeeded Beeson as chairman of internal medicine in 1965. Bondy was enthusiastic, well-liked and down-to-earth. We had become friends since he solicited me for a contribution to the Alumni Fund of Harvard Medical School which we had both attended at different times. The day that his appointment was officially announced I happened to see him in the corridor and I greeted him as "Dr. Bondy" and congratulated him on his appointment. He thanked me for the good wishes and told me that I should continue to call him Phil as I had in the past, and that he urged the other members of the department to do the same. In my opinion, that was a mistake because when some members of the department did not agree with "Phil", they did what they wanted to do instead of respecting the chairman and doing what he determined was department policy. Bondy and I also discussed a new problem that was just beginning to show itself. As house physicians were more frequently being asked on

rounds by attending physicians about the laboratory and x-ray results on patients and less and less about the history and physical examination, their histories and physical exams were less thorough and they bonded less with the patients. Even some patients noted it and mentioned it. Knowing that Bondy was a humanist in the tradition of Beeson and Soma Weiss and William Osler I suggested to him that the 40<sup>th</sup> anniversary of Francis Weld Peabody's famous Harvard lecture to second year students on "The Care of the Patient" published by popular demand in the Journal of AMA on March 19, 1927 (JAMA 1927; 88:877-882) was worth reading or rereading by all medical students and that we should republish it in the Yale Journal of Biology and Medicine (YJBM) and distribute a reprint to all the students, particularly those entering their clinical years.

Francis Weld Peabody, MD was an eminent scientific investigator and clinician who combined his keen interest in people with public service. None but those most intimately associated with him knew that he had been offered, in turn, the chairs of medicine at the University of Chicago, at Columbia, at Johns Hopkins, at Yale, and at Stanford University as well as the deanship of the University of Chicago Medical School—all of them declined in order to serve Harvard as Professor of Medicine and Director of the Thorndike Memorial of the City Hospital, where he developed an institution unique in the history of clinical teaching. As adviser to the YJBM, Bondy arranged to have Peabody's lecture published as a special article in YJBM, January 1968, 32:52, and asked me to write the introductory remarks. It was an impressive lecture/article and ended with Peabody's immortal words, "The good physician knows his patient through and through, and his knowledge is bought dearly. Time, sympathy and understanding must be lavishly dispensed, but the reward is to be found in that personal bond which forms the greatest satisfaction of the practice of medicine. One of the essential qualities of the clinician is interest in humanity, for the secret of the care of the patient is in caring for the patient."

Dr. Bondy asked me remain an assistant professor in internal medicine when I decided that I did not want to go to the University of Minnesota. My primary position would be as assistant PI on an immunology research project that had been submitted to the NCI by Frank Epstein, MD, chief of the renal service, a brilliant nephrologist, and it was the only salary he anticipated would be available to the department that semester. If approved and funded, it would pay my salary for at least two years. When I read the proposal that had been submitted, I felt that the immunological justification was weak and it would not be funded. Instead, I suggested to Dr. Bondy that I would like to study the use of high dose chemotherapy followed by bone marrow transplantation for the treatment of lymphoma as advocated by N.B. Kurnick et al., *Ann Intern Med* 1958; 49:973. As part of my interest and work in immunology, I was somewhat familiar with early marrow transplant studies by E.D. Thomas (who later shared a Nobel Prize for his work in this area). Bondy pointed out that studies of tissue typing were still primitive and a high incidence of rejection could be expected. There were no basic science studies of tissue antigens at Yale of which he was aware, and a clinical program without a scientific base was a set up for failure. He was correct. The time was not yet ripe for such an approach at Yale. The renal service grant application was not funded. My wife urged me to give up academic research and go into clinical practice. She liked the New Haven area and wanted to raise our three daughters here. During the first four years of our marriage when I was caring for individual patients, she took a particular interest in the patients as people and always inquired about their welfare, whether their pain was controlled, whether a new drug might help to extend their life or perhaps even provide a cure. (When she died in 1999, I endowed the annual Iris Fischer Memorial Lecture in her memory. It was designed to bring leaders in the field of compassionate palliative care and/or new therapies for cancer to YSM).

Sherwin Nuland, MD suggested that I should not abandon patient care and instead, answer the call of some of my surgical colleagues and go into the community as the first medical oncologist in New Haven. After much soul searching, I decided to do just that. It should have been a seamless transition since I already had full admitting privileges at YNHH. However, the Executive Committee of the Medical Board at the time was chaired by Hugh Dwyer, a community general internist. He told me that to be admitted to the staff automatically, one had to have been a full faculty member for five years and I had been for only three years. In addition, he informed me that the Medical Board had recently voted to establish a moratorium on the acceptance of new physicians in internal medicine because there were too many in New Haven. I protested that I wanted to practice medical oncology and hematology and there were no community medical oncologists on the staff and only one hematologist, Harvey Kaetz. Dwyer said that the medical board did not recognize medical oncology as a specialty (was this a reprise of what DeVita and Chu had suggested was the attitude at Yale about chemotherapy and medical oncology?) and that I was just trying to get around the moratorium to practice internal medicine. Dr. Bondy, as Chairman of the Department of Internal Medicine, and Dr. David Clement, Clinical Professor-of Pediatrics and the only pediatric hematologist in town at that time, supported the application, but to no avail. Finally, Dr. Bondy suggested that I join Marvin Zimmerman and Edward Scherr, two very fine internists in their practice in Branford, eight miles from the hospital and build up a medical oncology/hematology practice there. I did as he suggested and was granted YNHH admitting privileges. I had obtained admitting privileges at HSR almost as soon as I submitted my application to them and I set up the first solid tumor oncology board there. Within two years I was able to limit my practice to medical oncology and hematology and move to an office in New Haven as the only medical oncologist/hematologist in private practice. We will return to the cancer program at Yale and in the community after we discuss the Yale Cancer Center (YCC).

The 1971 National Cancer Act was signed into law on December 23 by President Richard M. Nixon to mobilize the country's resources to make the "conquest of cancer a national crusade." The original vision was spearheaded by Mary Lasker, Dr. Sidney Farber and the American Cancer Society, among others, to create a broad-reaching national program that would accelerate the pace of basic cancer research and its translation into clinical trials for adults and children and effective cancer treatments and to provide effective cancer education and prevention methods to the surrounding communities. The Act granted special authority to the National Cancer Institute (NCI) and its director to spearhead the nation's fight against cancer through the development of a National Cancer Program. Key provisions of the Act include:

1. Establishment of a National Cancer Advisory Board (NCAB), whose 18 scientific and lay members are appointed by the President to advise NCI on major initiatives.
2. Creation of the President's Cancer Panel, a three-member panel of experts, including a consumer, who independently appraise the progress of the national program and submit an annual report directly to the President.
3. Bypass budget authority for the NCI, which enables the Institute to "bypass" traditional budgetary mechanisms and submit a budget directly to the President without approval from either the National Institute of Health (NIH) or the Department of Health and Human Services (HHS).
4. Broad authority for the NCI director, a presidential appointee, to develop and carry out—in consultation with the NCAB—the many compelling and competing priorities of the nation's cancer research enterprise. The NCI director has the authority to create new cancer centers and personnel training programs, to appoint advisory committees to explore new research opportunities, to award research grants, and to expand the physical plant of the NIH, as well as cancer research facilities across the country.

Vincent T. DeVita, Jr., MD, a graduate of the College of William and Mary, earned his MD at George Washington University and was a resident in internal medicine at Yale in 1965-66 before he returned to the NCI where he worked in the Medical Branch. Later he became Chief, Medicine Branch. As such, he was directed by the NCAB (of which Mary Lasker was a member) to inaugurate the Comprehensive Cancer Centers Program. He had led the team at the NCI that showed that a four-drug combination (based on nitrogen mustard) could cure a majority of patients with Hodgkin's disease (HD). This was the paradigm for the future of treatments to cure other solid tumors (although some people lump HD with leukemia and not solid tumors, a semantic question). Just shortly before this, another team at the NCI led by Emil Frei showed that the acute lymphocytic leukemia of childhood could be cured in many cases. These successes spurred the hope that with enough money to support outstanding scientists and physicians, cancer could be cured in a reasonable time (notwithstanding that cancer is more than a hundred diseases that will have to be cured one-by-one). The politics of how the 1971 Act came about and the details of how the Comprehensive Cancer Centers (CCC) came into being will be detailed in a book by Dr. DeVita to be published soon.

Before the 1971 Act, there had been interest in applying basic science to the treatment of illness in patients at the bedside and Building 10, a 500 bed hospital had been built in the 1950s on a campus in Bethesda, Maryland that was later called the Warren Magnusen Clinical Center. The NCI soon became the largest user of the facility. In the next decade, a large cancer grant was made (in 1966) to the Memorial Sloan-Kettering Cancer Institute (MSKCC) in New York City and similar grants were soon made to the M.D. Anderson Hospital and Research Institute (MDAH) in Houston, and the Roswell Park Cancer Center (RPCC) in Buffalo, NY. Once the 1971 Act was implemented, there were additional grants to the MSKCC, the RPCC, the Fox Chase Cancer Center (FCCC) in Philadelphia, and the Dana-Farber Cancer Institute (DFCI) in Boston. The original plan was to have 15 CCCs distributed across the United States. Yale was considered in that group but had to apply and justify its possible selection.

The Yale School of Medicine (YSM) had an amazing number of talented people working in the cancer field. Accordingly, a cancer committee was set up that was chaired by Lewis Thomas, MD, dean from 1972-1973. A year later, a Division of Oncology was established as an interdepartmental organization to make plans to integrate the existing cancer studies at Yale as well as new programs of cancer research, patient care and education in the hopes that this effort would result in a program that would make YSM one of the most outstanding programs so that it would be designated as an NCI – CCC. This effort is detailed in an article in the Spring 1973 issue of *Yale Medicine*. The Division of Oncology was to have a director and assistant director who would be assisted by an executive committee of members of both the basic science and clinical departments. Joseph Bertino, MD, professor of medicine and pharmacology, was appointed as acting director. A clinical division was headed by James Fischer, MD, PhD, (no relation) chairman of the Department of Therapeutic Radiology (RT) and a basic sciences division was headed by Sherman Weissman, MD, professor of human genetics, medicine and molecular biophysics and biochemistry.

The Division of Oncology began to catalogue its strengths in people and programs. Scientists like Dr. Paul Howard-Flanders and Charles Radding, MD were international authorities in the field of recombination of genetic material and related phenomena, fundamental for understanding the basis for mutations and the ways in which viruses can become associated with cells and change their behavior. On the main campus, Dr. Peter Lengyel, professor of molecular biophysics and biochemistry and human genetics, a leading authority in the field of protein biosynthesis had recently turned a portion of his laboratory to-

ward the investigation of protein synthesis in virus-infected cells and the mechanism of action of interferon. He would be a major asset to a cancer research program. The strengths of the Department of Pharmacology, one of the foremost in the country, have already been detailed, except for the mention of Paul Greengard, PhD, professor of pharmacology who was recognized for his research in cyclic AMP which he initiated at Yale and completed at the Rockefeller Institute and for which he was awarded a Nobel Prize in Physiology or Medicine.

In the Department of Internal Medicine, the program in gastroenterology with Dr. Howard Spiro, section chief, and with Drs. Frank Troncale and Elliot M. Livstone, had a strong clinical and research interest in cancer. Dr. Spiro had been instrumental in forming the Gastro-Intestinal Study Group (GITSG) with Dr. Charles Moertel of the Mayo Clinic. It was a consortium of university hospitals and comprised medical oncologists, radiation oncologists, pathologists and gastroenterologist, among others. At Yale, Dr. Livstone was PI of GITSG at one time and Dr. John Marsh was PI at another time. They published a number of seminal studies as a cooperative cancer study group. Dr. Stuart Finch, section chief of hematology had an active interest in cancer. The section of Medical Oncology (formerly Clinical Pharmacology and Chemotherapy) under the direction of Dr. Bertino (and including Drs. John Marsh, Roland Skeel, Ronald DeConti, Robert Capizzi and Malcolm Mitchell) was conducting active research in a variety of solid tumors. Dr. Aaron Lerner, chairman of dermatology, was internationally known for his studies in skin pigmentation and melanoma. Pediatric hematology/oncology was participating in cooperative studies of leukemia and solid childhood tumors, particularly Wilms Tumor, under the direction of Dr. Howard Pearson. In 1958, Yale committed itself to a long-range program in support of research in clinical radiation therapy and radiobiology with the building of the Hunter Radiation Therapy Center and that program had prospered, initially under the direction of Dr. Morton Kligerman (as chief of Radiology which included Radiation Therapy) and then James Fischer, who became the section chief of the of radiation therapy and later its first chief. Radiation therapy and medical oncology had collaborated successfully in a program of combined modality therapy for HD proposed by Kligerman and J. Fischer and joined by Bertino that attracted national attention when it was taken up by Leonard Prosnitz in RT, Ronald DeConti in medical oncology and by Leonard Farber, first as a fellow and then as a community physician.

Several groups were actively involved in studies of phenomena related to viral oncology. Dr. George Miller, associate professor of pediatrics and epidemiology, was investigating the biology of herpes viruses and cells transformed by them. Dr. William Summers, associate professor of radiology and molecular biophysics and biochemistry, had recently initiated a research program of the molecular biology of herpes viruses and speculated that the virus was related to more than one kind of cancer. Dr. Mark Bitensky, associate professor of pathology was exploring the basic functions of cells, somatic cell genetics and the biology of cell regulation. Dr. Sherman Weissman had an active program in the molecular structure of genetic material of SV 40, an oncogenic virus. Dr. Byron Waksman, professor of microbiology, had long been recognized as a leader in lymphocyte biology. Understanding the function of the lymphocyte is important in the body's defenses against cancer, as well as infection. Dr. Richard Gerson, associate professor of pathology, was working on a program of immune reactions that modify tumor growth and transplantation.

In addition, many others in both the basic science and clinical areas had been involved in cancer research and treatment. Dr. Jack Cole, chairman of surgery, and Drs. John Kirschner (chief of otolaryngology), Thomas Krizek (chief of plastic surgery), Ira Goldenberg (breast surgery) and Mark Hayes (general surgery) had made important contributions to cancer treatment, as had Dr. John M. Morris, professor of gynecology and Dr. Ernest Kohorn, associate professor of obstetrics and gynecology. With all this

strength in Yale's cancer program, it seemed reasonable to expect that the NCI would designate Yale as one of its earliest CCCs. The application was supported by Robert U. Massey, M.D., Dean of the School of Medicine at the University of Connecticut.

Dr. Joseph Bertino was made Director of Oncology and put in charge of the application in July 1973. It was his understanding from Dean Thomas that he was to be Director of the Cancer Center when it was officially authorized. He detailed the strengths of the institution, particularly in the basic sciences related to cancer and outlined a plan to build a bridge over Cedar Street to connect YNHH to the YSM to house the cancer clinics and to have some of the cancer research laboratories in the building. It would also be adjacent to and lead into the Hunter Radiation Building. I remember being invited to a site visit meeting about late 1973 because the reviewers were concerned that Yale, being in a small city with a small clinical service, would have difficulty recruiting enough patients for clinical trials. They wanted to be assured that I and the other oncologists in the community would put a substantial portion of our patients into clinical trials at the Cancer Center when and if it was officially authorized. At the time I had been in medical oncology-hematology practice in the community for 6 years, and two years earlier I had a full enough practice that I was unable to absorb the hematology practice of Dr. Harvey Kaetz that I had been offered when Kaetz became full-time chief of the internal medicine section of the Yale Health Plan. One of our trainees, Leonard Farber, MD, was ready to come into community practice in 1971 and I helped him take Kaetz's practice so that we could cover for each other. Both he and I had participated in Yale research protocols, and since we were then the only oncologists in private practice, it was easy to assure the site visitors that we would actively participate in clinical trial protocols that could be done in the community, and both of us participated quite actively.

John W. Yarbro, MD, Associate Director for Cancer Centers at NCI addressed a letter, dated March 5, 1974, to Joseph R. Bertino, MD, Director, Division of Oncology, School of Medicine, Yale University, and was very reassuring. It was a response to a letter of February 26, 1974 indicating that there was a very generous financial commitment by Governor Meskill, representing the State of Connecticut, toward a CCC at Yale. Yarbro noted, "This evidence of local support is indeed gratifying. As you know we at the National Cancer Institute have been highly pleased with the level of scientific excellence attained by your institution and with your commitment to research and treatment in cancer. Responsible as I am for the development of cancer center programs across the nation I can assure you that academically, clinically, and in terms of local commitment, your program stands out as one of the best in the nation."

Bertino testified before the Senate-House Finance Committee in Washington on March 14, 1974 about the construction grant application and a core program grant application to establish a State Comprehensive Cancer Center at Yale. The total construction cost of the Cancer Center would be \$6.2 million. Yale would offer a match, or \$2.4 million, which is a proportion consistent with that offered by other institutions. The State of Connecticut would contribute \$1.2 million and Yale University would contribute \$1.2 million. This would be a one-time-only request and no future building was now planned, but it was assumed that in future years, the budget would increase and additional construction would be necessary. There would also be a request for \$6.2 million for a "core" program for 3 years and this annual budget would increase and did not require matching funds. The proposed CCC at Yale would be an important statewide resource. It would serve as a model for top quality cancer care and research and would be an invaluable resource to the individual cancer patient, the community physicians and other health care organizations and facilities.



Yale was officially established as a NCI CCC in May 1974 and Bertino became the first Director of the YCCC. The order of official selection is not what I or most people would have expected. In a brochure put out jointly by the American Cancer Society (ACS) and the Association of American Cancer Institutes (AACI), dated October 2007, the order of the early NCI designated CCCs and Research CCs is listed. The first NCI CCC was University of Texas-M.D. Anderson Hospital (MDAH) in 1971. This was no surprise since NCI had been funding MDAH for five years. To my surprise, the NCI designations in 1972 were to the Herbert Irving CCC of Columbia University, and to the Albert Einstein CCC of Yeshiva University. The 1973 NCI designees were Memorial Sloan-Kettering CCC (MSKCC), University of Wisconsin CCC, Abramson CCC of University of Pennsylvania, Duke University CCC, Mayo Clinic CCC, Dana-Farber Cancer Institute (DFCI), Sidney Kimmel CCC of Johns Hopkins University, and Norris CCC of University Southern California. Thus, there were 11 CCCs that were designated a year or two or three before Yale. Those designated in 1974 were: Yale CCC (YCCC), Roswell Park Memorial CCC, Lineberger CCC of University North Carolina, Ohio State University CCC, Fox Chase CCC and Massey CCC of Virginia Commonwealth University. In 1975, New York University CCC and in 1976, Jonsson CCC of University of California at Los Angeles (UCLA) were added to the list.

Bertino was running a very productive research laboratory in pharmacology with several fellows and he was chief of the section of medical oncology at the same time that he was serving as Director of YCCC. He was fortunate to recruit Roland Glenn, a lecturer in psychiatry, as his Executive Director and Henry Mandel as Associate Director of YCCC for Outpatient Services and Regional Affairs. Together they obtained the grant to build the bridge across Cedar Street which eventually contained the offices of the Cancer Center, the outpatient clinics, meeting rooms for conferences, and adjoined the Hunter Radiation Center for collaborative work between medical oncology and RT. The basic scientists continued to produce excellent research. The clinicians began to look into doing translational research and more clinical trials and enlarging the fellowship program. Marion Morra was hired to run one of the first NCI Cancer Information Services in the U.S. and she went on to become an Associate Director of YCCC. Just as all this was coming together, Bertino was offered a Career Research Professorship by the American Cancer Society as Robert Handschumacher had been in 1964. It was too good to turn down. It would allow Bertino to devote more time to his basic research in his pharmacology laboratory and to his clinical research interests as chief of medical oncology, but it would not permit him to spend time as an administrator, especially not one so demanding as Director of a Cancer Center. He resigned effective June 30, 1975.

Jack Westley Cole, MD, was Ensign Professor of Surgery and Chairman of the Department of Surgery at Yale from 1966 to 1974. When Bertino stepped down, Cole was no longer Chair of Surgery, but he was a tenured professor and he was available. He was appointed Director of the Cancer Center and Director of Oncology. Cole had been an outstanding surgeon at Western Reserve School of Medicine, known for his dexterity, meticulous technique and good judgment. He rose from chief resident to Professor of Surgery there. Unfortunately he developed a mild case of poliomyelitis (I was told by Dr. Stephen Ariyan, one of Cole's most distinguished mentees) which resulted in difficulty in fine hand movements and limited his surgery somewhat. None-the-less, he became Professor and Chairman of Surgery at Hahneman Medical College for several years before coming to Yale. According to Ariyan who was one his residents, Cole was "a surgeon's surgeon." He was seriously considered for Dean of the Medical School in 1967 when Vernon Lippard stepped down and Albert Snoke, executive director of YNHH recommended Cole and the suggestion was supported by Philip Bondy, Chairman of Medicine. However, President Kingman Brewster appointed Fredrick Redlich, Chair of Psychiatry as Dean and Cole continued as Chair of Surgery for a time. He improved the department with a fine selection of new faculty appointments and top flight residents whom he treated as colleagues.

Cole had been a skillful cancer surgeon but he had little or no background in basic science research or medical oncologic research. He did support chemotherapy and clinical trials of new chemotherapy drugs and did not interfere with the research that was being done but he was not actively involved in it. He still considered surgery the prime modality of cancer therapy for the present and the near future. When the NCI announced a new round of available funding for the early CCCs for building additional facilities, for core resources and equipment, and for expanding medical oncology training, Cole chose not to submit any grant requests, although urged to do so by Roland Glenn and Marion Morra. Whether he felt that Yale did not need the additional funds because the basic scientists were well funded directly and the cadre of clinical oncologists was small, or because the bridge over Cedar Street for the CCC was still being constructed, or whether Dean Robert Berliner advised against a grant request is not known to me. What is known is that when Berliner was at the NIH as Director of Research at the National Heart Institute, he opposed the concept of Comprehensive Cancer Centers and suggested that the funds could be used to greater benefit in other venues. However, Berliner later became a supporter of the YCCC. The failure to take advantage of the newly available financing in 1977 made it difficult for YCCC to get substantial funds thereafter because the NCI funding formula subsequently was based on a percentage of previous funding.

Cole did reach out to the community for cooperation and participation. The Cancer Center assisted in the foundation of the Connecticut Oncology Association (COA) in 1975 and Leonard Farber, MD, a community physician became its first president. In 1977, when I became president of COA I met with Cole and found him to be a true gentleman and supportive of COA and community oncology collaboration with the YCCC. In spite of his lack of familiarity with chemotherapy, he encouraged Marion Morra, who was responsible for outreach activities for the YCCC, to become secretary-treasurer of COA and through her office was able to provide COA with some financial support. That included having the YCCC do its mailings and to help arrange for some out of town lecturers who came to Yale CCC (and received a Yale honorarium) to also speak to the COA as part of the same trip.

Bertino's section of medical oncology tried to increase their accrual to clinical trials by reaching out to the COA physicians. Farber and I put quite a few patients on those protocols and participated in writing the reports and are listed as coauthors on some of the papers. However, when Yale began to participate more actively in placing patients on protocols of the ECOG of which John Marsh was PI, and the GITSG, of which he was also PI and Elliot Livstone was the facilitator, it became increasingly difficult to continue to put private patients on those clinical trials. This was partially because the HIC (IRB) consent forms became too long and complicated and it took too much valuable office time to fully explain all the information and our secretaries and/or nurses, had to recopy (by hand) laboratory results onto the special report forms we were given. We began to enroll fewer patients on protocols because patients who were interested in participating in a clinical trial often went directly to Yale and the full-time faculty oncologists. In a private medical office, time is money and our participation was becoming increasingly costly (we had no fax machines or computers in those days). Yale did not provide data collectors. Full-time faculty who were on salary could spend time explaining the investigative studies or have their fellows or research nurses do so and the department derived some funds from the cooperative groups, although probably not enough to cover the costs.

Bertino was appointed Associate Director for Clinical Research in the YCCC in 1979 by Cole to enhance participation in clinical research. However, the Chairman of Medicine, Samuel O. Thier, MD appointed Edwin C. Cadman, MD as co-chief of Medical Oncology for clinical affairs in 1980. Cadman was a good clinician and investigator and had been Bertino's fellow from 1974-76, then an assistant professor

1976-79 and became an associate professor in 1979. Although both were very able, they did not work well together. In 1983, Cadman left Yale to become chief of medical oncology at the University of California in San Francisco. In 1982, while he was Chairman of Pharmacology, Alan Sartorelli became Deputy Director of the YCCC to coordinate the very substantial basic science research in cancer and to attempt to increase clinical translational research. He worked very closely with Bertino. When it was time to write a new YCCC grant application in 1984, Cole did not feel capable of adequately presenting the basic science area, the main strength of the YCCC and resigned three months before the site visit and left the grant renewal process to his successor.

Alan C. Sartorelli, PhD was appointed the third Director of the YCCC in 1984, the same year that Berliner stepped down as dean. President A. Bartlett Giamatti (more famous to the public as Commissioner of Baseball than as President of Yale) considered Sartorelli and Leon E. Rosenberg, MD as the two finalists for the deanship and eventually gave it to Rosenberg. In 1984, shortly after he became director, Sartorelli proposed a new building that would join the medical school building and its laboratories to the Memorial Unit of YNH where most of the cancer patients were. Nothing came of the proposal because the new dean gave it no support. Sartorelli wrote a strong grant proposal based on the strength of the basic sciences. He had clinical and budgetary oversight responsibilities for the Cancer Center as its director, but he had no authority to appoint clinical staff. Those appointments were made by the department chairmen, and for the Section of Medical Oncology, that authority resided with the Department of Internal Medicine (DIM) and its chair. We will return to this issue. When the NCI site reviewers came to New Haven, Giamatti joined Sartorelli in suggesting that Yale was finally ready to build a cancer building, and that the University would help financially. The YCCC grant was approved for five years, the first two years were approved unconditionally, but at the end of that time, additional supportive evidence had to be submitted to justify the funding for the three additional years. With Sartorelli's strong leadership, that proved to be no problem.

The proposed new cancer building did not get built (as previously mentioned) because Dean Rosenberg decided he wanted the University and other funds (royalty funds from the staduvine patent of William Prusoff and Tai-Shun Lin) to be used for a new building on the corner of Cedar Street and Congress Avenue for DIM research that many years later came to fruition and was named the Anlyan Building. Giamatti had a reputation as a man of his word and I had the great pleasure of discussing educational policy with him and he was kind enough to send me an autographed copy of his book on educational policy. Why did a man of such integrity fail to push a new cancer center building? Traditionally, Yale Presidents allow their deans to run their own schools unless they are inept, and then they find a new dean to do the job. They rarely overrule a dean.

Sartorelli was an able administrator and a well-respected scientist. He ran up against a number of problems as director. The authority to make faculty appointments was in the hands of the chairmen and the dean. The most important clinical components of YCCC were medical oncology and hematology and they were sections of the DIM which controlled their finances and appointments. The DIM had become the largest department in YSM with the most professional personnel and it was difficult for the chairman to adequately keep abreast of what was going on in all of the sections. The section that received the least attention and support, supposedly because it was losing money (actually an erroneous supposition as we will later learn) was medical oncology. Radiation therapy was a separate department and had its own chairman who controlled its funding and did not necessarily look to the Cancer Center Director for leadership. The Director received little support from YNH, which was happy to treat the inpatients referred

by the medical oncologists, but it seemed to Sartorelli that YNHH administration did not feel that it was a part of the YCCC or even a partner. In spite of these problems, after four years of leadership by Sartorelli, the 1988 NCI Cancer Center Support Grant (CCSG) was renewed based on Sartorelli's demonstration of the excellence of the basic sciences program and the high quality of the cancer prevention and control program and received the highest priority score of any cancer center grant that year. The summary statement of the lead reviewer, Mr. Raymond Morrison is marked "Privileged Communication," but since it is now more than 20 years later, I think it is legal to reproduce it here:

"RESUMÉ: Yale School of Medicine is applying for renewal of its Cancer Center Support Grant. This Cancer Center program includes 13 program areas, nine shared resources, administration development, planning and leadership. This program is currently in its fourteenth year and is requesting \$905,206 for year 15 with a five-year request of \$5,193,127 in direct costs. The Yale Comprehensive Cancer Center (YCCC) has made tremendous progress under the Directorship of Dr. Sartorelli. The basic sciences have and continue to provide outstanding science. The clinical science programs have improved and have made significant progress in their interdisciplinary coordination with some of the basic science programs. The clinical research has been structured around disease-oriented teams. Some of these show substantial promise while others remain weak. The authority of the Director and the organizational capabilities are exceptional because of Dr. Sartorelli. He is effective because of his own abilities, independent of the formal authority granted by the Institution. In addition, the Institution gives the Center Director authority over YCCC space, some positions and institutional funds. The institutional commitment to the YCCC has been substantial over the past five years in terms of space, funds and facilities. There is promise of continued support with major consideration being given to expanded facilities. Approval is recommended for five years for this revitalized center program with high enthusiasm".

Sartorelli was able to get some NCI funds later for core support of research and training, but only a percentage of what he would have obtained if Yale had availed itself of the grants it could have had in 1977. In addition, Bertino was restricted in medical oncology by the Department of Medicine in hiring and was not able to bring in any appointee at the associate professor level. Carol Portlock, an expert in lymphoma, from Stanford Medical School, was recruited as an assistant professor in 1978 and was promoted to associate professor in 1980 in less than the usual three year period. Susan Pitman, from Dana Farber Cancer Center started here July 1986 as an assistant professor. All new appointments (to the best of my knowledge), were at the assistant professor level and those promotions followed the usual time track and included Drs. Gerald Kennealey, John Kirkwood, Marc Ernstoff, Daniel Vlock, Dennis Cooper, Christopher Benz, William Hait, Mary Todd, Jill Lacy, and Michael Reiss. Appointments were primarily of fellows who stayed on. When Dr. Samuel O. Thier left in 1986 to become the President of the Institute of Medicine (IOM), Cadman was appointed to succeed him. Bertino, who had been given two firm offers by Stanford University School of Medicine, which he turned down, suddenly accepted an offer by Memorial Sloan-Kettering Cancer Center (MSKCC) to become a Member and Co-Head of the Program in Developmental Therapy and Clinical Investigation. Carol Portlock accepted a position at MSKCC in 1988. Kirkwood, Vlock and Ernstoff, who were heavily involved in the melanoma program, went to Pittsburgh in 1986, where Kirkwood became Chief of Medical Oncology and some years later Ernstoff went to Dartmouth as Chief of Hematology/Oncology and Deputy Director of its Cancer Center, and Vlock went into industry.

William N. Hait, MD, PhD, who had been a fellow here 1982-83 and was appointed assistant professor in 1984, was made Acting Chief of Medical Oncology 1986-88. In 1987 he was promoted to associate

professor and then became section chief from 1988-92. It was an excellent appointment because he was a good clinician, teacher and researcher. I knew Bill quite well and had invited him to join me in private practice when he completed his fellowship, but he had invested a lot of time in research for his PhD and felt that he was uniquely qualified for an academic career and wanted to at least try it. Hait did very well as section chief with the faculty and resources that he had and he improved the clinical program. He also served as director of the breast cancer program, co-director of the lung cancer program and an associate director of the YCCC. Hait was fortunate to have John C. Marsh, a full professor and an outstanding clinician and a group of young assistant professors, most of whom were fellows who stayed on as junior faculty. That included Dennis L. Cooper, Jill Lacy, Michael Reiss, Mary Todd and Andrea Silber. He recruited Antonio Buzaid in 1988 for the melanoma program, and Roger Strair and Lee P. Schacter in 1989, all at the assistant professor level from outside. He promoted several able fellows to faculty at the assistant professor level, including Sandra Schnall, Wen-Jen Poo Hwu, John Murren, and Thomas Fynan, but always found his section short of funds. Accordingly, he was unable to bring in any outsider with proven experience in developing a strong clinical trials program. That would have required an associate professor level appointment at least and the Department of Internal Medicine denied him appointments at that level.

The Chairmen of the Department of Internal Medicine were:

George Blumer	1910-1920
Francis Gilman Blake	1921-1952
Paul Bruce Beeson	1952-1965
Philip Kramer Bondy	1965-1972
Louis Welt	1972-1974
Samuel O. Thier	1974-1985
Edwin C. Cadman	1986-1994
Ralph I. Horwitz	1994-2003
David Coleman	2003-2006 (acting)
Jack A. Elias	2006-

A disgruntled faculty member accused Hait and members of the section of medical oncology of scientific misconduct on an NCI grant, so an investigative team from the NCI came to New Haven to check whether Federal funds were being misused. Several investigations completely exonerated Hait and the section of medical oncology, no surprise since all the other members of the faculty were convinced of the innocence and integrity of Hait and his section. However, Cadman as Chairman of the Department of Internal Medicine indicated that he thought that the episode had cast a shadow on his leadership/integrity and on YSM. When Hait realized in 1992 that he did not have the confidence of his chairman, he left. This was a big loss because Hait's leadership was highly respected and with his departure, the momentum and continuity of the section was lost for several years. In 1993, Hait became the Director of the Cancer Institute of New Jersey. He took two faculty members with him, Mary Todd and Henry Durivage very shortly thereafter. The following year, Hait became Co-Director of the New Jersey Comprehensive Breast Care Center, Chief of Medicine and eventually he succeeded in making the University of Medicine and Dentistry of New Jersey (UMDNJ) into the 40<sup>th</sup> NCI Comprehensive Cancer Center of which he became the director. Michael Reiss became acting chief of medical oncology 1992-1993 at Yale. In 1994, Hait recruited Roger Strair, and in 2001, Michael Reiss went from Yale to join Hait at UMDNJ. Sartorelli's second five year term as director ended in 1993, and he left a greatly improved YCCC in basic science

research, but it could have been much better in the clinical area if he had received more financial support and cooperation from YNHH, Yale University (YU), YSM, and its department of medicine, and had not lost Hait.

“Follow the money” if you want to know why most things are done, was an aphorism that I was taught as a college student majoring in political science. We have seen how insufficient funds limited the development of the YSM and NHH in their early and middle years, and how it inhibited the growth of the YCCC and particularly the Section of Medical Oncology. The insufficiency of funds, especially for cancer therapy, was multi-factorial. Insufficient reimbursement for cancer care affected the YSM and YNHH and also affected those of us in community practice as well. I can illustrate the effect of these problems with some personal observations since I was involved in three issues that had significant bearing on the economics and hence the practice of medical oncology.

Blue Cross/Blue Shield insured a large proportion of those less than 65 years of age across the U.S. However, in Connecticut, Blue Cross (BC) only paid for services in the hospital. There was no Blue Shield in Connecticut. An entirely separate organization unrelated to BC, called Connecticut Medical Service (CMS), had been set up to pay fees for professional services incurred outside the hospital. Many patients had both BC and CMS. If a physician treated a patient with IV chemotherapy in the hospital, BC would pay for it. If he treated a patient in the office with IV chemotherapy, CMS would pay him a professional fee but refused to pay for the chemotherapy drugs or for their IV administration. When we only had 5-fluorouracil which cost \$1.10/dose and methotrexate which cost \$14.10/dose, it was difficult but tolerable for most patients to be treated in the office. When cyclophosphamide (Cytosan) became available at \$20/dose it became more difficult. When doxorubicin (Adriamycin) was marketed at \$125-250/dose, office therapy was out of the question. (It should be noted that doxorubicin cost substantially less in Europe at that time. Farmitalia, the pharmaceutical company that developed and marketed it, priced it at “what the market would bear” in the U.S. When there were no repercussions by the government or the insurance companies, virtually all subsequent drugs were priced higher and higher in my opinion, with only slight regard to developmental or manufacturing costs. The pharmaceutical industry has claimed otherwise publically, but I believe a careful study would support this opinion). As a result of these disproportionate and rapidly rising prices at that time, I had 12 to 20 patients in the hospital on any given day. Other oncologists had the same problem and in 1977, when I became president of the Connecticut Oncology Association (COA), some members asked that the organization do something about the CMS problem. I contacted CMS and they suggested that I admit such patients with BC and CMS coverage to the hospital and let BC pay for chemotherapy. When I went to the BC leadership to ask them to pay for chemotherapy in the office for patients who had the dual insurance, they said they would pay whatever it cost in the hospital, be it hundreds or thousands of dollars, but not a single dollar for treatment in the office.

T.F. Gilroy Daly, Esq was an attorney in private practice in Connecticut from 1964 to 1977. He gained prominence when he won freedom for Peter A. Reilly of Litchfield County, Connecticut who had been convicted of murdering his mother. Taking on the appeal pro bono, and with the help of a private investigator, Daly uncovered new evidence that resulted in Reilly being cleared of the crime and released from jail. I mention this episode because Daly was appointed Connecticut’s Insurance Commissioner in early 1977 and this was the kind of human being he was. I appealed to Commissioner Daly to direct CMS to pay for office chemotherapy since it would prevent many costly hospitalizations. He discussed the matter with BC, but they were adamant in their positions. He asked me to do a survey of COA members and

estimate how much money would be saved if office chemotherapy was covered by the insurers. Our survey (which did not include drugs given in the hospital outpatient clinics) showed that about one million dollars would be saved. He asked BC to do a similar survey and their figure was \$500,000. When BC came up for a rate increase, Daly invited me attend the hearing in Hartford and asked me to testify under oath, about the cost savings. He then asked the BC vice-president (VP) to testify under oath, (which was apparently unusual, as most of those testifying at rate hearings do so without oath, I was told). After the jocular suggestion by Daly that the VP intended to deceive him, the VP testified under oath and said that BC needed a rate increase and would go into bankruptcy if it was not granted and the \$500,000 they would save by paying for chemotherapy in the office would not avert such a dire result.

Daly suggested to BC that saving the rate payers of Connecticut \$500,000 or \$1,000,000 was no small thing and he wanted to see BC and CMS merge so that it would be in the interest of BC/CMS to pay for office chemotherapy and other fiscal economies of size and reduce unnecessary hospitalizations which were a major determinant of high health care cost. Daly denied the rate increase and mentioned that if BC went into receivership, he would be the likely trustee and would merge BC and CMS. If BC did not go into bankruptcy, he would have to consider whether the VP had committed perjury under oath. A month later BC and CMS announced their merge and the rate increase was granted. The merged organization immediately started paying for office chemotherapy and hospital admissions solely for chemotherapy dropped remarkably rapidly at a great saving for society and a great convenience for patients. However, there were other economic problems that limited care.

Medicare, an agency of the then Department of Health, Education and Welfare (HEW) after 1966, paid for 80% of what it deemed the usual and customary fees for the over-65 patients. For patients with cancer who received intravenous (IV) chemotherapy drugs, they would pay 80% of the wholesale cost of the IV drugs if the physician purchased the drugs and administered them, and accepted Medicare payment. However, if the patient was given a prescription for the IV drug and went to a pharmacy, the patient incurred the entire cost of the drug and there was no Medicare reimbursement. Many physicians refused to lay out the money for the drugs because some patients would not pay the 20% co-insurance, some patients would get the 80% reimbursement and keep all the money. I had a few such patients but Medicare payments were often delayed so that I did not know of my losses until it was too late to recoup anything. Even when the patient was a responsible individual and paid the co-insurance, the physician accepting Medicare reimbursement was losing money because he (at that time most Connecticut community oncologists were male) had to invest money up front (sometimes paying interest if he did not have the cash) to pay for the drug and would not be reimbursed for many months. Additionally, there was some breakage of vials and errors in reconstituting lyophilized drugs which were losses to the physician. Most community physicians could not buy the drugs at wholesale prices but only at retail, and lost additional funds. As a result medical oncologists had low incomes compared to specialists in other areas of internal medicine and it was therefore not a subspecialty that was attractive to young internists.

Dr. Vincent T. DeVita, Jr. became president of the American Society of Clinical Oncology (ASCO) in 1977. At that time I advised him to set up a Public Issues Committee similar to the one that the American Society of Hematology (ASH) already had and suggested that appropriate reimbursement for oncologists might be an issue that such a committee could address in the name of ASCO. He graciously agreed to create such a committee and asked me to be its chairman. Dr. Virgil Loeb of Washington University in St. Louis agreed to be vice-chairman. Together we built a committee with multistate representation. After some discussions and a review of available data, the committee concluded that not enough young physi-

cians were becoming medical oncologists because reimbursement levels were the same as for primary care physicians. Considering the time it took with each cancer patient for the physician to explain the nature of cancer and the treatment options, and perhaps later, the end-of-life options, it was economically undesirable to have spent five or six years training to do medical oncology and then receive reimbursement that was less than similarly trained internal medicine specialists or even some general practitioners. When the patient needed chemotherapy, which was time consuming, it did not generate extra income and might potentially lead to a loss. The committee agreed that we needed to contact HEW and appeal for higher professional fees for oncologists. Dr. DeVita, being Clinical Director of the NCI at the time, was better informed about the workings of Washington and suggested that we discuss the matter with the Chairman of the Ways and Means Committee of the U.S. House of Representatives. I wrote to the Chairman of the Committee but after a month had received no reply and became quite discouraged.

Albert H. Owens, MD, Director of the Johns Hopkins Cancer Center was the next President of ASCO (1978-79) and reappointed me as Chairman of the Public Issues Committee and urged us to persist in our goal so that the field of oncology could grow and attract well trained young people. Fortunately, one of our COA members from Hartford introduced me to Congressman William R. Cotter.

Congressman William Cotter had been deputy insurance commissioner of Connecticut from 1957 to 1964 and commissioner from 1964 through 1970, when he was elected as a Democrat to the Ninety-second Congress and served from January 3, 1971 until his death from pancreatic cancer on September 8, 1981. (The William R. Cotter Federal Building in Hartford was named in his honor). When I explained to him the economic problem of oncologists, he immediately understood because of his experience as insurance commissioner. He also just happened to be on the Ways and Means Committee of the Congress and agreed to discuss the problem with the then chairman, Al Ullman, Democrat of Oregon. Shortly thereafter I was invited to Washington by Chairman Ullman who then turned me over to his Health-care Aide. She explained that based on what I (as ASCO representative) and Congressman Cotter and oncologists from his own state had told him, the Chairman had determined that there was merit in our case. However, Medicare could not raise reimbursement for oncologists because surgeons, other cognitive specialists (internists, pediatricians, general practitioners) and the AMA would protest and criticize such a decision. He had noted that gastroenterologists no longer made most of their income from cognitive services, but that a significant portion of their income came from procedures like colonoscopy. Similarly, cardiologists made a significant proportion of their income from procedures like EKGs, stress tests, cardiac catheterizations, stents, etc, and oncologists needed a procedural “gimmick.”

Chairman Ullman suggested that he would ask the Medicare/Medicaid program to allow oncologists to charge a 10% markup on the IV drugs that they purchased and a significantly increased charge for administering IV therapy, whether it was by the physician himself or by a nurse under his direct supervision. This suggestion was accepted and when implemented significantly changed the fabric of outpatient chemotherapy. It made oncology a competitive sub-specialty of internal medicine and contributed to an enormous growth of the field of medical oncology and of oncology nursing. I might add that the system worked well for about 4 or 5 years. In the mid-1980s, some of our colleagues were influenced by a cultural change epitomized by the motion picture “Wall Street” (1987 – Director Oliver Stone) in which the character, Gordon Gekko (played by Michael Dougllass) famously declared, “Greed is good.” Along with the “Reagan Revolution,” many of our colleagues became greedy and started to “game” the system by raising the markup to 15% or even 20%, allowing oncology nurses to give chemotherapy infusions when no physician was present (and charging for their supervision when there was no supervision), and selecting the



newest and most expensive drug with which there was less experience but potentially increased toxicity instead of less expensive drugs with proven benefits and less toxicity. One can only presume that in some (but not most) cases, the selection of the more expensive drug was primarily intended to raise physician income rather than improve patient outcome. In addition, when some new support drugs became available, like erythropoietic drugs, in some cases, the drug markup and administration fee and the support drug yielded more than the cognitive fee. I did not foresee this sad turn of events at the time.

Cisplatin was identified serendipitously by Barnett Rosenberg, et al. in 1961 and developed into an effective drug for non-seminomatous testicular carcinoma and for ovarian carcinoma and approved by the FDA for those indications in the early 1970s. Several independent groups demonstrated significantly improved survival of non-small carcinoma of the lung with the drug and the NCI began to use it frequently in some of their protocols by the late 1970s. In early 1979, Dr. Arthur Rosenberg (no known relation to Barnett Rosenberg) contacted me as President of COA to ask for help with obtaining reimbursement for cisplatin which he had used with superior results (compared to previous therapy) on several of his patients at the Greenwich Hospital. The hospital had run up a bill of over \$25,000 and Medicare had refused payment because cisplatin had not been approved by the FDA for lung cancer and considered it experimental for lung cancer. I know that YNHH had it on our formulary for testicular and ovarian carcinoma because I have been the sole medical oncology/hematology member of the Pharmacy and Therapeutics (P & T) Committee since 1971. We restricted its use in our closed formulary to the FDA indications because we knew that we would not be reimbursed for “off-label” use (that is lack of FDA approval). However, Arthur Rosenberg’s use was reasonable in view of its use “off-protocol” by the NCI and the strong supporting peer-reviewed literature.

To try to help get reimbursement for cisplatin, I contacted Congressman Cotter and he wrote an amendment to the Medicare Act, but it was not called up by the Ways and Means Committee immediately as we had hoped and we were all afraid to use cisplatin as long as it was off-label lest we create a big out-of-pocket expense for the patient or a big loss for the hospital. A previous request to Medicare, a division of the Department of Health, Education and Welfare (HEW), was answered by their representative Mr. Earl Gruhn who indicated that “the reason Medicare does not pay in this type of case stems from section 1862(a) (1) of the Medicare law and the policies we have adopted in applying this payment exclusion. This section of the law prohibits payment under Medicare for items or services ‘which are not reasonable and necessary for the diagnosis or treatment of illness or injury.’ In applying this requirement a basic consideration is whether the particular item or service is one generally accepted by the professional medical community as being safe for the purpose used. If it is, Medicare may make payment, on the other hand, if the item or service is one that is not generally accepted, is rarely used, novel, or relatively unknown, then authoritative evidence must be obtained to establish it is safe and effective before Medicare may make payment. In such cases we obtain advice from the medical staff of the public health service which consults with specialists and professional groups who are authorities in their particular fields. Based on the advice they provide us, we develop and issue appropriate instructions to our contractors.” The simple answer was, no.

Marion Morra, Program Director for Cancer Communications suggested that I write to her friend, F. Peter Libassi, Esq, General Counsel of HEW as a representative of ASCO and COA. I wrote to him on February 20, 1979 and indicated that, “A number of patients have had treatment for cancer disallowed because they were treated with a drug that was not yet approved by the FDA although it was distributed by the National Cancer Institute.” I went on to suggest that, “if a drug is distributed by the cancer therapy

section of the National Cancer Institute it would seem that that is a reasonable drug to use. I would certainly agree that a drug that has not been approved by a legitimate agency of the government should not be paid for under Medicare. However it seems unreasonable to me from the Medicare law alone for HEW to decide that their guide should be the FDA and not the cancer treatment section of the National Cancer Institute...It would be most helpful to us if you could indicate from the legal point of view just what the law in this respect is and whether the secretary of HEW could in fact pay for drugs that have been approved by the Cancer Treatment Section of the National Cancer Institute.”

Mr. Libassi analyzed the relevant portions of the law in some detail, reviewed the Congressional hearings leading to its approval and concluded, “As I understand it, investigational drugs approved for use by the National Cancer Institute have demonstrated a certain degree of safety and therapeutic effectiveness, even though they have not been finally approved. As long as they are being used for therapeutic purposes with the approval of the NCI, and are approved for use by an appropriate committee of a hospital’s medical staff, they would appear to qualify for payment under the provisions of Section 1861(t), its legislative history, and the overall purpose of the Medicare legislation.” I sent copies of the letter to all members of COA, to Drs. DeVita and Owens, to the ASCO committee members, to the cooperative oncology groups and to our area Medicare payment office. The Greenwich Hospital received its reimbursement shortly thereafter. Actually, I had made an error in my letter to Mr. Libassi. I said, “A number of patients have had treatment for cancer disallowed because they were treated with a drug that was not yet approved by the FDA although it was distributed by the National Cancer Institute.” What I meant to say, was “not yet approved by the FDA for that indication.” If the drug had not been approved at all by the FDA (at least at that time), the pharmaceutical company could not charge for it and had to distribute it for free as an experimental drug. Once it was approved by the FDA, they could charge for it but unless the drug was used for the specific malignancy approved by the FDA, in this case, ovarian and testicular cancer, they would not reimburse for treating lung cancer. That was the issue I meant to call to his attention and I am certain that Mr. Libassi knew that far better than I did. Two days after receiving his letter, I was called by HEW and told to return the letter because Secretary Joseph Califano had not seen nor approved the letter. I returned the original copy, but I had already distributed more than 20 copies and so informed HEW. They were mainly upset that Mr. Libassi’s letter might be misconstrued to imply that a drug not yet approved by FDA but used by NCI had to be reimbursed if there was peer reviewed support and a hospital’s P & T Committee approved its use in the hospital.

It did not really matter if NCI used the drug because under the law setting up FDA, there could be no payment unless there was FDA approval. The crux of the matter was reimbursement for “off-label” use, in this case, for lung cancer. HEW conceded this and the freedom to use “approved” oncology drugs “off-label” and be reimbursed was established by this opinion when there was good peer-reviewed evidence of efficacy accepted by NCI and the local hospital P & T Committee. Since then, our P & T committee has been adding to our formulary only drugs approved by FDA and has restricted their use to the “label use.” However, when there is substantial evidence in peer-reviewed literature of the efficacy of an approved drug for another indication that FDA has not considered, our P & T will, on request of one of our chemotherapy credentialed physicians, consider the drug for “off-label” use. While off-label use is reasonable in some cases, too many physicians are now using drugs for disorders for which there is no scientific support, and some of these are very expensive chemotherapy or biotherapy drugs being used inappropriately for benign and malignant diseases.

Off-label use of erythropoietin (EPO) at YNHH became a major issue in the 1990s. Erythropoietin- $\alpha$  (Epogen, Procrit) was the first erythropoiesis stimulating agent (ESA) and was approved by the FDA in 1989 for use in treating the anemia of end-stage renal failure. It was produced by recombinant DNA techniques and has the same biologic effects as endogenous EPO produced primarily in the kidney and to a lesser extent in the liver, to stimulate division and differentiation of red blood cell (RBC) precursors in the bone marrow. It was generally agreed that ESAs were indicated to reduce or eliminate the need for RBC transfusions in patients with end-stage renal disease. However, some of our physicians were using EPO for anemic patients with malignancies who were fatigued, but only minimally anemic. In 1993, the ESA epoetin (Epogen) and in 2002, a long acting preparation, darbepoietin (Aranesp), were FDA approved for the management of the anemia due to cancer treatment (with chemotherapy) for non-myeloid neoplastic diseases. This opened a flood-gate of use of this expensive biological. Soon it was being used for treating many other anemias, including those due to radiation therapy, and in general for fatigue and to “improve the quality of life.” Although it could not be detailed by the companies for such use, a large number of studies of “fatigue” began to appear regularly in medical journals and use became widespread. The companies recommended that ESAs be pushed to “normalize” the hemoglobin to 12 or 12.5 gm/dL. YNHH along with almost everyone else followed these guidelines because there seemed to be minimal toxicity, although there were reports of worsening hypertension and more frequent thromboses in patients on ESAs. When I became chairman of the Transfusion Committee in 1998, I noticed that our guideline for RBC transfusion was a hemoglobin (Hgb) of seven gm/dL or less except in special circumstances like active bleeding, ischemic heart disease, pulmonary insufficiency, cerebral vascular insufficiency, significant anemia just prior to surgery and a few others.

Why was the indication for ESAs different from all others? In 2001, as the hematology/medical oncology representative on the Pharmacy and Therapeutics (P&T) Committee, I presented that question to the P&T Committee and suggested that the indication for the use of ESAs should be an Hgb of less than 10 gm/dL. The nephrologists would not hear of this and pointed out that the American Kidney Society agreed with the 12 gm/dL goal and I pointed out that I wondered about an organization making such a suggestion when 25% of its total budget at the time came from the ESA manufacturers, but to no avail. To its credit, I was able to convince the P&T Committee to compromise and mandate that the indication for ESA use for in patients with chronic kidney disease (CKD) would be a hgb of 11 gm/dL or less and for cancer induced and chemotherapy induced anemia it would be (after ruling out iron deficiency, hemolysis, folate deficiency, B-12 deficiency, etc.) 10.5 gm/dL and the target for cancer patients would be 11.5 gm/dL and 12 gm/dL for CKD at which level the ESA would be discontinued. In 2006, the committee also agreed to have patients sign a consent form before the administration of ESAs, just as they do before administration of blood or before undergoing elective surgical procedures.

In 2007, the FDA released a safety information report based on four papers that appeared in the world literature indicating that patients with cancer treated with ESAs had a “higher chance of serious and life-threatening side effects or death with the use of ESAs. These research studies were evaluating an unapproved dosing regimen, a patient population for which ESAs are not approved, or a new unapproved ESA. FDA believes these new concerns apply to all ESAs and is re-evaluating how to safely use this product class. FDA and Amgen, the manufacturer of Aranesp, Epogen and Procrit, have changed the full prescribing information for these drugs to include a new boxed warning, updated warnings, and a change to the dosage and administration sections for all ESAs.” Eventually, the FDA black box read: “WARNINGS; INCREASED MORTALITY, SERIOUS CARDIOVASCULAR and THROMBOEMBOLIC EVENTS and INCREASED RISK OF TUMOR PROGRESSION OR RECURRENCE.” The warning goes on to

indicate that there is a risk of tumor progression or recurrence in some patients with breast, non-small cell lung, head and neck, lymphoid and cervical cancers.. They urged physicians to decrease these risks by using the lowest dose needed to avoid RBC transfusions and noted that “ESAs are not indicated for patients receiving myelosuppressive therapy when the anticipated outcome is cure.” The company now mandates the use of a consent form before ESAs are administered. YNHH guidelines anticipated the eventual national procedures, our patients were spared the added risk and our controversial early decisions were vindicated. In 2007, Procrit had world-wide revenue of \$2.9 billion for Johnson and Johnson (J&J) and Aranesp had \$3.61 billion in sales in 2007 for Amgen and I do not have figures for Amgen’s Epogen. To its shame, ASCO and ASH (note: I am a member of both organizations) fought the changes. Both organizations received generous support from J & J and Amgen as did their members. One can only speculate on why both community and academic medical oncologists and hematologists opposed questionable use of ESAs. Some have suggested that the drug companies supported ASCO meetings and journals and that the high price of the ESAs combined with generous discounts resulted in a large net profit for practitioners or hospital pharmacies that did not pass on the discount to patients or the third party payers. Some commentators have suggested that the profit for those physicians who administered a dose of an ESA in the office, exceeded the office visit fee. The main losers in this situation were the taxpayers and those who paid for health insurance. President Eisenhower warned us to be aware of the collusion and resulting power of the military-industrial complex and its effect on government spending. Do we need to be similarly aware of the pharmaceutical-medical complex and its effect on government spending in a time of budgetary distress?

Gerard Noel Burrow, MD, became Dean of YSM in 1992. He was a graduate of YSM class 1958 and stayed on as a house staff member, became chief resident, then a post-doctoral student and then fellow in internal medicine, an assistant professor in 1966 (when I first met him), an associate professor in 1970 and Professor of Clinical Medicine in 1975. It is worth noting that until about the mid-1970s, the promotion track was based almost entirely on scholarly publications and grants, as Welch had told me in 1966. This traditional system apparently worked well in the medically related basic sciences as it did in the University generally. However, it was becoming increasingly clear that in the clinical realm, YSM was losing some of its best teachers and physicians because they did not publish enough or get enough grants. Later the system was modified so that some associate professors could be reappointed with tenure and might or might not be promoted to full professor, but did not have to leave the institution. That was apparently the basis of the rank of Professor of Clinical Medicine, a full-time position. In 1981, I was promoted to Clinical Professor of Medicine (a part-time faculty position) based on a pretty good record of continuing publications, teaching in the clinics and on the inpatient units and serving as a preceptor each year for one student for a full month who would see office and hospitalized patients with me all day . This rank entitled me to sit on the Board of Permanent Officers. The senior faculty on that Board were still not satisfied with the traditional and clinical tracks and appointed a committee chaired by the late Norman Siegel, MD, Pediatrician-in-Chief, to suggest a better system. As I remember it, the traditional track was preserved, but full-time faculty could also be promoted in the clinical scholar track and the clinical educator track up to full professor but were not guaranteed tenure. They would have to generate at least their salary and benefits.

The promotion system I have described is how it looked to a part-time faculty member. It is best to view it as an insider saw it. In his *A History of Yale’s School of Medicine*, Dean Burrow says, “Despite the primacy of medical education, promoting faculty members for their teaching abilities has been extremely difficult. The presumed commitment to education has more often been honored in the breach. Young

faculty members have been advised to resist teaching commitments that will not foster their academic careers. Lack of objective criteria makes it difficult to evaluate educational excellence or clinical judgment, in contrast to research, where peer-reviewed publications and grants all provide objective evidence of excellence. As a consequence, a medical school's reputation is often linked to research prowess. At Yale, tenure appointments have been largely based on research accomplishment, reflecting the culture of Yale College and the Faculty of Arts and Sciences, which makes promotions on the basis of achievements in scholarship. Basing tenure primarily on research accomplishments is certainly a feature of other medical schools, but at Yale, the school's close ties with the college have made this focus more apparent. The basic-science orientation of the medical school grew from its association with the college dating back to Benjamin Silliman."

Burrow goes on to say, "Tenure appointments are jealously guarded by the university, because they incur long-term financial obligation. At Yale, a faculty member must achieve tenure within ten years or leave. The 'up or out' rule was intended to prevent faculty exploitation by administration, but it works to the disadvantage of individuals who take time off (to, say, raise a family). A continuing-appointment track was instituted at the medical school to alleviate pressure on limited senior appointments. Associate professors on this track are not required to leave after ten years if they fail to be promoted, but the number of professorial slots in the track is limited. Professors on this track can be terminated only by eliminating the entire track for reasons of financial stringency, but the number of faculty qualified for promotion to professor increased faster than the number of positions the university was willing to make available. Recently, a third academic track has been added at the medical school which offers less long-term security but allows attainment of professorial rank."

When Burrow became dean in 1992, he soon realized that the YCCC was a great asset to YSM and YU because of its strong basic science departments, but that its clinical component was weak and underfunded and because it had no support from YNHH and little from YU, it had never built the facility that it had led NCI to believe it would build, and that Sartorelli had tried to get YU to assist in building. With Sartorelli stepping down, Burrow sought support from YU for resources to recruit a new director who would be an outstanding clinician and scientist and an experienced administrator and thought that he had such a commitment for funds. With the selection of Vincent DeVita whom he had known at Yale in 1965-66, he knew he had the right man for the job.

Vincent T. DeVita, Jr, MD. had a remarkable scientific and administrative career and some of it has already been mentioned. Suffice it to say that in addition to his pioneering work in developing a curative therapy for Hodgkin's disease, he had been Clinical Director, NCI 1975-1980 and appointed by the President, Director NCI, National Cancer Program, NIH 1980-1988. At the end of his term, he had become Physician-in-Chief (9/88-7/91), and Attending Physician and Member, Program of Molecular Pharmacology and Therapeutics (9/88-9/93), MSKCC. Burrow invited him to become Director of YCCC in 1993 and DeVita accepted. I was personally delighted because I felt that the clinical program at YCCC needed a strong clinician with the resources to revamp it into a leader in the field. I was also pleased because I knew DeVita personally from when he was President (1977-78) of ASCO. I knew that he was smart, experienced, and knowledgeable and I thought he was the best person for the YCCC job. DeVita was the fourth Director of the YCCC.

The Directors of the Yale Comprehensive Cancer Center were:

Joseph R. Bertino	1974-1975
Jack Wesley Cole	1975-1984
Alan C. Sartorelli	1984-1993
Vincent T. DeVita, Jr.	1993-2003
Richard L. Edelson	2003-2009
Thomas Lynch	2009-

When DeVita arrived, he found the YCCC still strong in basic science research as a legacy of Sartorelli's stewardship, but the in-house clinical program in medical oncology was weak. One reason for this may have been the relatively large number of well-qualified medical oncologists who were clinical faculty practicing in the community and included: Kathleen Bober-Sorcinielli, Samuel N. Bobrow, Ricki Lahn Chopyk, Leonard Farber, David S. Fischer, Kay A. Haedicke, Jacqueline Henchel, Martin E. Katz, Arthur L. Levy, W. Bruce Lundberg, Joseph O'Connell, Jeffrey A. Orell, and Roy Glen Wiggans. Each was practicing a full range of medical oncology and only beginning to think about specialization. There were fewer full-time medical oncology faculty members but they had been starting to carve out areas of special interest a few years earlier. DeVita was fortunate to have John C. Marsh, a full professor and an outstanding clinician to anchor the group, and several young assistant professors, most of whom had been fellows and stayed on as junior faculty. They included Dennis L. Cooper, Jill Lacy, Mary Todd, Wen-Jen Poo Hwu, Andrea Silber (at HSR), John R. Murren, Joseph Germino, Thomas Fynan and Michael Reiss. In addition, Roger Strair remained until 1994 and Lee P. Schachter remained until June 2000. Rose Papac was very ably running the Yale medical oncology program at the West Haven Veteran's Administration Hospital (WHVAH), a favorite rotation of the fellows.

Paul Harold Laviertes, MD received his BS degree from the Sheffield Scientific School in 1927 and his MD degree from YSM in 1930. He was an assistant professor of medicine from 1937-1946 and worked closely with Dr. John P. Peters in endocrinology. He went into private practice in New Haven in 1947. In 1958 he was a founding editor of the Yale-sponsored Medical Letter on Drugs and Therapeutics along with Arthur Kallet and Dr. Harold Aaron and he remained a long-time member of the advisory board. The Medical Letter is unique in that its articles are written by an outside expert or an in-house editor, edited in-house by Medical Letter staff and sent unsigned to a large number of reviewers, including the first authors of all articles cited in the text. The final version of the article incorporates the suggestions of the reviewers and the editorial board into a consensus document and is published unsigned. It provides unbiased information on new and existing drugs and other therapies. It is completely independent, supported solely by subscription fees, and accepts no advertising, grants or donations. Thus, it can use the expertise of some authors with special knowledge who also have conflicts of interest because their bias should be tempered or eliminated by the expert reviewers who have no conflict of interest. This proved to be very important when it was realized that almost all drug experts had financial conflicts of interest with pharmaceutical companies. In fact, the New England Journal of Medicine largely abandoned its series of periodic drug and topic updates when it became evident that it could rarely find an expert with no conflict of interest. Accordingly, in 1979, when Laviertes asked me to become a "Reviewer for the Medical Letter" in oncology and hematology, I was delighted to do so pro bono, and it is a position that I continue to fulfill to the present day. Laviertes also had the distinction in 1971 of becoming the founding medical director of the Community Health Care Plan in New Haven until his retirement in 1981. When Laviertes stepped down at the Medical Letter, James D. Kenney, MD, a rheumatologist in private practice and a

part-time Associate Dean for Graduate and Continuing Medical Education became a member of the advisory board and set up the system for testing so that the Medial Letter could be used for CME credits that were then certified by YSM. Lavietes and Kenney and YSM played a major role in disseminating accurate and unbiased drug information and this is particularly important in the area of cancer drugs which are very expensive, often quite profitable for the pharmaceutical manufactures and heavily promoted. Sandip K. Mukherjee, MD of YSM cardiology is now one of the 13 contributing editors, so the Yale connection continues.

The Hospital of St. Raphael was another favored rotation of the fellows. Its contribution to the Yale Cancer Program is important. As I previously indicated it offered an alternative for patients and for admitting physicians who did not wish to or were unable to use the NHH and later the Y-NHH. In 1957, it opened the first radiation therapy facility in Connecticut under the direction of Wayne Whitcomb, MD. Many years later, when he died, I was instrumental in convincing the search committee to hire Arthur Knowlton, MD, a radiation oncologist at YNHH who was known for his skill as a radiation therapist, his outstanding devotion to compassionate patient care and keen understanding of the value of interdisciplinary therapy. When I came to Connecticut in 1962, HSR had some distinguished physicians practicing there and most notably Theodore Evans, MD, a hematologist who had written one of the major monographs on monocytic leukemia and was chief of medicine. For a time, he was chief of medicine on the General (Grace) Service at GNHCH. After years of being known for quiet, compassionate care, areas of leadership developed in several specialties at HSR, most notably in cardiology and gastro-enterology, as young Yale trained physicians moved into community practice and put their patients in both hospitals and demanded an equal standard of care. In 1958, Max Carter, MD used the first heart-lung machine to perform open heart surgery, the first community hospital in the state, and probably in New England, to do so. In 1963, HSR opened its first intensive care unit, and in 1965, Oscar Roth, MD, designed and opened the first coronary care unit in Connecticut, the second in New England, and among the first half dozen in the U.S. The Cardiac Diagnostic Unit that HSR opened in 1977 was heralded at the time as the only one of its kind in the U.S. as it combined the disciplines of nuclear medicine, cardio-vascular radiology, echocardiography and cardiology in one location. New Haven's first, and Connecticut's second, laparoscopic cholecystectomy was performed there in 1990. Many services became outstanding.

Robert Zanes, MD became the head of hematology at HSR on the retirement of Dr. Evans, his mentor. When I joined the staff of HSR in 1968 as a hematologist and medical oncologist, Zanes was then the only trained hematologist there but he had no training or experience in solid tumor chemotherapy. He graciously welcomed me and asked me to co-chair the biweekly hematology conference. In a few months, we set up a biweekly medical oncology (MO) conference that I chaired so we alternated weeks with hematology one week and MO the next week, and I chaired MO and regularly attended hematology. My colleagues there were anxious to give their cancer patients the newest and best therapy and soon 50% of my patients were at HSR. In 1979, I was honored to be asked to serve as President of the Medical Staff and served on the Medical Board as president elect in 1979, president in 1980 and past president in 1981. My life was complicated one week after I accepted the presidency at HSR by the nominating committee at YNHH offering me the presidency of the Yale medical staff. I could not do both, and so they offered it to Leonard Farber, MD who had joined the staff in 1971 and had participated in the medical oncology and hematology conferences. From 1983 to 1987, he was Principal Investigator of the Clinical Community Oncology Program (CCOP) at HSR, which accrued a great many patients to clinical trials and helped demonstrate that clinical trials could be performed at community hospitals. He was also instrumental in convincing administration that we had reached a critical mass of oncology patients and that we needed

a separate, dedicated medical oncology and hematology service with specially trained nurses capable of giving chemotherapy intravenously and orally. One of the newest and best units at HSR was so dedicated and worked very well. At that time YNHH did not have a dedicated medical oncology unit and our patients were scattered on the medical service. It did not take long for YNHH administration to realize the need for such a unit at Yale. Unfortunately, it was placed on Winchester I, which was an old ward with poor lighting so that patients who were depressed by their disease were further depressed by their medical unit surroundings. Mr. Smith, the administrator and I had some strong words about that situation before the medical oncology unit was first moved to a light and airy unit on Hunter 4, but still across the street from the main medical service in the Memorial Unit (MU). Eventually it was moved to the remodeled quarters in the MU and is now moving to the Smilow Cancer Hospital.

The Father Michael J. McGivney Center for Cancer Care opened in 1994 at HSR. It was named for the local New Haven priest who was the founder of the Catholic fraternal order, the Knights of Columbus, which is now nationwide and has evolved to be a major insurer of its members. Many people called it a "Cancer Center" and equated it with the one at Yale. However, it was appropriately named as a "Center for Cancer Care" and not for basic science research. As noted, a Clinical Community Oncology Program was able to do some clinical trials and after that program closed, some patients from HSR were entered into YSM clinical trials. The teaching program in oncology is strong at HSR and Andrea Silber, MD, who was a Yale intern, resident, fellow and full-time YSM faculty member runs a remarkable breast clinic there. She has done considerable work with minority patients and has published extensively on disparities in health care for breast cancer. She gives several lectures to the YSM fellows here every year and is the consulting oncology editor of Connecticut Medicine. I frequently refer patients to her and they have all been delighted with the care that she has given. The oncology fellows find the time spent in her clinic at HSR is one of the most rewarding of their rotations. In 2007 she was the recipient of the ACS Lane Adams award.

DeVita recognized that YCCC was working as a series of small shops, with each physician doing excellent work in his/her small domain and specialty. Although the basic scientists had much interdisciplinary cooperation, clinicians collaborated only at tumor boards. DeVita set out to make those interdisciplinary tumor boards the nexus of a series of interdisciplinary disease units that would work together to give the patient the best therapy available. There is an old aphorism, "a man with a hammer sees a nail everywhere he looks." Our therapy had to avoid the problem of a patient being treated with surgery if the first patient contact was with a surgeon or radiation therapy if the first referral was to RT and similarly with chemotherapy if the first contact was with a medical oncologist. If all three physicians saw the patient at the same visit and then considered the best therapy together, it was more likely that the patient would get the best therapy, and this is what DeVita was determined to make happen at YCCC.

Hait left Yale in late 1992 for reasons previously detailed. Michael Reiss became acting chief of medical oncology for the remainder of 1992 and the first half of 1993. When DeVita became Director of YCCC, he also assumed the role of Chief of Medical Oncology until a new chief was appointed. In that period, there were several new faculty appointments, including Ann Berger, RN, MD who set up a pain and palliative care program; Michael Reale, who had a particular interest in genito-urinary (GU) oncology; Emile Sal-loum whose major interest was lymphoma and stem cell transplantation; Barbara Burtness, who trained at MSKCC and came with an interest in breast cancer, esophageal, and gastric cancer.



How and why I returned to work at YSM after 25 years of practicing medical oncology and hematology in New Haven, initially alone and later with partners: In November 1992 I was struck by an automobile while crossing the street near my office. I was thrown up in the air and my head went through the car's windshield. I sustained a comminuted fracture of the left tibia and fibula and an external ear was almost severed. I was admitted to YNH and I was extensively worked up with CT scans of the head, chest and pelvis and plain x-rays of the legs. As was typical with patients at that time, I was worked up by the house staff of the trauma team and told nothing, except by my friend, James Dowaliby, MD, an ENT surgeon who skillfully reattached my external ear and assured me that it would heal and look relatively normal, and events proved him correct. About 30 minutes before I was scheduled to go to the operating room to reduce the fracture, I was informed by someone in a scrub suit that I did not know, that he was going to operate on me. I asked where was the attending surgeon with whom I was familiar and that I had requested five hours earlier. He said that the surgeon I requested was in Chicago and that he had just joined the group of eight about four months earlier after completing his residency and that he was going to do the operation. As it was now 7:00 PM, the other members of the group (who I knew and who knew me but had not been informed that I had been injured) had all gone home and I was put on the operative schedule as an emergency. If I did not consent to have him do the surgery as an "emergency add-on," I would have to wait three days until the group had its next elective operative day and I would be responsible if infection or other complication occurred because of the delay. Reluctantly, I allowed him to do the procedure. Afterwards, he assured me that the insertion of a metal rod with fixation at both ends and the reduction of the fracture had resulted in perfect position and a likely prompt healing. I was skeptical. I asked one of my interns to bring me the post-op x-rays and I noted through the short-leg cast that a relatively large space had been left between the fragments. When my selected surgeon returned from Chicago, I expressed my doubts about healing and asked him to take me back to the OR to get a proper reduction where the bone fragments would be close enough to heal. He assured me that I was young (62) and healthy and it would heal in three months.

Three, and then four months later, x-rays showed a non-union and progressive loss of bone with the fragments even further apart. I was advised that amputation and a good prosthesis would be my best option. I refused amputation and suggested that we return to the OR, take out the fixed rod that was keeping the fragments apart and put in a rod with fixation at only one end so the fragments could be allowed to approach each other and put in some bone chips to provide an additional matrix for healing and accepting the risk that my left leg would be shorter than the right one. This was done and a full leg cast applied. My condition was complicated after the initial operation by the development of reflex sympathetic dystrophy, a condition that occasionally follows an extremity injury or operation and is characterized by severe pain which is increased after minimal stimulation and often includes severe sensitivity to cold. It persisted after the second operation and even the weight of a sheet on my toes caused severe pain, and my foot was always cold. I had to take two oxycodone-acetaminophen tablets every four to six hours. I was bed to chair bound for about six months until there was x-ray evidence of enough healing to start using crutches. As I gradually was able to reduce my pain medication I went for hydro-therapy and when I thought that I had improved enough, I tried to return to practice on crutches. I lasted one day in the office because of the profound fatigue of walking with crutches and I was still in so much pain that I was still taking some oxycodone and thinking more about pain relief than about the patients' care. My partner and I decided to close the office. After three additional months, I was able to walk with a cane and gradually reduce my pain medication and discontinue all narcotics.

On my first trip to YSM more than a year after my injury, I encountered Dr. DeVita after a lecture and he asked me what I was doing now that I had closed the office. I told him that as I was able to walk better and was gradually increasing my strength and endurance, I was beginning to think about my professional future. He asked me if I would help him a half-a-day a week with the ACoS program that was taking more of his time than he could spare. I agreed to do so temporarily. One thing led to another and Dr. Robert Levine finally enlisted me to become a member of the HIC (I say “finally,” because he had asked me several times earlier to join but I could not spare the heavy time commitment required to do it right and maintain a busy private practice). Since I seemed to be doing a good job at both volunteer tasks, Dr. Edward Snyder, Director of the Blood Bank, asked me to chair the Transfusion Committee, and the P & T Committee asked me to resume my role as oncology-hematology representative. As I worked on the ACoS Cancer Committee, we started doing more and more and it was taking two days and often three days a week. I had to have an office, a telephone and a computer to do the work effectively and it was not long before Dr. DeVita and Dr. Deisseroth arranged to provide those necessities for me and I have been working at YSM and YNNH three days a week since then.

Albert B. Deisseroth, MD, PhD received his PhD in 1968 and his MD in 1970 from the University of Rochester School of Medicine. He completed his internship and residency at Beth Israel Hospital in Boston and was a Fellow in Medicine at Harvard Medical School. Following several years of training at NIH and at the Dana Farber Cancer Center, he joined the Pediatric Oncology Branch of NCI as head of the Experimental Hematology Division. He was also Professor of Medicine at UCSF and Chief of Medical Oncology/Hematology at the San Francisco VAMC. Later, he was Anderson Professor of Cancer Treatment and Research and Chairman of the Department of Hematology at the MD Anderson Cancer Center. In 1995, DeVita was finally able to recruit Albert B. Deisseroth as Professor of Medicine and Chief of Medical Oncology. This was the only full professor he was able to appoint as far as I know. His credentials were impeccable and his research outstanding.

In the Winter 1996 issue of *Caring*, Yale Cancer Center, volume 1, number 1, Deisseroth is called: “The gene doctor.” “In his new position as the Yale Cancer Center’s associate director for clinical research, and head of the gene therapy program, Albert B. Deisseroth, MD, PhD, describes himself as a ‘matchmaker’— someone who can bring together researchers in the basic science laboratories and in the clinics and guide them in developing new programs of cancer therapy. But he is also a pioneer himself, charting new frontiers in cancer research through the emerging field of gene therapy, a revolutionary new technique in which a normal gene is inserted into the cells of a patient in order to treat diseases. It has been described as ‘the ultimate treatment— coaxing the body to heal itself.’ It is Deisseroth’s combined expertise as a molecular biologist and gene therapist— along with his ‘unbelievable energy’— that convinced Cancer Center Director Vincent T. DeVita, Jr. that he would be a tremendous force at Yale. ‘He is driven,’ says DeVita of his longtime colleague. ‘He wants to discover new things, but is always aware of linking the lab and the clinic. He does things with the patients in mind.’”

Deisseroth set up a fine research laboratory and embarked on exciting gene therapy projects with attempts to introduce new genetic material into cells with viral vectors. We had a gene therapy board meeting monthly and talked about potential vectors and how they could be used in specific tumors. However, to the best of my recollection, we did not initiate a clinical trial. All the work was done in laboratory animals. In the clinical area, Dennis Cooper, MD was involved in the medical treatment of Head and Neck cancers (H&N) and also set up an autologous stem cell transplantation program in 1993 and an allogeneic transplant program in 1997. The clinical program was very successful with the collaboration of Bernard

Forget, MD, chief of hematology and Edward Snyder, MD in Laboratory Medicine. Frank Hsu, MD was recruited from Stanford Medical School in 1996 as both a basic investigator and clinician in lymphoma. Emile Salloum, MD, a fellow here who had become an assistant professor and worked in the lymphoma and stem cell transplantation area, left in June 1997. Joseph P. McGuirk, DO, had been a resident at Yale before he spent some time at MSKCC and in South Carolina with Dr. P.J. Henslee-Downey and her team studying haplo-transplantation. He came to Yale in 1997 hoping to start a haplo-transplantation service, but it did not succeed. Stuart Seropian, MD, finished his medical oncology fellowship here in June 1997 and joined the faculty to work with Cooper in lymphoma and stem cell transplantation. Together they run the lymphoma tumor board which I attend regularly and is also a favorite area of instruction for fellows. Their stem cell transplantation program is distinguished for having one of the highest U.S. transplantation survival rates.

Michael Reiss, MD, headed the breast cancer clinic with Michael DiGiovanna, MD, PhD, a YSM graduate who had graduated the fellowship program in 1997 and helped in the breast cancer clinic and also worked in the laboratory on tamoxifen and related drugs. He also headed the second year student clinical module where he made oncology one of the favorite modules of the students while he was one of their favorite teachers. Jill Lacy, MD, became specialized in gastrointestinal (GI) cancer and neuro-oncology and in 1997 became fellowship director (and still is); Barbara Burtness, MD, worked on esophageal and gastric cancer and breast cancer until she left to join the staff of the Fox Chase Cancer Center. John Murren, MD, headed the lung cancer chemotherapy program and developed a program in phase I drugs. Michael Reale, MD, transferred his major activities and his special interest in genitourinary cancer to the WHVAH and Wen-Jen Poo Hwu, MD, PhD, took over the medical oncology GU service and headed the medical oncology melanoma program after Antonio Buzaid, MD, left to become Executive Director of the Oncology Center in a hospital in Sao Paulo, Brazil. Giuseppe Pizzorno, PhD, PharmD, was an Associate Professor of Internal Medicine, Pediatrics and Pharmacology and Director of Research of the Yale Pediatric Pharmacologic Research Unit. He had trained with Handschumacher and Bertino and concentrated his research on anti-folate antimetabolites and on the evaluation of new fluoropyrimidine-based regimens and biochemical modulations. He left Yale in June 2008 to become Director, Division of Translational Sciences at the new Nevada Cancer Institute which he and John Murren had helped to establish. Ann M. Berger, MD, RN, MSN started a palliative care program with an emphasis on pain control. DeVita encouraged Berger to arrange to edit a book on palliative care because that was a much neglected field. She was senior editor with Russell K. Portenoy and David E. Weissman as coeditors. They published *Principles and Practice of Supportive Oncology*, a major addition to the field. Berger left Yale in 1996 to set up a palliative care unit at Camden Hospital, an affiliate of the University of Medicine and Dentistry of New Jersey and later she became the Chief, Pain and Palliative Care Service at the Surgical Unit at the NCI.

DeVita was a great mentor and when I showed him a small pamphlet on the follow-up of cancer that I had edited for the Connecticut Division of ACS for its second and third editions with contributors from other Connecticut physicians, he encouraged me to transform it into a full book with multiple authors from across the country that I edited (*Follow-up of Cancer: A Handbook for Clinicians*, 4<sup>th</sup> edition). I am sure that he helped many others to be more productive. We tended to think locally and he sought the best from around the country and around the world.

Edward Chu, MD was recruited as associate professor of medicine and pharmacology (with tenure) and chief of medical oncology/hematology at the WHVAH in 1996 when Rose Papac wanted to return to the YSM central campus. This was only the second (Deisseroth was first) direct tenured appointment

DeVita was able to make. Many of the assistant professors were promoted to associates professors, but none in the traditional tenure track. This “freeze” on promotions was tied to the allegation that medical oncology was not earning enough and that the Department of Internal Medicine (DIM) had to assume its \$3 million a year deficit. This alleged deficit was related to the fact that medical oncology billing went out through the office of the DIM which did not completely understand the complexities of oncology billing which differed from billing in other areas and DIM under-billed for oncology services. Sometimes they did not submit bills within 120 days to Medicare/Medicaid or to some HMOs in 90 days, and those bills became uncollectable. In addition, they failed to recoup the fees for drugs and drug administration that were supposed to be credited to medical oncology and were probably many millions more per year than the alleged \$3 million deficit. Instead, that money went to YNHH pharmacy and nursing and only a little found its way back to medical oncology. As I detailed previously, it was a long and hard fight to make the practice of medical oncology a viable field financially. In office practice, approximately one-third of income came from professional fees and two-thirds from drugs and drug administration fees. There was no way that medical oncology could be fiscally viable without the administration and drug fees. Congress knew it. Medicare/Medicaid knew it. No one wanted to talk about it publically lest it become a political issue and as a result, some people who should have known, did not. Without it, a strong section of medical oncology was not possible, and the YCCC clinical program and its clinical trials accrual program were not viable without medical oncology and some support from the University or the Hospital or both.

DeVita attempted to have a private group with experience in medical oncology billing do the billing for the Section of Medical Oncology to ameliorate this situation, but this was not agreeable to the Dean. To transfer fiscal and academic control to the Cancer Center, he proposed an arrangement similar to the situation at New York University School of Medicine. The best compromise he could get was that the Cancer Center was free to make its medical oncology appointments without clearing them with the DIM and could run its own financial affairs and transfer its fee collection out of the DIM, but the confirmation and level of academic appointments would continue to be made in the DIM. For good reason, the department of surgery had allowed some subspecialties to become departments, like neurosurgery, orthopedics (and in the near future, urology), but internal medicine was holding tenaciously to sections that might prosper with more independence. It was difficult to hire and retain physicians with a dedication to compassionate patient care and patient oriented teaching of house staff and fellows. The situation improved a little when promotions could be made more easily in the clinical scholar track. With that change, it was possible for DeVita to appoint Dennis Cooper as a full professor, effective in 2004. The clinical track allowed for more clinicians. Still there were problems.

On January 5, 1999, I noticed an article in the New York Times that seemed to address some of the problems that we had at YNHH and the YCCC. I decided to share it with Mr. Brian Condon, Senior V.P. of YNHH, its representative on the Cancer Committee and a knowledgeable, cooperative and dedicated administrator. In view of subsequent developments, the letter and his response may be of some general interest.

“Dear Brian: I hope you read the page one article in yesterday’s New York Times on the race in New York City to provide “patient friendly” cancer care in an out-patient setting in order to enhance the in-patient hospital census. The NY Times is announcing what we already know, that cancer will eclipse heart disease as the major hospital activity in the next two decades and the financial future of hospitals will depend on their ability to make an appropriate response. We are not. The NY Times points out that Memorial Hospital was not, but has learned a lesson and is now trying harder to become “patient friendly.”

They just succeeded in stealing one of our best oncologists in that category, Dr. Wen-Jen Poo Hwu.

“If you read the article, you may appreciate why I have been making such a fuss over improving the ambience in the Mammography area, in the Medical Oncology Clinic, and pushing for a formal patient library area with a computer and a librarian to help patients and patient’s families, and why I pushed to get a senior representative of the Dean’s office on the Cancer Committee. I do not believe that the higher levels of the Medical School get the message of the NY Times article. Perhaps in negotiations between the Hospital and the Medical School that message can be pushed because the two entities will prosper or decline together. We are clearly not doing as good a job as we should be doing. A medical school cannot prosper on research alone, it needs to do a creditable job in patient care and education as well, especially since the object of the educational process is to produce doctors who will render patient care, although they may also do research. You do not need a MD to do research. Excellent research is conducted by PhDs all the time. Patient care requires a cadre of excellent physicians and nurses, support personnel, and adequate facilities. The NY Times discussed competition between Memorial and the Beth Israel and St. Lukes-Roosevelt Hospitals, but the fact is that they are also our (YNHH’s) competition. I point this out because I want to see this medical center grow, prosper, and become a better center of excellence. There is no personal agenda, other than the pleasure or disappointment, depending on the outcome. Have a happy New Year. Dave Fischer”

Mr. Brian Condon replied: “Dave: Your comments are timely for two reasons. First your assessment of the relationship between the New York Times report of the situation in NYC and YNHH is very accurate....Secondly, we ARE about to launch our Cancer Service Line planning effort to another level with the support of the dean and Joe Zaccagnino who should be sending out letters this week to significant medical center persons involved with cancer inviting them to join a high charged action oriented planning process that is intended to tell us what we have to do to be successful in the regional market, and how we have to be organized to achieve that success...It will focus on patient needs, facilities, and organizational changes... You are one of the persons who will be asked to join the group that is going to report on the clinical practice needs which I am sure will look at MD and patient friendliness improvements on all levels.... The groups are expected to conclude their reviews in about 90 days.... And will be facilitated by a professional consultant with whom we have previously worked...who is actually very familiar with the Salick operations...We are looking at this as a major opportunity...Thanks again for your continued interest.....Brian.”

One week later, a letter from the YNHH President and the YSM Dean was sent out and said, in part, “Over the past year, Yale-New Haven Hospital and the Yale University School of Medicine have been involved in a process to identify the complex market place issues that influence our oncology program. We retained Ronning Management Group (RMG) to assist us in this effort. Recently, RMG presented a comprehensive analysis of our oncology program and its position in the market. Two of the study’s primary recommendations were to reorganize our clinical services to better meet patient expectations and to develop an appropriate synergy between the administration and financial organizations at the School of Medicine and the Hospital. It was recommended that the two work groups be charged to develop models that would address both of these issues.

“We would like to invite you to participate as a member of the Clinical Services Delivery group. This group will meet for 4 to 6 sessions every other week beginning in January. The objectives of the Clinical Services Delivery group would be to formulate a patient-focused clinical integration of the outpatient,

inpatient and faculty clinic services and design a patient services delivery process that is competitive in the marketplace. Additional information such as goals and deliverables, guiding measures and committee members are attached.”

The Clinical Services Delivery group was carefully selected. It included the Assistant Director of the YCCC, the Chief of Staff of YNHH as co-chairmen, the YNHH COO, the YCCC Director (Ex Officio), two department chairmen, the section chief of medical oncology, the chief of gynecologic oncology, three members of YNHH administration, eight physicians (including me), two nurse managers and a representative of RMG. It was an excellent group of dedicated health care professionals. We worked together and made many good suggestions for improvement, some of which were implemented and led to better patient care and increased patient and family satisfaction. A patient oncology library was created and staffed with relevant printed materials and three computers (one donated by the American Cancer Society) and computer-knowledgeable volunteers intermittently were present to help patients and families who were unfamiliar with computer use. More space was provided for clinics and more trained interpreters were provided for those who did not speak or understand English. Nursing improvements were made. Physicians were encouraged not to over-book their clinics and to diminish waiting times. What could easily be done was done. We discussed the need for additional space for cancer clinics either in rented space or building a new cancer center and bringing together the inpatient cancer services. However, there was no decision to start significant improvements that required large financial commitments, like building a new cancer unit or a cancer hospital.

As early as October 1999, I recognized that in spite of the improvements, we were approaching a situation that might lead to a non-renewal of the NCI designation. I took the opportunity of writing to Dean David Kessler, MD, JD, on October 10, 1999, after he had sent me a note thanking me for setting up an endowed lectureship in memory of my late wife, Iris. In a five-page letter, I detailed my concerns about the future of medical oncology at YCCC and even the survival of the NCI designation of the YCCC. I sent copies to Yale President Richard Levin, PhD, YNHH President Joseph A. Zaccagnino, Ralph I. Horwitz, MD, chair of DIM, and a copy to Dr. DeVita. President Levin responded and thanked me for my concern and said he would look into the matter. Dean Kessler, at a party in my honor, told me verbally that he had received my letter. Dr. Horwitz replied in part, “. . . I cannot help but express my support for your remarks concerning clinical oncology at Yale. Your comments are all the more meaningful because they are so very authentic. I know you are aware of the strong commitment, in words and dollars, the Department of Medicine has made to Medical Oncology clinical services. Nothing is more central to this effort than the work now underway to strengthen the clinical faculty in Medical Oncology.”

The bridge over Cedar Street bore the label, “Yale Cancer Center,” but YSM had no other construction specific to the cancer program. Cancer patients were on designated adult cancer units and pediatric cancer units, and the cancer clinics were scattered in the hospital and in the Faculty Practice Plan building, and later in a rented facility at the Long Wharf. DeVita proposed the construction of a building on the corner of Howard Avenue and York Street, then and now a parking lot, that would be connected to the main buildings of the YNHH by an over the street bridge. It would have oncology clinics on the lower floors and cancer research laboratories on the upper floors. Dean Kessler objected and suggested that a University owned lot on Amistad Street, two blocks from YNHH would be a more suitable location for such a facility and it could have inpatient units. The Department of Radiation Therapy objected and indicated that it was not feasible to transport patients from the proposed facility by ambulance or van to the existing Radiation Therapy facility. No building was built there at that time.

Deisseroth's tenure as section chief was also compromised by his "luke warm" support and DeVita's lack of support for the promotion of Wen-Jen Poo Hwu (who was bringing in relatively large grants from pharmaceutical companies) because she did not have enough peer-reviewed publications. She spent long hours in the clinics and also saw her inpatients each and every day. She had a melanoma clinic estimated at 600 patients and had much data to publish, but no help to organize the material and no one to help her write in a language that was not native to her. I helped her write two papers and she graciously added my name as a coauthor because she said that they would not have been written without my help. Although she had ample funds from pharmaceutical contracts to hire a secretary, she was not allowed to do so (because her coworkers could not) and she had to share a secretary with two other faculty members. That certainly interfered with her ability to organize her data for publication and write it up. When she went to MSKCC there was no one to do genito-urinary medical oncology and that was referred to the community oncologists. At MSKCC she had more help and many more peer-reviewed publications. She was later recruited to MD Anderson Cancer Center.

Deisseroth had to assume the burden of the estimated 600 patients in the melanoma clinic and those admitted to the hospital. It so consumed his time that he had little time left during the day for supervising his research laboratory. I remember him working late into the evening and sometimes the night, because my office was a small area carved out of his laboratory, and when things were quiet, we could hear each other. He also spent a lot of time on administrative problems including his inability to promote Michael Reiss in the Clinical Scholar track because Michael had started in the Traditional track and DIM would not permit the switch. He was almost frustrated when he tried to hire Ercut Bahceci, MD, from the National Heart, Lung and Blood Institute in July 2006 to help in the bone marrow (stem cell) transplant program. The Chair of DIM, Ralph Horwitz said that he was only able to fund one third of the necessary support because medical oncology was always losing money (as previously noted, it only looked that way because of the way its income was misallocated and credited elsewhere). Dr. DeVita was able to offer only one third from YCCC funds. Realizing the importance of this appointment to the transplant program, and having known Horwitz for many years, I obtained DeVita's permission to negotiate for the financing. Horwitz was more interested in hiring an interventional cardiologist because he said that they generated income for the DIM and oncologists generated losses. I was able to convince him that the hospital needed an additional physician for the stem cell transplantation program which was already generating steady income and needed an additional physician to continue to succeed. He finally agreed to fund one-third of the funds necessary. Then I approached Peter Herbert, MD, YNHH Chief of Staff and he knew that the program was a money maker for the hospital and arranged for YNHH to give the other third and Bahceci came to YCCC. This was just another example of the problem of operating a section with insufficient funding.

Dean David Kessler, MD, JD, has been criticized by me, but in all fairness, I must point out that he said that when he came to YSM he was told that the school was \$23 million in the red and that part of his job was to get the budget into the black. This resulted in his ordering a near freeze of faculty salaries, some reductions in salaries for some surgeons, with the result that a few left. New hires were minimal unless they were to replace departing staff. The faculty at a Board of Permanent Officers (BPO) meeting complained about salaries. The BPO ratifies all promotions and appointments, and advises the Dean on curriculum and goals of the school. At Yale College and Law School, it plays a role in governance of the school and did for many years at YSM before Dean Kessler came and scheduled meetings only for promotions of faculty or students. President Levin has since made it clear that the BPO's role beyond approving promotions and appointments is at the discretion of the Dean of the particular school. In response to

the question on salaries, Dean Kessler promised to present his budget at the next meeting. The expenses exceeded the income by about \$3 million, but one item caught the interest of the members. There was a transfer of \$45 million to the University that the Dean could not explain other than to say it was about the same as when he took the job and approximately the same or slightly larger every subsequent year, but he assumed that it was for electricity, security, other administrative functions and property repairs, but he had never questioned it. The faculty questioned it and he promised to have his financial officer explain it at the next meeting. That did not happen, but the Dean later explained that it was for indirect costs that were included in grants, which was somewhat different from the situation on main campus. President Levin has since explained to the faculty that half of the budget of the University is represented by YSM and it contributes only about 25% of the University's administrative support, so he considers the transfer of funds appropriate, but admits that reasonable people could argue that it should be less. In fairness, I note that in approximately 2004 and again in 2007, the University contributed many millions of dollars to YSM and much of it was to improve the YCCC and help fund the building of the Smilow Cancer Hospital at Yale New Haven. Mr. Joel E. Smilow told me, "I learned about the hospital project in a 3-5 minute snippet during a three hour lunch with Inga Reichenbach [then Sr. VP of Development for Yale University]. There was no formal solicitation and I don't think that she had any encouragement from me when she left the meeting...The terms of the gift had already been formalized and approved by Rick [Yale President Richard Levin] and we had the final acceptance in his office."

Deisseroth had many frustrations before he was offered the opportunity to become CEO and President of the Kimmel Cancer Center in La Jolla, California. He accepted the appointment and left YSM in early 2001. On October 2, 2001, he wrote to me: "David: Thank you for the congratulatory note. Things are going great here. The difference is that in this free standing cancer center, there are no political struggles that arise from struggles for dominance between the pro-cancer lobby versus the anti-cancer lobby. It was a real emancipation to be free again to aggressively pursue obvious goals. I have raised 14 million dollars since I have been here in the last three months and completed three recruitments. My lab is about moved and we will start up our laboratory research....It certainly was a wonderful personal experience for me at Yale and I accomplished many research goals." After many years at LaJolla, he went to the FDA.

DeVita had assumed the YCCC Directorship in July 1993 and soon realized that a major deficiency of YCCC was insufficient accrual of patients to clinical trials. He had attempted to increase the accrual of patients to therapeutic clinical trials by approaching the medical oncologists in New Haven who had clinical appointments at YSM and admitting privileges at YNHH. He was aware of the fact that in 1984, the community oncologists of the Connecticut Oncology Association (COA) had collaborated on a study of the treatment of advanced non-small cell lung cancer (NSCLC) and published their findings (R Folman, et al. Proc Amer Soc Clin Oncol 3:232, 1984). In collaboration with a full-time YSM faculty member (C Portlock) and two oncology fellows (K Haedicke and A Koletsky), the COA oncologists extended their study and reported on 70 additional cases (K Haedicke, B Camp, L Farber, A Koletsky, S Bobrow, B Lundberg, A Levy, M Katz, D Fischer, R Folman, C Portlock, Proc Amer Soc Clin Oncol 5:186, 1986). To recapture the enthusiasm they had demonstrated in clinical trials research, DeVita encouraged them to put patients on Eastern Cooperative Oncology Group (ECOG) protocols and local YSM protocols and arranged for data collectors to visit the New Haven offices and collect the data. He even invited them to participate in the planning of some of the local protocols, and in July 1994, published an YCCC Referring Physician Guide that included the participating New Haven community oncologists. This increased clinical trials accrual from the community oncologists somewhat.



DeVita hoped to increase accrual further and assigned Lee Schacter, MD, PhD, an assistant professor who had joined the faculty in 1989 from industry, to identify groups of well-trained oncologists in Connecticut affiliated with seven other hospitals who would be willing to participate in clinical trials with YCCC. At that time I was chairman of the membership committee of YCCC and we reviewed the credentials of all of them and appointed 58 of them as affiliates of the YCCC and members of the YCCC network. Most of them were graduates of our own fellowship training program and some were from MSKCC or other cancer centers and had participated in clinical trials during their training. In 1998, a revised edition of YCCC Referring Physician Directory was published with each physician listed with the site and year of his/her medical school, residency, fellowship, board certifications and areas of special interest and competency. It was widely distributed throughout Connecticut and looked good. Unfortunately, no funds were available to YCCC for data collectors to go to offices outside of New Haven (faxes and computers were not being widely used by physicians at that time), and the participating physicians could not bear the expenses of the considerable data collection necessary and the anticipated increase in accrual never materialized. I regarded this as another example of a failure due to the underfunding of the Cancer Center's mission.

The Cancer Center Support Grant (CCSG) was reviewed by the NCI in 1988. The overall evaluation of the scientific quality of YCCC was rated as excellent, but the relatively poor accrual of patients onto clinical trials was most troubling. Nonetheless, as previously mentioned, the grant received an excellent score and it was the highest score of any cancer center that year. In the year following the CCSG review, the YCCC leadership reviewed the findings and embarked upon a program to correct the deficiencies and maximize the strengths of the center. This included serious in depth analyses with YNH of its role in the YCCC. Clearly there was a need for major structural changes and YNH hired a nationally recognized outside consulting firm (the previously mentioned RCG) to help in this reconfiguration. They recommended a formal modification to the YSM-YNH affiliation agreement to recognize the role of the YCCC and to formalize the authority of the Director over interdisciplinary cancer care in both inpatient and outpatient. They further recommended that the Director's salary be paid in equal parts by YNH and YSM with an offset from the CCSG. There was a recommendation for an increase of 10-12 medical oncologists as well as new cancer-related clinical faculty in surgery, pediatrics, gynecologic-oncology, neuro-oncology and therapeutic radiology. I did not notice any significant increase in clinical oncology faculty in this period.

By 2001, I was so apprehensive about the future of YCCC, that I wrote to President Levin directly on June 25, 2001 and said, "When Yale was first considered for designation as a comprehensive cancer center, I testified in its support. I did so enthusiastically because we had a strong basic science program in cancer and the potential for a good clinical program. YCC received the NCI designation based on its basic science strength. Today, the NCI insists on both clinical and basic science excellence and has withdrawn its designation from institutions that could not maintain outstanding programs in both areas. Unless we enhance our clinical cancer program, I fear that we will lose our NCI designation with a resulting loss in federal funds, in the ability to deliver superior cancer care to our patients, and it will be an embarrassment to the YSM and Yale University. I hope that you will personally intervene to prevent such a disastrous scenario."

President Levin replied on July 25, 2001, "Although I am aware of the many issues you raised, your professional expertise and depth of experience with the Section of Oncology and the YCCC have added to my understanding of the challenges facing these organizations. I share your concern regarding the current

dearth of visible progress in enhancing cancer care at Yale and want to assure you that the creation of an ambulatory cancer center and the reinvigoration of the clinical practice of the Section of Medical Oncology are top priorities of the leadership of the School, the University, and the Yale New Haven Hospital. The Provost and I have engaged personally with the Dean in developing and implementing strategies intended not just to remedy recent losses in clinical areas and to maintain NCI accreditation but to raise cancer care at the Yale New Haven Medical Center to unprecedented levels of quality and distinction.” Since President Levin said that Dr. DeVita had conveyed a similar message to him, I think that he was sincere in his engagement and intentions and wished to improve the situation. I know that he was concerned that Yale had not built a Cancer Center facility in 30 years.

Brian Kimes, PhD, Director of NCI’s Office of Centers, Training and Resources, visited YCCC in December 2001, to evaluate a request for a two year administrative extension of the renewal submission date to allow the YCCC to implement the extensive changes that would be necessary to submit a successful application. He met with the YSM leadership including the Dean, the relevant chairs of departments, the research program leaders, YCCC Directors and the President of YNHH. He also met with President Levin and was impressed with the commitment of YU and YSM to YCCC and with the new and increasingly positive attitude of YNHH, but he was troubled by the lack of synergy between the DIM and YCCC in nurturing clinical investigative programs. He suggested moving the Section of Medical Oncology from the DIM to the YCCC. He also raised a question about increased physical facilities.

On November 26, 2002, Dr. DeVita had reported to Dean Kessler, “It is important to recall that the NCI granted the funded extension with an expectation that a competing renewal application would be submitted in October 2003. An unsatisfactory progress report may jeopardize the Comprehensive Cancer Center designation. If so, it would be extremely difficult to reacquire. It would also have a significant negative impact on the Medical Center as a whole. For example, several million dollars more would be forfeited from programs like the million dollar a year Cancer Information Service contract. It comes up for renewal next year, and is only competed to Comprehensive Cancer Centers. Three other educational grants totaling approximately \$700,000 per annum are at risk for the same reason. The Medical Oncology Training Grant has already received an unfundable priority score for lack of appropriate sectional leadership. Failure to maintain Comprehensive Center designation by the NCI would also mean the loss of considerable philanthropic support, programs, and contracts built over the years, all of which support the approximately \$8 million annual operating budget of the YCC Office of the Director, all a considerable disincentive for a new Director. As a result there are a limited range of options at our disposal.”

DeVita’s report continued, “The robustness of the therapeutic clinical trials effort in the disease-oriented programs must be strengthened to retain designation and support. This has historically been the weakest area at Yale, and remains so. This program serves as the ‘translational research’ arm at all NCI Cancer Centers and a vehicle for moving science from any research program, basic or clinical, to the bedside....At the time of the last review, the NCI noted that with the additional faculty, as planned, the Center was on track to reach 700 to 1,000 patients per year by the site visit originally scheduled in 2003, an acceptable target for a Center of our size....Failure to meet accrual targets activates stopping rules, which creates conservative projections, so this is very likely an accurate estimate. The Section of Medical Oncology, it should be noted, carries the weight of the Clinical Trials Program, which is normal for most Cancer Centers, but its contributions have been limited by the number of faculty.” Copies were sent to YNHH President Zaccagnino and to Richard Edelson, at that time Assistant Dean for Clinical Affairs who had been assigned by the Dean to chair the search for a new YCCC Director.

Dean Kessler had appointed a search committee to select a new Chief of Medical Oncology but did not accept their recommendation. He made himself chair of a new search committee and as such made an offer to a well regarded Harvard clinical oncologist to fill the position of Chief of Medical Oncology, but the selectee inquired about whether DeVita would be reappointed and if not, who would be the new YCCC Director. When told that DeVita would not be reappointed and a selection had not yet been made for a new Director, he asked that he be considered for that position. The Dean subsequently made the offer to him. While the selectee considered the post of YCCC Director, a substantial package of financing for YCCC was pulled together by the University to support the new Director's application to renew the NCI designation and a cancer hospital was planned with YNHH. After considering the package for nearly a year, the designee was awarded a Spore grant and a promotion at his own institution and then declined to accept the Yale offer. Meanwhile, the problems of YCCC seemed to be increasing as the days wore on. The NCI Core Grant was to Vincent T. DeVita, Jr., MD from July 1, 1998 to June 30, 2003 and needed to be renewed.

After the first candidate for new YCCC Director turned it down, a second candidate, a physician/basic scientist, also from Harvard, was offered the position. It was soon clear that YCCC had been put on probation because it had fallen behind on a scale on which the NCI graded Cancer Centers and YCCC was put on official notice that we were in jeopardy of losing the NCI designation. There were many problems:

- 1) Inadequate development of the clinical investigation program;
- 2) Poor linkage of clinical programs with clinical translation of research;
- 3) Inadequate recruitment and sustenance of clinical trial investigators;
- 4) Insufficient enrollment of patients on clinical trials;
- 5) A low level of institutional support;
- 6) Insufficient coordination of research and clinical facilities to be an NCI designated CCC.

The new designee went with Edelson to Bethesda to meet with Dr. Kimes in December 2002 to discuss the steps being taken by Yale to meet the deficiencies, and to determine what more the NCI considered necessary. They were initially not received warmly. It was clear to Edelson, as the Dean's representative, that Dr. Kimes was requiring the YCCC to meet the precise four milestones that DeVita had previously identified. First, it needed to recruit at least five nationally recognized clinical trialists and another five talented young medical oncologists. Second, it needed to build a Clinical Cancer Center. Third, it needed to substantially expand the clinical trials patient base. Fourth, it needed to more intricately weave the clinical and scientific bases together. And, it needed to accomplish all of these goals prior to being redesignated as a CCC. It was while making those pledges to Kimes that Edelson realized that the Dean's promise, made through him, was essentially a contractual agreement since at the time he was "Deputy Dean for Clinical Affairs." At that point, it seemed to Edelson that the NCI had decided to drop the YCCC. The designee decided that he was not interested. Edelson called DeVita for help and the next day they met with Kimes. DeVita was warmly greeted by Kimes and a host of other NCI people who had worked with him when he was Director of the NCI. Together, Edelson and DeVita proposed that Yale be allowed to retain the NCI CCC designation for two years while it attempted to meet the conditions Edelson had just promised to fulfill. Kimes supported the request for two years beginning July 2003. He stipulated that NCI would support the Center for one year but it would receive no federal funds the second year and would have to rely on Yale University while it brought its programs up to the standards for the NCI to reconsider a new application. This was approved by the NCI Director. There was one further stipulation. There had to be an YCCC Director to succeed Dr. DeVita by July 1, 2003 and NCI had to know who that person would be by January 2, 2003. With only a month left to name the new Director, Richard L. Edelson was asked by

the Dean to assume the position effective July 1, 2003.

Shortly after his appointment as Assistant Dean for Clinical Affairs, I began to meet with Edelson and recounted the problems of the YCCC as I viewed them from the perspective of the CC. I showed him my correspondence with Dean Kessler and President Levin and we discussed the need for additional resources in terms of additional faculty and facilities. When he was asked to be Director of YCCC, I told him about the lesson I had learned almost 30 years earlier from Dr. Welch when Beeson left and a new Chair was being considered for DIM. Bondy was the leading choice and Welch told me he opposed that appointment because a new internal Chair would get little support, whereas an outside recruit would not come without an attractive package of funding. I then reminded him of the problem that Dean Burrow had with his expectations of support for the YCCC and his disappointment when it was not made available to DeVita. We both knew that the outside candidates had a substantial offer of support and I advised Edelson not to take the position without at least that level of support, and to get the commitment in writing. Also, since this was to be truly an YSM-YNHH joint project, there had to be a commitment for a new clinical facility or NIH would not renew.

Richard L. Edelson, MD was Chairman of Dermatology and Assistant Dean for Clinical Affairs. He had graduated from YSM in 1970 and gone on to do important work in the immunology of cancer. He came back to YSM in 1986 from Columbia University's CCC where he was Head of the Immunobiology Group and Associate Director of their General Clinical Research Center to become Chair of Dermatology, a department established by Aaron Lerner, MD, PhD one of the most outstanding clinical and research dermatologists in the U.S. Edelson increased the size and eminence of the department with his research and managerial skills. It was unusual for a dermatologist to be Director of a Cancer Center, so the announcement of his appointment explained: "Dr. Edelson is internationally acclaimed for his fundamental contributions to the study of Cutaneous T-Cell Lymphoma (CTCL), a disease caused by malignant T lymphocytes that affect the skin. His research group has played a central role in deciphering the basic biologic properties of CTCL cells, in delineating the pathogenesis of that serious malignancy, and in developing effective scientifically grounded therapies for it. Dr. Edelson and his research team were the first to successfully use anti-T cell antibodies in the treatment of a lymphoma and have recently demonstrated that CTCL is an antigen-driven malignancy."

"Dr. Edelson devised and implemented the first FDA approved selective immunotherapy for any cancer, a treatment now referred to as transimmunization. Transimmunization has been administered worldwide to patients with Cutaneous T Cell Lymphomas and to patients with graft versus host disease. This treatment has proved to be a remarkably safe and clinically effective cellular 'vaccine' for CTCL patients. Transimmunization is one of the most impressive examples that immunotherapy of advanced cancer is possible. Dr. Edelson regularly receives CTCL referrals from around the world and continues to direct his own clinical research program". He continued as Chair of Dermatology while serving as Director of the Cancer Center. As Edelson became Director, Dean Kessler left for an appointment as Dean and Vice-Chancellor at the University of California Medical School at San Francisco.

Dennis D. Spencer, MD, Professor and Chairman of Neurosurgery, was appointed interim Dean of YSM. He did a splendid job. While Dean Kessler had established good relations with the medical students and clinical chairs, he generally failed to engage with the lower-echelon faculty and had poor relations with YNHH administration. Spencer was approachable by students, junior faculty and chairs and was generally well liked by them. He decided to have a copy of all books published by faculty in

the Dean's office and as he requested that we donate copies of books we had published while at Yale, he thereby met many of us he had not previously known. He worked well with YNHH and his counterparts in the University and brought together many diverse communities. President Levin commented that Dennis Spencer had "brought this faculty together in a way it hadn't been for some time, and he worked very hard to collaborate, not only within the medical school but also with the university and hospital, in ways that were welcomed by all of us." What he could not do was make some senior appointments.

Jill Lacy, MD was made acting Section Chief of Medical Oncology in 2002. She was a 1978 graduate of YSM, an intern, resident, chief resident (1981-1982) at YNHH and a fellow in oncology at YCCC. She was then an instructor, assistant and associate professor in the clinical educator track. Since 1997, she has been and remains the Director of the Medical Oncology Fellowship Program. She was and is a member of the neuro-oncology and G.I. units.

Edward Chu, MD was born in Michigan but spent his early life at Yale. His mother, Ming Chu, PhD and his father, Shih-Hsi Chu, PhD were cancer pharmacology researchers when Arnold Welch was chairman. I knew Ming well. She worked with Glen Fischer while Shih-Hsi worked with Henry Mautner and they both were recruited to Brown University Medical School when Paul Calabresi became Chair of Medicine there.

Ed received his BS and MMS in Pharmacology from Brown University and his MD from Brown School of Medicine. He spent nine years at NIH and as previously noted, was recruited by DeVita to Yale in 1996 to head the cancer program at WHVAH. After Deisseroth left in January 2001, Chu was promoted to full Professor of Medicine and Pharmacology in July 2001 with the likely intention of making him Chief of Medical Oncology. However, that did not occur for reasons not clear to me. When Dr. Robert Alpern became the new dean in 2004, Edelson was able, with his approval, to appoint Chu as Chief of the Section of Medical Oncology effective July 2004. The announcement stated that he had "achieved international acclaim for his research in fundamental aspects of aberrant cellular proliferation in cancer. In particular, his research group has elucidated the regulation of thymidylate synthase, a critical target in cancer chemotherapy, with a specific focus on novel translational autoregulatory mechanisms. Currently he and his research team are actively involved in developing novel compounds and strategies for the treatment of colorectal cancer as well as other human malignancies. Among the many national posts he has held, Chu served a three-year term as Chair of the NIH Experimental Therapeutics I Study Section. He is the founding editor-in-chief of Clinical Colorectal Cancer and is a current member of several editorial boards of cancer journals focusing on basic science and clinical research."

The Chiefs of the Section of Medical Oncology (called Clinical Pharmacology and Chemotherapy from 1963-68 and Cancer Chemotherapy 1968-74) were:

Paul Calabresi	1963-1966
Joseph R. Bertino	1966-1986
Edward Cadman	1980-1983 (co-chief for clinical affairs)
William N. Hait	1986-1988 (Acting)
	1988-1992
Michael Reiss	1992-1993 (Acting)
Vincent T. DeVita, Jr.	1993-1995 (Interim)
Albert B. Deisseroth	1995-2001
Vincent T. DeVita, Jr.	2001-2002 (Interim)

Jill Lacy	2002-2004 (Acting)
Edward Chu	2004- 2010
Roy Herbst	2011-

After Kimes' suggestion to enlarge the clinical faculty, there were several new faculty appointments. Warren Shlomchik, MD was recruited from the University of Pennsylvania Medical School in 1999 to do immunology and lymphoma research and later he was selected to head the immunology unit. Mario Sznol, MD was recruited in July 2001 to head the medical side of the melanoma program and work with the surgeon, Stephen Ariyan, MD who had made YSM a major melanoma center. Together, they established a very successful clinical trials program. Sznol had been a Senior Investigator and subsequently Head of the Biologics Evaluation Section of the Investigational Drug Branch at NCI where he also attended on the inpatient/outpatient services of the Biological Response Modifiers Program and the Immunotherapy Service of the Surgical Branch. However, he was recruited from his most recent job as Vice President for Clinical Affairs and Executive Officer at Vion Pharmaceuticals and also served as assistant chief of the Section of Medical Oncology.. Gina Chung, MD was promoted from the fellowship program in 2001 to the faculty to work in breast cancer. Harriet Kluger, MD was promoted in August 2002 from the fellowship program and started research in breast cancer but made melanoma and kidney cancer her major commitments and actively participated in the clinical trials program with Sznol while she continued some of her very productive laboratory research. Diamand Psyrrri, MD was promoted from the fellowship program in August 2002 and became interested in clinical and laboratory research in the Head and Neck (H & N) Cancer Program and contributed to our understanding of the role of Human Papilloma Virus in the development of some H & N cancers. When Dennis Cooper dropped out of the H & N tumor program to concentrate on stem cell transplantation, Psyrrri assumed H & N program responsibility.

When Chu became chief on July 1, 2004, he hired Joseph O'Connell, MD, who had trained at MSKCC and had been in clinical practice with me for 10 years (before we mutually agreed to close the practice), to work part-time to help John Murren, MD in the lung cancer program. Murren also set up a phase one program of clinical trials that grew steadily until his tragic death from metastatic melanoma. Hari Deshpande, MD who had trained primarily in Leeds, England, was recruited in December 2004 from the private practice of Oncology and Hematology in New London, CT to enhance the general clinic program where he has done a splendid job, and took over the medical portion of the H & N Cancer Program (after Psyrrri left to return to Greece), and for a time was the director of outpatient clinics. Then in 2005, in quick succession, eight additional faculty members were hired. Francine Foss, MD an internationally known authority on T-cell lymphomas was recruited from Tufts Medical School and set up an active clinical trials program in her area of expertise; Wasif Saif, MD a G.I. oncologist with particular interest and expertise in pancreas cancer, came from the University of Alabama and headed an active clinical trials program in G.I. diseases with an emphasis on pancreatic cancer; James Lee, MD came from the NCI to work in G.I. oncology with a major interest in colorectal cancer but he left after two years for a position in his native Korea; Maysa Abu-Khalf, MD was promoted to faculty from the fellowship program to work in the breast cancer program and to initiate additional clinical trials in breast disease; William Kevin Kelly, MD was recruited from MSKCC where he was a national P.I. for several CALGB trials to head our G.U. program and he successfully involved us in clinical trials; Kenneth D. Miller, MD came from private practice in Washington, D.C. to set up a supportive care and survivorship program that was such a great success that he was recruited to the Dana Farber Cancer Institute; Scott Gettinger, MD came from the Beth Israel Hospital in New York City to work in the Thoracic Oncology Program and took over the medical leadership of the thoracic cancer program when John Murren died; Lyndsay Harris, MD was recruited from

Dana-Farber Cancer Institute to head the medical component of the breast cancer center and expand the clinical research program in breast diseases. That completed the additional faculty members that Kimes had suggested were necessary for YCCC to cease its role as a small CCC and begin to strive to become a major CCC.

Under Edelson' leadership the YCCC began to behave like it was going to become a major cancer center. Basic scientists and clinicians began to come together, to know each other and each other's work. Discussions about translating laboratory observations to clinical trials were initiated. Kelly, Saif, Sznol and Kluger put many patients into clinical trials and Kelly was P.I. on several CALGB national trials. Unfortunately, other sections put fewer patients on clinical trials. Nonetheless, more patients were seen in clinics which began to overflow and a facility had to be rented at the Long Wharf, about a mile away, for the solid tumor clinics. Edelson pointed out that Ed Chu's contributions to the recruitments, clinical investigation program development and writing/presentation of the YCCC grant were absolutely critical. He told me to quote him: "There is no way that we could have accomplished these goals without Edward Chu's exceptional multidimensional contributions."

As of December 2008, the end of this history, the Section of Medical Oncology faculty was: Maysa Abu-Khalaf, Edward Chu (Chief), Gina Chung, Dennis Cooper, Hari Deshpande, Michael DeGiovanna, Vincent DeVita, Jr., Francine Foss, Scott Gettinger, Lyndsay Harris, William Kevin Kelly, Harriet Kluger, Jill Lacy, James Lee, Kenneth Miller, Joseph O'Connell, Wasif Saif, Stuart Seropian, Warren Shlomchik, Mario Sznol, and Stephen Wrzesinski (who finished his fellowship in June 30, 2008 and became faculty). Of course, all of these oncology clinicians, indeed, most of all the clinicians who are full-time faculty at the YSM, are employees of the Yale Medical Group (YMG) which functions as a large multispecialty group of medical specialists. Under the able direction of David J. Leffell, MD, CEO of YMG and Deputy Dean for Clinical Affairs, who primarily does dermatologic surgery, the group has expanded and is taking in some primary care physicians and trying outreach to the community specialists also. To help in this endeavor, Ronald J. Vender, MD, a community gastroenterologist with a sterling reputation was recently recruited to be CMO of YMG and Associate Dean for Clinical Affairs. The group seems to be prospering in the stormy and constantly changing sea of healthcare and is trying to anticipate whatever the evolving government battle over healthcare finally produces. The community oncologists are also having difficulty with the changing healthcare environment, but most retain some affiliation with the YSM and YNHH and may someday join the full-time faculty as a group. Those who were active in 2008 include Samuel N. Bobrow, Jeremy S. Kortmansky, John C. Rhee (left in mid-year); Andrea Silber who heads the Yale teaching program at HSR and its breast cancer program; Kay A. Haedicke, W. Bruce Lundberg, Thomas S. Fynan, Martin E. Katz, Johanna M. LaSala, Jeffrey A. Orell, Daniel Y. Reuben and Wajih Zaheer; and three physicians who practice primarily in Meriden but have YNHH privileges, Kathleen E. Bober-Sorcinelli, Rajani P. Nadkarni and Gary F. Tasino. Arthur L. Levy and Leonard R. Farber, who were in community clinical practice for many years, joined the full-time faculty in 2009. (The story of the cancer program would not be complete without at least listing the approximately 230 fellows who came through the medical oncology program and taught us as we taught them. Some of them are now full-time faculty and some are part-time faculty, and some have gone on to careers elsewhere in clinical practice or academia. I am in debt to Savannah Woods for compiling the list of oncology fellows which is appendix 1).

After all the faculty recruitments, Edelson and his clinical and research senior staffs were able to put together a strong application for a renewal of the NCI CCSG. All along we had an outstanding basic science program; indeed, it was one of the main reasons that YSM was originally selected to be a CCC. Most basic science members of the YCCC were affiliated with one of the YCCC Research Programs. Those clinicians who were doing research that fit with a research unit's program, were invited to join the unit. The programs change and the leadership changes from time-to-time, and even now they are undergoing some changes, but as of the end of 2008, they consisted of:

#### YALE CANCER CENTER RESEARCH PROGRAMS

	<u>Program</u>	<u>Program Leader</u>
1	Signal Transduction	David Stern, PhD Joseph Schlessinger, PhD
2	Cancer Genetics	Allen Bale, MD
3	Immunotherapy & Immunology	Michael Girardi, MD, Clinical Leader Francine Foss, MD, Clinical Co-Leader Warren Shlomchik, MD, Basic Science
4	Developmental Therapeutics	Yung-chi Cheng, PhD Ed Chu, MD
5	Gene Regulation and Functional Genomics (Molecular & Cellular Oncology)	Jeffrey Sklar, MD, PhD Sherman Weissman, MD
6	Molecular Virology	Daniel DiMaio, MD, PhD
7	Prevention/Control	Susan Mayne, PhD Ruth McCorkle, MSN, PhD
8	Radiobiology and Radiotherapy Research	Peter Glazer, MD, PhD Patrick Sung, DPhil

Another major strength of the YCCC is an outstanding population cancer program headed by Susan Mayne, PhD in the School of Public Health. The missing component was the clinical program, and now it is well staffed with many more individuals with clinical trials experience. In addition, YSM and YNHH now have new leadership that is finally committed to the cancer center program and we are fortunate to have that new leadership working together. As I mentioned, Acting Dean Dennis Spencer had done an outstanding job, but as an interim dean, he was not in a position to make long-term commitments and the CCSG submission was delayed a year with NCI approval.

Robert Alpern, MD came as Dean in June 2004 from Southwestern Medical School where he had achieved recognition as an outstanding renal researcher and medical school dean. Ms. Marna Borgstrom, who had been Chief Operating Officer (COO), became President and CEO of YNHH in 2005, and she was uniquely well prepared for her job. The CCSG was finally submitted with their strong support, an enhanced faculty, many improvements in governance and the promise to build a new physical facility for cancer therapy. The YCCC financial suspension was lifted and full designation and support was restored for the period April 1, 2007 to March 31, 2012. In addition, both Dean Alpern and President Borgstrom were ready to work together to start a drive to put up "real money" to build a cancer hospital. The Memorial Unit (East Pavilion) of YNHH had been built originally as part of a design of an X with four pods. The South Pavilion was the second pod, the Children's Hospital was the third (West) pod and a new Cancer Hospital would complete the original design as the fourth (North) pod of YNHH. President Levin helped by suggesting to the Smilow family that a major gift to the University could be put to good use as



the founding gift for the new cancer hospital which would then be called the Smilow Cancer Hospital at Yale New Haven. The story beyond that commitment and construction is not a subject for this history.

A great many people have contributed to the Yale Cancer Program, and my story would not be complete without a mention of some of those who I have known or know about. Regrettably, I will omit the role of many worthy individuals because of my ignorance. The additional areas that I briefly review for their role in the cancer program are: adult hematology, pediatrics and pediatric hematology/oncology, surgery, radiation therapy, gynecologic oncology, pathology, nursing, the founding of Connecticut Hospice, medical ethics in relation to cancer and end of life studies and a few additional observations on the Cancer Committee.

Adult hematology began at YSM when Dr. Beeson began to put more emphasis on having internists who had developed expertise in specialized areas and he invited Stuart C. Finch, MD from Harvard and the Peter Brent Brigham Hospital to cover hematology as Allan J. Erslev, an instructor, was leaving. Finch came as an assistant professor and set up the section of hematology in the DIM and served as its section chief from 1953 until 1975 with a few years away to be chief of the Atomic Bomb Casualty Commission in Japan. While he was away, Paul Calabresi served as acting chair for two years and Pasquale E. Perillie served for two years, but I cannot pinpoint those exact years.

The Chiefs of the Section of Adult Hematology were:

Stuart C. Finch	1953-1975
Paul Lebowitz	1975-1976 (Acting)
Bernard G. Forget	1976-1987
Edward J. Benz, Jr.	1987-1992
Bernard G. Forget	1992-1993 (Acting)
Bernard G. Forget	1993-2005
Nancy Berliner	2005-2006 (Acting)
Thomas P. Duffy	2006-2008 (Acting)
Madhav Dhodapkar	2008-

During the period of Finch's leadership, the section did clinical hematology and some clinical research in leukemia and lymphoma, some drug testing in association with pharmacology and more research in the red cell area. Yale Nemerson, MD devoted his research to coagulation studies, particularly the study of thrombogenic tissue factor and he made major contributions to the development of the modern theory of blood coagulation. His two seminal papers were Kinetics of Factor IX Activation via the Extrinsic Pathway (J Biol Chem 1980; 255:5703-5707) and The Dual Role of Factor VII in Blood Coagulation (J Biol Chem 1982; 257:5623-5631). I worked with Nemerson on an extensive characterization of a cryoprotein and became friendly with his talented coagulation technician, Lionel Clyne because of my previous experience with coagulation in Seattle. However, Nemerson and I never completed the paper for publication. He left YSM in 1975 to go to Stony Brook University where budget cuts doomed his plans and in 1977 he moved to Mt. Sinai where he stayed for the remainder of his brilliant career. Clyne stayed on to do clinical coagulation at YNH and in 1981, when I had been in community clinical practice for many years, we published a study of a circulating Factor XI antibody and disseminated intravascular coagulation (Arch Intern Med 141:515-517).

When Peter McPhedran, MD graduated from fellowship to faculty in 1970, he took up the clinical coagulation leadership after Nemerson left. McPhedran was then recruited to head the Clinical Hematology Laboratory for YHH but continued to see patients in the hematology clinic. In 1975, Bernard G. Forget, MD, an associate professor of pediatrics at Harvard Medical School, already a distinguished investigator in red cell biochemistry and molecular genetics, was invited to become chief of hematology to set up a basic science oriented research program which he did when he arrived in 1976. His research productivity has been outstanding and he attracted and mentored more than 100 fellows in his program (see appendix II), many of whom went on to distinguished academic careers. One of his trainees, Edward J. Benz, Jr., MD succeeded him and served as section chief for five years, then became Chairman of Internal Medicine at the University of Pittsburgh, then Chairman of Internal Medicine at Johns Hopkins and is now President of the Dana Farber Cancer Institute. Another trainee, Nancy Berliner, MD, became acting section chief when Forget stepped down in 2005, and then she left Yale at the end of 2006 to become Chief of the Division of Hematology at Brigham and Women's Hospital.

Thomas P. Duffy, MD was recruited by Forget in 1976 from Johns Hopkins to handle the clinical hematology program and manage leukemia and lymphoma patients as well as other aspects of clinical hematology. He is a clinical investigator with major interests in mast cell disease, hemolytic anemia, thrombocytopenia and the hematologic and medical problems and complications of pregnancy. He is also a master clinician and teacher and was chosen for an outstanding teacher award in 1980, 1992, 1994, and in 2003 received two separate teaching awards. Duffy was also very active in special teaching sessions to sensitize students and house staff to ethical issues. After Howard Spiro's retirement, Duffy became director of the Program in Humanities in Medicine, which Spiro had created and led so well. We will revisit Duffy and Spiro in the section on ethics.

When McPhedran became emeritus and reduced his participation to 40% and Duffy assumed administrative responsibilities that reduced his clinical activities to 50% and Joel Rapoport, M.D. had a disabling accident in 2004 which virtually assured his retirement in 2005, Lawrence Solomon, MD was rehired in 2005 as an associate professor and the Director of the Adult Sickle Cell Program and as an attending in hematology. Solomon had been a member of the department (assistant professor 1975-1980 and associate professor 1980-1990) and worked primarily at the WHVAH on red cells and was Assistant Chief of Internal Medicine at WHVAH and of the clinical hematology service there 1988-1990. He left to serve as Medical Director of Connecticut Hospice 1990-1993; then served as a medical staff member and hematology consultant at the Yale University Health Plan before he returned to the full-time faculty as an associate professor in hematology in 2005. In 2007, he became Director of the Adult Palliative Care and Pain Service.

Peter W. Marks, MD, PhD was recruited in 2006 to run the clinical program. He earned his M.S., M.D. and Ph.D. degrees at New York University and had his resident and fellowship training at Harvard's Brigham and Women's Hospital and he spent a few years working in the pharmaceutical industry. His research interests are in the treatment of leukemia, and problems in thrombosis and hemostasis, but his broad and deep knowledge in the entire field is respected and he works longer and harder than anyone I know. He has done an incredibly good job of patient care and combines the latest therapy with a sensitive and compassionate approach to patients that serves as a model for house staff and fellows, who feel that he is one of the best educators on the staff. He is also active in nursing education and is associate clinical professor of nursing in addition to associate professor of medicine. In addition, Marks is chief of the leukemia service and was recently appointed Chief Clinical Officer of the Smilow Hospital.

Joel M. Rapoport, MD graduated from Yale College in 1961 and received his MD degree in 1965 from Tufts University. His residency was at Tufts and his hematology fellowships were on Harvard services. He joined the Harvard faculty and rose to associate professor in 1984. There he was a pioneer in the emerging technology of bone marrow transplantation for neoplastic and non-neoplastic hematological disorders, collaborating with his mentor, Dr. David Nathan, to establish the bone marrow transplantation service at the Peter Bent Brigham Hospital and the Children's Hospital Medical Center. He came to YSM in 1987 as the founding Director of the Bone Marrow Transplantation Program at YNHH, primarily an allogeneic bone marrow program which he directed from 1987-1997. He was also the director of the Sickle Cell Disease Program at YNHH from 1998-2003. He held a joint appointment as a professor in internal medicine (hematology) and in pediatrics and established a program that treated children and adults with leukemia, lymphoma, aplastic anemia and sickle cell anemia. As a result of the program, the Frisbee Foundation was set up to memorialize one of his patients and has supported hematologic research and established the Frisbee Cell Processing Laboratory, a sterile laboratory and storage facility for freezing stem cells and other tissues in liquid nitrogen. Although Rapoport retired in 2005 because of a disabling accident in 2004, the collaboration of the Laboratory Medicine Program with the cancer program grew out of some of his work and the placement of the Frisbee laboratory there. The Department of Laboratory Medicine (DLM) now plays a crucial role in the Progenitor Cell Transplant Program since its inception in 1987.

Edward L. Snyder, MD, Professor of Laboratory Medicine and Director of the Blood Bank and Apheresis Service and his staff, provide the services needed to support the clinical Stem Cell Program, which was undertaken by Dennis Cooper in 1993 with the introduction of autologous stem cell transplantation primarily for lymphomas and was expanded to allogeneic transplantation in 1996. That program now includes Stuart Seropian, Francine Foss and Walter Shlomchik. The Blood Bank and Apheresis Program includes Edward L. Snyder as overall program director, Yan Yun Wu, MD, PhD Associate Blood Bank Director; Diane Krause, MD, PhD, Associate Blood Bank Director and Director of the Frisbee Cell Processing Lab; and Mark Shlomchik, MD, PhD, Associate Director of the Blood Bank who assists with the overall guidance of the program. Dr. Christopher Tormey is Assistant Blood Bank Director at WHVAH. For the past twelve years, I have had the pleasure of being Chairman of the Transfusion and Tissue Committee and working with Dr. Snyder and the associated blood bank staff.

The Hematology Training Program always emphasized research opportunities and collaborative research projects between its trainees and faculty members in both basic science and clinical departments. As described by Forget, "The Program has, from its inception, been tightly linked to the outstanding basic science resources of the Yale University School of Medicine. Drs. Forget and Benz were the first investigators to bring molecular genetics expertise to a clinical department at Yale. Dr. Forget has had a long history of productive collaboration with Dr. Sherman Weissman, a founding member of the Department of Genetics. Both Dr. Forget and Dr. Nancy Berliner of the Hematology Section held joint faculty appointments in the Department of Genetics, and were highly active within the department. The department is among the nation's strongest genetics programs and a number of its faculty are participating faculty members of this training grant, including Dr. Daniel DiMaio, Dr. Peter Tattersall, and Dr. Sherman Weissman. Dr. Forget has an ongoing research program on the molecular and cellular biology of the membrane skeleton and that program has led to close collaborative interactions with the Department of Pathology." The section of hematology has made its most important contributions to the cancer program in the basic science field and translational medicine and also in its collaboration with the stem cell transplantation program with Drs. Cooper, Seropian, Foss, W. Shlomchik and Snyder.

Madhav V. Dhodapkar, MBBS was invited to be Professor of Medicine and Immunobiology and Chief of Hematology in 2008. He is a graduate of All India Institute of Medical Sciences in New Delhi and trained at St. Louis University and the Mayo Clinic. He came to Yale from the Rockefeller Institute where he studied the biology of dendritic cells, the regulation of immune responses, the immunobiology of multiple myeloma, the role of the cancer microenvironment and the relation of immunity to lipids in inflammation. He is nationally recognized for these contributions and his leadership in the management of multiple myeloma. In December 2008, the faculty of the section of hematology consisted of Madhav Dhodapkar, chief, Thomas Duffy, Bernard Forget, Stephanie Halene, Alan Lebowitz, Peter Marks, Peter McPhedran, Deborah Ornstein, Lawrence Solomon, and Mathew Strout. Overall, this is a very successful section. The fellows have contributed to this success and thanks to Savannah Woods and Richard Carr, the list of the 104 hematology fellows is appendix 2.

Pediatrics at Yale dates back to 1820 when Dr. Eli Ives was professor of materia medica and botany as well as diseases of children. He has been called America's first academic pediatrician. Recently, some of his lecture notes as recorded by students were found in the Yale Historic Library by Howard Pearson, MD. Pearson has written an excellent pamphlet, entitled, Histories of Pediatrics in New Haven and the Department of Pediatrics, Yale University School of Medicine for the 200<sup>th</sup> anniversary of the legislative charter of what is now the YSM. I cannot improve on it, so I won't try. The chairs of pediatrics were all quite eminent.

The Chairs of Pediatrics since 1921 were:

Edward A. Park	1921-1926
Grover F. Power	1926-1951
Milton E. Senn	1952-1964
C. Davenport Cook	1964-1974
Howard A. Pearson	1974-1986
Joseph F. Warshaw	1986-2000
Norman Siegel	2000-2002 (Acting)
Margaret K. Hostetter	2002-

Since this is a history of the cancer program, there is not much to say until 1946. David Clement, MD graduated Yale College in 1931 and Harvard Medical School in 1935. He took most of his training at the Boston Children's Hospital and spent much time with Dr. Louis Diamond, one of the pioneers of pediatric hematology. During World War II he served in the U.S. Army and participated in the liberation of the Buchenwald Concentration Camp. He came to New Haven in 1946 and engaged in the practice of pediatrics. He served ably at YNHH as Associate Chief of Pediatrics and did all the pediatric oncology therapy, largely leukemia and lymphoma, until Dr. Pearson arrived in 1968. When I came to New Haven in 1962, he graciously agreed to be pediatrician for my oldest daughter and to the other two when they were born. When I went into clinical practice, he sent adolescent patients with leukemia to me for therapy. We were both delighted when Howard Pearson came to Yale in 1968. Pearson says that when he was considering moving to New Haven, he was reluctant to displace David Clement who was another "Diamond Chip" and a friend. When he called Clement, David said, "I am the strongest proponent for getting you here."

Howard A. Pearson, MD was born in the Panama Canal Zone and had his early schooling (to age 10) there. He attended Dartmouth College and then its two year medical school and finished his last two years at Harvard Medical School. His postdoctoral training was mainly in the National Naval Medical Center in Bethesda except for a year of research at the Boston Children's Hospital where he worked with Dr. Louis Diamond. I first interacted with him when I was a physician at Womack Army Hospital and was treating an adolescent with acute lymphocytic leukemia. I managed to get the youngster into remission for six months, but when he relapsed, further therapy was unsuccessful and I referred him to Walter Reed Army Hospital. They said they had nothing more to offer than what I had done, and sent him back. I was unwilling to let a 14 year old die without at least one more try. I called the National Naval Medical Center and spoke to a Commander Pearson and described the situation and asked him to accept the adolescent for experimental chemotherapy since, as a military dependent, he was ineligible for care at NCI. I suggested that Pearson might visit NCI a few blocks away and the boy and his family were agreeable to experimental therapy. A few weeks later, the patient returned in apparent remission, having been one of the first patients treated experimentally with vincristine plus prednisone. The youngster and his family were pleased with the remission which lasted about four months. Imagine my surprise when I was called to the office of the Commanding General of my Army Hospital for disciplinary action. The charge: "Captain Fischer violated procedural guidelines" (by sending an Army dependent to a Naval Hospital). I protested that I was a physician and did what was best for my patient. The General said, "Military procedures must be followed by all military personnel. There is a chain of command. You cannot pick your own consultants." When I failed to understand, he lost patience, and said, "Spare me two year civilian doctors. Don't ever do it again, and now get out of here."

Pearson came to YSM as the first Pediatric Hematology/Oncology Section chief in 1968 and promptly set up the first Pediatric Hematology/Oncology Clinic in Connecticut. In 1969 he set up the first neonatal screening program for sickle cell disease in the U.S. and he published many seminal articles in this field. He also studied and wrote about thalassemia, isoimmune neonatal thrombocytopenic purpura, leukemia and granulopoiesis in children with Down's syndrome and several other diseases. He identified two new diseases: refractory sideroblastic anemia with vacuolization of marrow precursors and exocrine pancreatic function (a syndrome that now bears his name), and chloramphenicol responsive neutropenia. He began a fellowship program and trained a cadre of young people, some of whom succeeded him later as chiefs of pediatric hematology/oncology. His first fellow was Richard T. O'Brien who succeeded him as section chief from 1974 to 1978 and then went to head pediatric hematology /oncology at the University of Utah in Salt Lake City. The second was Sue McIntosh who was on the YSM faculty for many years and was one of the first to point out that the combination of parenteral methotrexate and radiation could cause severe diminution of cognitive function in children. In 1978, she opened the first Connecticut private hematology/oncology practice in Guilford, CT. A. Kim Ritchy was the third fellow and he became head of the pediatric hematology/oncology at the University of West Virginia in Morgantown and is now head at the University of Pittsburgh. The fourth was Jack von Hoff who served as acting head of the section here from 1998-2000 and again from 2002-2008 and is now head of pediatric hematology/oncology at Dartmouth Medical School. With his fellows, Pearson treated patients with leukemias and with solid tumors, particularly, Wilms tumor, on protocols and worked with the Pediatric Oncology Group (POG) initially and later with the Children's Oncology Group (COG) when POG was incorporated into it. They put about 80% of their cancer patients on protocols.

The American Board of Internal Medicine [ABIM] conducted its first examination in hematology in 1972 and its first examination in medical oncology in 1973. ABIM continues to certify the two subspecial-

ties separately. In 1970, pediatric members of the American Society of Hematology (ASH) were concerned that there was no credentialing of sub-specialists in pediatric hematology and oncology. They convinced the American Board of Pediatrics [ABP] to establish such a board and to make it a combined board which conducted the first subspecialty combined examination in hematology/oncology (as distinguished from the ABIM which continues to test for them separately) while the ABP continues to test for them in a single examination. When the first qualifying examination in pediatric hematology/oncology was conducted in Chicago, Philadelphia and San Francisco in 1974, Howard Pearson and Diane Komp took it in Philadelphia and both passed and Pearson was noted to have attained the top score in the country. Hematology as a subspecialty at Yale began as a separate section in 1953 and medical oncology (then called clinical pharmacology and chemotherapy) began in 1965 as a separate section. Pediatrics had them as a combined specialty from the start. An excellent reference for more information is Pearson, HA, History of Pediatric Hematology Oncology, *Pediatric Research* 2002, 542:979-992.

Pearson stepped down as chief of pediatric hematology/oncology in 1974 to become chairman of the Department of Pediatrics and continued in that position until 1986. When he became chairman, he decided not to continue to treat children with cancer because his administrative responsibilities would interfere with his continuity and availability. He continued to see children with non-malignant conditions and so became a “benign hematologist.” In an entirely different but ground-breaking role, he became the founding Medical Director of the “Hole in the Wall Gang Camp” that was started by Paul Newman in Ashford, CT, to serve children with cancer and blood disorders. Pearson served as medical director from 1986 to 2004.

The Chiefs of the Section of Pediatric Hematology/Oncology were:

Howard A. Pearson	1968-1974
Richard T. O'Brien	1974-1978
Diane Komp	1978-1985
G. Peter Beardsley	1985-1998
Jack van Hoff	1998-2000 (Acting)
Greg Plautz	2000-2002
Jack van Hoff	2002-2008 (Acting)
Gary Kupfer	2008-

The pediatric oncologists continued to put the vast majority of their patients on clinical trials, which may be one of the reasons that we have a greater proportion of cures and longer survivals in pediatric cancers than we do in adult cancers where only 3% of cancer patients in general are treated on clinical trials, and perhaps 5% to 10% in academic institutions or cancer centers. We have a lot to learn from our pediatric colleagues.

Surgery was the sole treatment for cancer since ancient times and until the beginning of the 20<sup>th</sup> century when radiation therapy was introduced, and they remained the main modalities until the mid-twentieth century, when hormonal therapy and chemotherapy were beginning to demonstrate some efficacy. In that sense, the YSM cancer program can be said to have begun with the appointment of Nathan Smith in 1813 as professor of the theory and practice of physic, surgery and obstetrics. His outstanding reputation drew others to New Haven to work with and learn from Smith.

The Chairmen of the Department of Surgery were:

Nathan Smith	1813-1829
Thomas Hubbard	1829-1838
Jonathan Knight	1838-1864
Francis Bacon	1864-1877
David Paige Smith	1877-1880
William Henry Carmalt	1880-1907
Joseph Marshall Flint	1907-1921
Samuel Harvey	1921-1948
Gustav E. Lindskog	1948-1966
Jack Wesley Cole	1966-1974
Arthur E. Baue	1974-1984
William F. Collins	1984-1993
Ronald C. Merrell	1993-1999
Robert Udelsman	1999-

A recent list of the full-time faculty of the Department of Surgery had 70 names. It did not include the part-time faculty or the faculty of the Departments of Neurosurgery, Orthopedics or Obstetrics/Gynecology because they are separate departments. Since I did not work in surgery, I have no special knowledge or insight to impart. Most of my interactions with surgeons were on the receiving end. They sent patients with cancer to me for palliative chemotherapy after a non-curative surgical procedure or for adjuvant chemotherapy after surgery that resulted in no evidence of disease (NED) in hopes of eliminating residual microscopic foci of cancer and achieving a long-term cancer free state that we call “cure.” Toward the end of my active practice career, we started to treat some patients with neo-adjuvant chemotherapy to reduce a tumor in size and try to convert an inoperable tumor into an operable one, and also to establish sensitivity to a drug program that might be used as post-operative adjuvant therapy. Hence, all I can do in discussing my surgical colleagues is to list those surgeons with whom I interacted at one time or another. When I first went into community practice, the surgeons to whom my colleagues sent their most difficult cancer cases were Mark A. Hayes MD of the full-time faculty and Max Taffel, MD a community physician. The choice was good and I did likewise and was never disappointed. Later, I sent my patients primarily to community general surgeons including Drs. Sherwin Nuland, Nicholas Passarelli, Robert Houlihan, Paul Barcewicz and Stephen Stein. For breast cancer, that list was extended to include Drs. Teresa Ponn, Nina Horowitz and Raymond Ippolito. On the full-time faculty, Ira Goldenberg, MD was a most outstanding breast surgeon and was one of the earliest in the U.S. to advocate lumpectomy with radiation therapy for well localized resectable breast cancers. He was also one of the founders of the Connecticut Hospice. After Goldenberg died, he was succeeded by Charles F. McKhann, MD who was an outstanding immunologist in addition to being a skilled breast surgeon. Barbara Ward, MD trained here and her excellence was recognized even as a resident and she developed a well deserved large following for breast surgery. When Ward left to head a breast cancer section at Greenwich Hospital and McKhann retired due to illness, Donald Lannin, MD was recruited to be chief of breast surgery and Teresa Ponn, MD and Baiba J. Grube, MD joined the faculty.

Lung and other thoracic cancer patients requiring surgery were directed by me to Drs. Harold Stern, Allan Toole and Ronald Ponn; all of them were outstanding surgeons.. After Stern and Toole retired, Ronald Ponn was appointed to be full-time chief of thoracic surgery at YNH, but tragically died at a

relatively young age of a sudden heart attack before he took office. Yale was fortunate to attract Frank Detterbeck, MD as chief of thoracic surgery from the University of North Carolina and he is building a fine section. In addition to his excellence as a thoracic surgeon, he has additional administrative roles as Associate Director of Clinical Affairs and co-vice chair of the cancer committee. Daniel Boffa, MD joined the thoracic surgery staff and has a special interest in esophageal cancer. Anthony W. Kim, MD just joined the staff. For very special surgery, full-time faculty members were the only ones who treated a sufficient number of cases to develop and retain those special skills. Liver and pancreatic cancers were sent to Elton Cahow, MD and later to Dana K. Andersen, MD. Endocrine surgical cases were sent to Barbara Kinder, MD. We now have a very active endocrine cancer section led by Robert Udelsman, MD and including Drs. Julie Sosa and Sanziana Roman. Thyroid cancer is the 6<sup>th</sup> commonest tumor in our registry since Udelsman's arrival.

The Section of Surgical Oncology was started in 1990 with T. Ravikumar, MD as chief. Ronald Salem, MD, an excellent general surgeon, became the section chief when Ravikumar left in 1994. That section is growing rapidly. We had excellent plastic surgeons in the community and I sent my melanoma patients from St. Raphael Hospital to Marvin S. Arons, MD, DMD who was Chief of Plastic Surgery there. The Yale patients with melanoma I referred to Stephen Ariyan, MD when he was full-time Chief of the Section of Plastic Surgery (1979-1991) at YNHH and later when he went into community practice. He is one of the most outstanding melanoma surgeons in the U.S. and perhaps the world. He established the Yale Melanoma Unit in 1976 and continues to lead it. He originated and developed several new surgical procedures for reconstruction of head and neck flaps that have become standard worldwide. He has authored or co-authored more than 200 scientific papers and four surgical books (one of them, *The Handbook*, has been published in three editions in English, Spanish and Japanese). His presence has made YSM a melanoma center and the commonest neoplasm in our tumor registry is melanoma. It has been a privilege for me to work with him at the melanoma tumor board. He edited the issue on *Cultaneous Melanoma* for *Clinics in Plastic Surgery* in July 2000 and asked many of us in the Melanoma Unit to contribute to it. I co-authored the chapter on *Clinical Classification and Staging*. Melanoma is one our best tumor boards and its excellence is due in no small measure to Dr. Ariyan's secretary, Carolyn Truini, who serves most effectively as the melanoma tumor board coordinator. As chief of the melanoma unit, Ariyan coordinates care with Mario Sznol, MD co-chief of the unit, and Harriet Kluger, MD, who together collaborate on patient care and lead the clinical trials and state of the art research. Deepak Narayan, MD, a plastic surgeon, does considerable melanoma surgery and regularly attends, as does Dwain Fehon, PsyD a psychologist who helps by providing psychological insight to patient problems and arranges psychiatric care as needed. My urology patients were sent to Drs. Richard Lena or Ralph DeVito in the community or to Bernard Lytton, MD at YNHH. Robert Weiss, MD is now Chief of Urology and John Colberg, MD heads oncologic urology. Difficult head and neck (H & N) cancers were sent to Eiji Yanakasawa, MD or K-J Lee, MD at HSR. Lee invited me to write the chapter on cancer chemotherapy for his *Essentials of Otolaryngology: Head and Neck Surgery* in 1983 and the revised edition in 1987; and for his *Textbook of Otolaryngology and Head and Neck Surgery* in 1989. Difficult H & N cancers were also sent to John Kirschner, MD at YNHH when he was chief of ENT and later to Clarence Sasaki, MD, our current chief of ENT. I have enjoyed attending the excellent H & N tumor board run by Sasaki, and attended by Yung Son, MD as the radiation therapist who uses brachytherapy when indicated in addition to or in place of external beam therapy. Other regular attendees are Drs. Roy Decker from radiation therapy, Hari Deshpandi from medical oncology, Diane Kowalski and Manju Prasad from pathology. H & N has become outstanding at YNHH. Orthopedic Surgery is a separate department headed by Gary Friedlaender, MD who does excellent oncologic orthopedic surgery.



The Section of Neurosurgery became the Department of Neurosurgery at Yale in January 1997. Interestingly, its roots reach back to Harvey Cushing, MD when he was Professor of Surgery at Harvard Medical School and surgeon-in-chief at the Peter Brent Brigham Hospital. Samuel Harvey, MD trained with him there and in 1917 worked with him at Base Hospital 5 in France. Harvey came to Yale and did general surgery and neurosurgery. He became chairman of surgery and established a combined surgical-neurosurgical training program at Yale. William German, MD had also trained with Cushing and came to NHH, and in 1933 was appointed Chief of Neurosurgery at NHH. When Cushing came to YSM in 1934, he was offered the position of Professor of Neurosurgery but chose to be Sterling Professor of Neurology. When he transferred his personal collection of rare medical books to Yale and combined them with the collections of John Fulton, MD and Arnold Klebs, MD, the Yale Historical Library was born, and has grown to become one of the outstanding medical historical libraries in the U.S. Cushing also transferred his collection of brain specimens and slides to Yale and they are now housed in a special section of the Yale Medical Library. In 1967, when German retired, William Collins, MD was appointed Cushing Professor of Surgery, Neurosurgery and Chief of Neurosurgery. When Collins was appointed Chief of Surgery in 1984, Dennis Spencer, MD was appointed acting and then Chief of the Section of Neurosurgery in 1987. When it became a department in 1997, he became the first Chairman of the Department of Neurosurgery. His major interest is in the study and surgical treatment of epilepsy and other seizure disorders. Joseph Piepmeier, MD heads the oncologic neurosurgery program and chairs the neuro-oncology tumor board. Joachim M. Baehring, MD has a joint appointment in neurology and neurosurgery and is an outstanding leader in neuro-oncology. Distinguished neurosurgeons in the community who did a substantial amount of oncologic surgery were Lycurgis M. Davey, MD, Alvin D. Greenberg, MD, Franklin Robinson, MD and Isaac Goodrich, MD. Members of the department in December 2008 were Dennis Spencer, chair, Philip S. Dickey, MD assistant chief, Khalid M. Abbed, Ketan R. Bulsara, Veronica L. Chiang, Charles C. Duncan, Murat Gunel, Joseph M. Piepmeier and Kenneth P. Vives.

Gynecologic Oncology was established at Yale in 1979 as a section within the Department of Obstetrics and Gynecology by Peter E. Schwartz, MD, who remained its chief for 26 years, and is still active as Assistant Chief of Obstetrics and Gynecology. It is interesting to note that Yale's first professor of surgery and physic, Nathan Smith, MD, was the second person in the world to operate on an ovarian tumor. He had seen one and at an autopsy on the case realized that the pedicle could be free and could be ligated. He did this in a patient and allowed the pedicle to fall back into the abdomen – at that time it was usual to exteriorize the pedicle. Smith's patient lived into her seventies. Before Schwartz's arrival, the section of gynecology was active in cancer care with Maclyn Wade, MD and Ernest I. Kohorn, MChir collaborating with Alan Sartorelli, PhD testing uracil mustard plus 5-fluorouracil in the treatment of ovarian carcinoma with some incomplete responses. Results with new drugs today are much better but cures of metastatic disease remain infrequent. Gynecology was primarily oriented to surgical treatment.

John McLean Morris, MD, a virtuoso surgeon, developed an interest in radiation therapy during his gynecological training at Massachusetts General Hospital and while on a sabbatical at the Radiumhemmet in Stockholm. He became convinced of the efficacy of intra-vaginal and intra-uterine brachytherapy with radiation sources in these two situations. Even before he arrived at Yale, he had conversations with Dean Hugh Long and the Chairman of the Department of Surgery, Dr. Gustaf Lindskog, about establishing a radiation center to serve all clinical departments. (see Kohorn, EI, Connecticut Medicine, 2009; 73:223-227). While Morris could perform brachytherapy with appropriate radiation sources and his own instruments, he was concerned about the lack of a centralized external beam radiation system for cancer patients at Yale. The Hospital of St. Raphael had just established the first radiation therapy center in

southern New England in 1951 under the direction of Wayne Whitcomb, MD and Morris worked with HSR to jointly purchase some radium for brachytherapy. He introduced and adapted the Stockholm system of intra-cavitary radiation in a highly original way and this was used until he retired and after-loading techniques were introduced. At Yale, an advisory committee was established in 1952 and it proposed the building of a radiation cancer center. Fortunately, Robert S. Hunter, a Yale graduate of 1911 provided the funds for the Hunter Radiation Center which was built and opened in 1954 and operated as a part of the Department of Radiology. Morris insisted that super-voltage machines be used and not rely on cobalt radiation. It was not until 20 years later that radiation therapy was identified within the Department of Diagnostic Radiology as a Section of Therapeutic Radiology with James J. Fischer, MD, PhD as section chief under the chairmanship of Morton Kligerman, MD. (More will be said about therapeutic radiology anon). Morris was the first to describe a large series of patients with testicular feminization in 1952, a condition in which a woman is phenotypically female but genetically male, with XY chromosomes. These women had an ovo-testis but were insensitive to testosterone. The syndrome is still known as Morris' syndrome. Ironically, Morris is most remembered as the co-developer of the "morning after pill."

Ernest I. Kohorn, MChir, trained in Cambridge, England and University College Hospital for his clinical work and took more advanced oncology training at the Chelsea Hospital for Women and at The Middlesex Hospital. He took special training in Glasgow, Scotland in the use of ultrasound. When he came to the U.S. he introduced and popularized obstetrical ultrasound in New England. Although it had been used in Denver, Colorado previously, ultrasound was virtually an unknown modality in the U.S. He also demonstrated its use to his general surgical colleagues before he went on to a distinguished career here as a gynecologic surgeon. In 1972, he developed a special interest in gestational trophoblastic neoplasia (GTN) and set up a Trophoblastic Center (TC) at Yale for specialized treatment. He was one of the early advocates of chemotherapy for GTN and over the next 40 years treated or consulted on 500 cases of this uncommon but now curable malignancy. No patient primarily treated for this at Yale's TC died. The hCG assays done here with antibodies developed at Yale had no false positives. Some 40 publications arose from this experience and significantly affected the staging and risk factor scoring of GTN. The Yale TC used to see 10 to 15 patients per year but the rate fell after Kohorn retired from clinical practice in 2002. His talents were recognized early and he was invited to serve a number of organizations: locally, as President of the Connecticut Society of Arts and Sciences; nationally, as President of the Society of Gynecologic Surgeons; and internationally, as President of the International Society for the Study of Trophoblastic Disease among others.

Peter E. Schwartz, MD was a graduate of the Albert Einstein College of Medicine and was then a resident in Obstetrics and Gynecology at Yale. He obtained further training in gynecologic oncology at the M.D. Anderson Hospital. After being recognized as both an outstanding surgeon and medical oncologist, he came back to Yale and set up a Fellowship Training Program in gynecologic oncology at Yale in 1980. The section has been an actively growing part of the Department of Obstetrics and Gynecology doing extensive surgery, bench research and clinical trials. His achievements and those of the section are nationally recognized and are so extensive that I cannot summarize them, but Peter Schwartz was kind enough to do it for me:

"Regarding significant contributions to the literature, I have reviewed my CV and have identified 12 areas where the division has made significant contributions to the literature.

1. Ovarian Germ Cell Malignancies: With my particular interest in these rare tumors we have now one of the largest series of patients treated and the largest reported series of women who were successfully

treated and then conceived normal pregnancies following treatment. When modern chemotherapy started at the M.D. Anderson Hospital with the VAC regimen, the treatment period was 2 years. I reduced the treatment to 3-6 four week cycles with the same results. I subsequently demonstrated that platinum-based chemotherapy was critical for the successful treatment of germ cell tumors that made AFP (alpha-fetoprotein). I was able to show that even women with stage III disease could preserve fertility and be treated with chemotherapy. Prior to 1984, the standard treatment for the dysgerminoma was radiation therapy. Dysgerminomas are the only ovarian cancers exquisitely sensitive to radiation therapy. However, using radiation therapy often meant the patients became infertile. I showed that dysgerminomas were exquisitely sensitive to chemotherapy and one could preserve fertility.

2. Hormonal aspects of epithelial ovarian cancer: Collaborating with laboratory investigators in our department, we were able to show that epithelial ovarian cancers express estrogen receptors and subsequently showed progesterin receptors in these tumors. This led to the first clinical trial of tamoxifen in advanced recurrent ovarian cancer. Having shown a role for tamoxifen in this disease, I then put together the division's second prospective randomized trial, a trial of doxorubicin and cyclophosphamide with or without tamoxifen for previously untreated advanced stage epithelial ovarian cancer. This was the first prospective randomized trial of ovarian cancer that used hormonal therapy as part of the initial treatment. Unfortunately, the addition of tamoxifen did not enhance the results, suggesting to me that the addition of one drug to a platinum regimen brings maximum results in ovarian cancer therapy. This observation seems to be true today (GOG 182). Working with Richard Hochberg, we were the first to try to image ovarian cancer using radio-labeled estrogens which he had synthesized.
3. The division has been one of the early leaders in the field of distinguishing benign pelvic masses from malignant ones collaborating with our colleagues in diagnostic imaging.
4. The division was one of the first to establish a role for circulating and urine tumor markers in the diagnosis and treatment of ovarian cancer.
5. The division had an early interest in the early detection of ovarian cancer and established either the first or one of the first early detection programs for ovarian cancer in the United States. Information gained from our work in collaboration with Diagnostic Imaging and our experience with circulating and urine biomarkers were incorporated into this program.
6. Working with Dr. Barry Zaret (cardiologist), we established a role for MUGA scans in detecting doxorubicin cardio-toxicity and showed how one could continue doxorubicin therapy beyond its normal cutoff levels using MUGA scans.
7. Working with Dr. Jennifer Kelsey and colleagues in the School of Public Health, we performed some of the earliest epidemiologic studies of ovarian and endometrial cancer.
8. I began treating selected patients in 1979 with neo-adjuvant chemotherapy for advanced epithelial ovarian cancer. Yale is internationally recognized as a leader in the field. We have established diagnostic imaging criteria (Nelson, et al) for who might benefit from this approach, showed that the patients' long term survival is not compromised and have provided data to suggest that neo-adjuvant chemotherapy should be considered a standard therapy for Stage IV disease.
9. We have had a strong interest in the molecular biology of chemotherapy resistance and cancer stem cells in ovarian cancer. The additions to our faculty of Drs. Gil Mor and Alessandro Santin have resulted in Yale being one of the centers for this research in the U.S. Dr. Mor has identified phenoxodiol as an agent that can reverse platinum resistance. It has gone through Phase I and II trials at Yale and is in an international Phase III trial.

10. We have one of the largest series of UPSC (uterine papillary serous carcinoma) patients in the country and have been on the forefront of its treatment and laboratory research.
11. We were the first to show that tamoxifen was associated with aggressive forms of uterine cancer.
12. We alerted the country to a particularly aggressive form of cervical cancer, so-called rapidly progressive cervical cancer. This led to collaboration with the NCI to identify risk factors for this disease.”

All of these contributions were annotated with full references listing the journals in which the articles appeared with volume and page citations. His colleagues included, among others: John McLean Morris, Thomas J. Rutherford, Robert Romero, Setsuko Chambers, D.C. Chapman, B. Edraki, J. Tangir, R.B. Hochberg, J.W. Walsh, L.A. Cole, Y. Wang, D. Chen, G. Mor, J.T. Chambers, and Ernest I. Kohorn. Thomas J. Rutherford, MD, PhD became the second chief of gynecologic oncology in 2005. The clinical faculty of the section of gynecologic oncology in December 2008 was: Masoud Azodi, Elena Ratner, Thomas J. Rutherford, Alessandro D. Santin, Dan A. Silasi and Peter E. Schwartz.

The Department of Diagnostic Radiology, now chaired by James A. Brink, MD, provides very important support to the cancer program, but it is hard to indicate particular individuals who work primarily in the area of malignant disease versus benign disease. They support our tumor boards and our daily therapeutic decisions. Those who regularly attended our tumor boards in 2008 included: Laura Horvath, Liane Philpotts, Regina Hooley, Liva Andrejeva, Jeffrey Weinreb, Bruce McClennan, Gary Israel, James Abrahams, Shirley. McCarthy, Howard Forman, Jonathan Kirsch, Robert Fulbright, Cindy Miller, Kenneth Baker, Robin Goodman, Gordon Sze, Anne Curtis, Amy Rabinowitz, and Myung Shin. From Nuclear Medicine, the main participants have been David Cheng and Indu Doddamane.

The Department of Therapeutic Radiology is a very active department providing radiation therapy to patients who need it. Originally, radiation therapy was a section of the Department of Radiology as previously noted. Morton M. Kligerman, MD was chairman of the department from 1958 to 1972 and headed both Diagnostic and Therapeutic Radiology. In the mid-sixties he began to confine his consultations and interest to Therapeutic Radiology (TR) along with Carl F. von Essen, MD and Samuel Hellman, MD and developed a cadre of clinical fellows, including Stanley Order, MD, James J. Fischer, MD, PhD and Leonard Proznitz, MD, that was primarily interested in TR. Kligerman was among the first to use halogenated pyrimidines to sensitize tumors to radiation, and he helped to develop WR-2721 (amifostine, Ethylol), an agent that protects healthy tissue from some of the effects of radiation. Based in large part on the work that he did, the drug was FDA approved. Many of the techniques that he pioneered, including three-dimensional CT treatment planning, three-dimensional conformational radiation therapy and patient immobilization before treatment, are still used today. Before he left Yale in 1972 to become chair of the radiotherapy division at the University of New Mexico Hospital and work at the Los Alamos National Laboratory, he suggested the use of adjuvant radiation therapy (RT) for patients with stage III or IV Hodgkin's disease (HD) who achieved complete remission (CR) with MOPP chemotherapy.

James J. Fischer, MD, PhD (not related to me) was appointed section chief of TR in 1968 before it was elevated to a separate department in 1972. He served as chair of the department of TR from 1972-2002 and grew the department into a major clinical facility, a strong basic science research group and a clinical research group. Many of its members went on to other institutions, including Daniel S. Kapp (to Stanford University); Arthur H. Knowlton (to Chairman at Hospital of St. Raphael); Michael G. Chen; Bernard Percarpio and Jeffrey Bitterman to Waterbury, CT; Barry M. Kacsinski; Bruce Haffty (to Chair at Robert Wood Johnson Hospital at University of Medicine and Dentistry of New Jersey); Leonard Prosnitz

(to Chair at Duke University). They and other members of the department have published extensively. The department has been distinguished in many areas. It introduced Americium-24 for the treatment of gynecologic malignancies. It has been a leader in the field of computerized dose calculation including three-dimensional imaging-based dose calculations. It was the first in Connecticut to incorporate on-line portal imaging in the management and treatment of patients. The gamma knife service is one of the largest in the U.S. The total skin electron beam program is also one of the largest in the U.S. with the other being Stanford. The head and neck brachytherapy program is one of the most active in the U.S. The stereotactic body radiotherapy program currently treats approximately 150 patients per year which is an extremely high volume. I will discuss its many publications about treatment of HD separately. Its basic science group, including Sally Rockwell, Ph.D., Dean Rupp, Ph.D. Susan Baserga, M.D., Ph.D. and others, has published important work

Peter M. Glazer, MD, PhD became the second chairman when appointed in 2002. He has enlarged the clinical faculty and the basic science faculty. Clinical faculty of the department now serve, supervise or consult on therapeutic radiology at Bridgeport Hospital, Lawrence & Memorial Hospital, Trumbull Oncology Center (associated with Bridgeport Hospital), William W. Backus Hospital, Veteran's Administration Hospital in West Haven, YNHSH Shoreline Medical Center, and of course, Smilow Cancer Hospital at Yale New Haven. In addition to routine radiation therapy services, the department provides intra-cavitary and interstitial brachytherapy; high-dose-rate remote afterloading (Gamma-Med) brachytherapy; prostate implantation, using the ultrasound-guided perineal approach; total body irradiation for bone marrow (stem cell) transplantation; total skin electron beam therapy for lymphoma of the skin and cutaneous T-cell lymphoma; and stereotactic radiosurgery for cerebral vascular malformations, pituitary adenomas, and intracranial benign and malignant tumors and lung cancers using a Gamma Knife Device. As of December 2008, its clinical faculty included: Peter M. Glazer (chair), Bryan Chang, Roy Decker, James J. Fischer, Susan A. Higgins, Jonathan Knisely, Sheida Mani, Meena Moran, Abhijit Patel, Richard E. Peschel, Kenneth B. Roberts, Yung H. Son, and Joanne B. Weidhaas. Lynn D. Wilson, MD is vice chair and clinical director. He has particularly distinguished himself by being able to manage a clinical program at seven sites and do fine research in mycosis fungoides, malignant tumors of the lung and total skin electron beam therapy for a number of skin maladies.

Leonard R. Prosnitz, MD, was acting chair of radiation therapy (1976-1977) and took up the idea of Kligerman and James Fischer that RT could increase survival of patients with HD who had achieved a complete remission with chemotherapy alone. His work with HD was in addition to his interests in breast cancer and head and neck cancer. Beginning in 1968, and working with the medical oncologist, Leonard R. Farber, MD, they pushed the idea that all patients with stage III or IV HD who went into CR on chemotherapy (CT) alone, or who had RT alone for stage I or II HD and relapsed and then had salvage CT and achieved a CR would get low dose radiation (20-30 Gy) to formerly involved areas to reduce the incidence of recurrence. (Henry Kaplan, MD of Stanford had established the standard dose for HD as 36 Gy). This adjuvant radiation therapy after CT was called combined modality therapy (CMT) and seemed like a brilliant idea to reduce late relapses and we all (medical and pediatric oncologists) bought into it. Early in the program, I entered many patients into the protocol, although it was being done as a routine therapy and not an investigation with an informed HIC/IRB consent form. However, after I had a 39 year old woman referred to me for treatment of a sarcoma in the radiation field of a stage IIA HD treated 20 years earlier and in CR of her HD; and soon thereafter, a 37 year old female with breast carcinoma in the radiation field of a stage IIA HD treated 18 years earlier and still in CR of her HD, I began to have second thoughts about the long-term safety of RT and the need for it in all patients in CR after CT.

The Atomic Bomb Casualty Commission was frequently being staffed by YSM faculty members including Drs. Averill A. Liebow, James W. Hollingsworth and Stuart Finch, among others. From their studies, it was becoming clear that the late consequences of the radiation exposure from the atomic bomb explosions resulted in acute non-lymphocytic leukemia, generally, in 4 to 6 years with a declining incidence thereafter, but an increasing incidence of thyroid cancer, lung cancer, sarcomas, and breast cancers beginning about 13 years later and increasing year by year with no obvious plateau. This added to my worry that we were setting up some of our HD CR patients (potentially “cured patients”) for second malignancies and we did not know the cost-benefit ratio of what we were doing. I suggested to Prosnitz that we continue to treat HD patients with bulky mediastinal disease (greater than one-third of the transverse transthoracic diameter of a standard P-A chest x-ray at the T5-T6 level) or other tumor greater than 10 cm in largest diameter with RT, but all other patients in CR should be randomized to receive either involved field radiation or just careful observation. Those who then developed a recurrence could be treated with salvage radiation plus or minus additional CT so that we would eventually know who, and whether, we were truly helping them. DeVita and the NCI group had by then treated Hodgkin’s disease patients with stage IA, IIA, IIIA and IVA and they all had a CR. The symptomatic group, IIB, IIIB and IVB did not. In a 20 year follow up of MOPP therapy for HD, Longo, DL, et al. (J Clin Oncol 1986; 4:1295-1306) noted that only one patient in their series of 198 who had received only combination CT developed acute leukemia, but 12 patients in that series who had both RT and CT developed acute leukemia and suggested, “Therefore, it appears that chemotherapy alone is the treatment of choice for asymptomatic advanced stage patients.” He also reviewed the data on treatment of stage IIIA HD with RT alone as compared to combination CT and commented, “Certainly, it appears that the combined modality approach does not provide superior results in any subset of stage IIIA patients and the increased incidence of acute leukemia (about 1% per year) that occurs in patients receiving combined modality treatments makes it desirable to use this approach only in patients for whom either radiation therapy alone or combination chemotherapy alone have proven inadequate for controlling the disease (e.g., patients with massive mediastinal or other very bulky disease).”

Prosnitz rejected the suggestion to randomize patients to RT or no RT because he said it was unethical to do a scientific experiment when he knew the answer and that answer was CMT, what he was already doing. He honestly believed that this additional radiation would save lives (and still does) and I honestly did not know, but was worried that treating patients in CR would expose many of them, to the long term risks and possible mortality of RT and cardiac injury and would benefit only the few who were destined to recur. Those who recurred could likely be salvaged. But I did not know for sure, and only a randomized trial could answer the question of whether CMT was doing more good or more harm. Thereafter, I discussed the risks and benefits with all my patients, had them sign an informed consent that I wrote, and subsequently most of my patients in CR who did not have bulky mediastinal involvement, chose not to have adjuvant RT. My decision led to the cooling of a warm friendship, but Prosnitz did what he believed to be correct and I did what I thought to be correct and we both relied on time for an answer. In the short term, only one of my patients in CR who did not have radiation relapsed with NHL and he responded to CTR for that and went into CR. In the short term, patients who had CMT had a slightly better freedom from treatment failure (FFTF), but most of the CT alone patients who relapsed could be rescued with additional CT or RT or a combination of the two. Their overall survival (OS) was not significantly different. In a 13 year follow-up study of Yale patients by Salloum E, et al. (J Clin Oncol. 1996; 14:2435-2443), they separated HD patients treated with full-dose radiation therapy (~40 Gy) and those treated with low-dose (15-30 Gy) radiation and demonstrated that those who received high-dose RT had a statistically significant increased incidence of second malignancies but those who received low-dose therapy did

not. They concluded that low-dose therapy was safe. The last word on this subject has not been written and may never be written. However, the general literature indicates that second malignancies (other than leukemias), usually show up after 13 years and may not for 20 years. The secondary malignancies and increased incidence of radiation induced heart disease may decrease overall survival in those treated. We have to remember the large number of patients in CR who were already cured and were unnecessarily exposed to radiation. A well controlled randomized study in the 1970s and 1980s would have answered the question long ago.

Salloum E, et al. (*Cancer J Sci Am* 1995; 1:267-273) also reviewed the series with 11 year follow-up data and extrapolated actuarial data to 24 years and attempted to show longer survival with CMT compared to other series with CT alone, admitting that the data is weak and that it would have been better to do a randomized study initially. At my suggestion (as acknowledged in their article), Doria R, et al. (*J Clin Oncol.* 1995; 13:2016-2022) studied the actuarial incidence and relative risk (RR): (1) of second solid malignancies (SSM), (2) solid tumors (ST) and (3) non-Hodgkin's lymphoma (NHL). They concluded that previously untreated patients with advanced disease who were treated with CMT had a modest but not significant increase in the RR of ST; however patients treated with CMT for recurrent disease had a highly significant increase in the RR of ST. They suggested that a possible explanation for the increase in ST in the previously treated group was a more cumulative RT dose or a greater carcinogenic effect of CT in previously irradiated patients, but it was also possible that the increase was simply due to a longer follow-up time in the second group.

Kenneth B. Roberts, MD is our current radiation therapy colleague whose special interests are the treatment of lymphomas and pediatric neoplasms. He came to Yale from Duke University School of Medicine where he trained and worked with Leonard Prosnitz, our former radiation therapy colleague with a major interest in lymphoma and the main therapist in the 1970s Hodgkin's disease study. Dr. Roberts was kind enough to provide me with a copy of an abstract he submitted, Roberts, K, et al., *Second Malignancies after Hodgkin's Lymphoma: The Thirty-Five Year Yale University Experience*, that reviewed the data of 550 HD patients treated at YNHH between 1970 and 2004 (it is incorporated in the Cancer Program 2009 Annual Report of YNHH – YCC), and a follow-up manuscript, Olmer, B, et al., *Risk of Second Malignant Neoplasms after Hodgkin Lymphoma*, that is being submitted for publication. It reports on 753 HD patients (26.7% under 20 years of age) treated consecutively at YNHH between 1970 and 2009. It is interesting that the charts of a total of 32 patients, mostly from the early 1970s could not be located. This is the first revelation of which I am aware of the loss of so many records, and they are the records of the earliest cases and hence those most at risk of a late malignant neoplasm. It is hard to put this in context when we were able to find the chart of the 1942 patient who was the first to receive nitrogen mustard therapy for a lymphoma and I don't personally remember any chart being lost at YNHH, although I am sure that it occasionally happens when a chart is misfiled. This again emphasizes my discomfort with the Yale HD studies, since long term studies have demonstrated a relatively high incidence of late malignancies in patients who received RT or CMT. The tragedy of not doing a randomized scientific study then is that we are still debating the issue 40 years later. Had we done a randomized study then, we could have answered the question definitively and possibly spared generations of patients, particularly those in CR from radiation therapy that may have been of no benefit and could potentially have caused a later second malignancy or later cardiac disease and an earlier death.

Today we know that an adolescent or young adult (under 40) treated with RT for HD has a risk of 1% per year of developing a second malignancy and it is 25% at 25 years (van Leeuwen, FE, et al, *J Clin*

Oncol 2000:18:487-97). Low dose radiation (20 Gy) increases breast cancer incidence, indeed, doses as low as 4 Gy substantially increase the risk of breast cancer (Boice JD Jr, *Med Pediatr Oncol* 2001:36:508-13). Even diagnostic levels of radiation increase the risk of breast cancer and the risk appears to increase linearly from 4 to 40 Gy (Boice JD Jr, et al, *Radiat Res* 1991:125:214-22). On a study-by-study basis or by meta-analysis, CMT does not improve survival of patients with HD compared with appropriate CT alone in advanced disease. Loeffler M et al., (*J Clin Oncol* 1998:16:818-29) concluded, "Combined modality treatment in patients with advanced-stage Hodgkin's disease overall has a significantly inferior long-term survival outcome than CT alone if CT is given over an appropriate number of cycles. The role of RT in this setting is limited to specific indications." There is also a substantial increased risk of breast and lung cancer, coronary artery disease and of stroke in patients treated with mantle-field radiation therapy after 17 years or so. In short, there seems to be no role for routine RT in the treatment of HD except in some special situations like bulky disease or frank recurrence not curable by additional CT alone. Today, many oncologists are still using CMT and we are still arguing about whether RT has any role in HD or whether it should be reserved only for the 5 to 7% special failure cases. A randomized Yale study would have answered the question 20 years ago. Sadly, we didn't do it then.

Belaboring this point with HD was necessary because radiation is still being widely used in HD and the idea that randomized trials are not indicated when the investigator thinks he/she knows the answer, still plague us. Current news stories tell of patients clamoring to use new drugs that some investigator or pharmaceutical company has suggested may be useful although the drugs have only gone through a phase I or phase II study. There are many examples of this, but I became involved when in the 1980s and 1990s, a number of oncologists advocated treatment of women with metastatic breast cancer with high dose CT and bone marrow transplantation (BMT) and published uncontrolled studies that seemed to support their thesis, (Williams SF et al, *J Clin Oncol* 1989:7:1824-1830); Antman K et al, *J Clin Oncol* 1992; 10:102-110; Peters WP et al, *J Clin Oncol* 1993; 11:1132-1143). The idea caught on and major academic hospitals around the country started to treat women with metastatic breast cancer with this modality. At least eight such patients were treated at YNHH with BMT (or stem cell transplantation).

In 1987 and again in 1990, I was approached by two of the largest insurance companies in the U.S. to advise them which of their insured patients they should fund for this therapy and whether it was standard or experimental (payment for experimental therapy was excluded by the contract, and on average, the procedure cost more than \$150,000). The V.P. for medical affairs of the Aetna Insurance company, Henry Williams, MD, (a MSKCC trained oncologist and the first medical oncologist in private practice in Connecticut) knew me from the year that he had spent part-time at Yale supervising the Clinical Pharmacology and Chemotherapy Service while Paul Calabresi was on sabbatical. He and I discussed the problem at length and he knew I agonized over the decisions because it was clear that patients with bulky disease would not respond. But would patients with limited metastases benefit or be cured? He offered me \$500 to review the English language word literature and give him a formal recommendation, which I did. Searching the literature took more than 30 hours and was exhausting but provided no positive guidance because there were no comparative clinical trials. I suggested to him that Aetna and the Travelers Insurance Company (which had also asked my opinion and both with headquarters in Hartford, CT) get together and offer to pay for a randomized clinical trial in the 10 largest institutions doing the procedure. Williams told me that Aetna had made the offer to the five largest groups doing high dose CT with BMT and had been turned down and were told by the transplanters, "we know that what we are doing is correct and it is now standard therapy."



Some of the insurance companies decided not to pay for what they thought was experimental therapy and not covered by the contract. George P. Canellos, MD, the editor of the *Journal of Clinical Oncology* at the time and one of the most outstanding medical oncologists in the U.S. and a good friend, wrote in an editorial, “How did this approach escape the scientific scrutiny that is expected in the practice of oncology.” He answered, “The third-party payers distanced themselves early on from participating in the evaluation and relied on the meta-analysis of poor results of early trials to defer payment. However, in the court room, the payers usually were defeated when the scientific merits of the issue had to be decided by a jury of layman.” It was true that when some patients went to court to overturn the decision they were successful. In a major trial where Marc E. Lippman, MD was the expert consultant for the plaintive, he solicited written opinions of more than 20 medical oncologists, including chairmen of departments, chiefs of oncology sections and heads of BMT services who claimed that BMT for metastatic breast cancer was either standard or so efficacious that their institutions were using it as if it were standard therapy. It was hard for a jury of laymen to ignore. Lippman was obviously a bright young man when I knew him as a Yale medical student and then as an endocrinology fellow here. He went on to a brilliant career at the NCI and was Chair, Department of Oncology at Georgetown University Medical School when he agreed to testify as an expert for the lead BMT patient.

Insurance companies had incurred my wrath in other contexts, but knowing that at least the Aetna and Travelers Insurance Companies had made a legitimate effort to organize and fund a randomized clinical trial to clarify the situation, I wrote a letter to the editor (*J Clin Onc* 1998; 16: 1237-1238) entitled, “Need Randomized Clinical Trials, Not Litigation” to set the record straight. While I admitted that a randomized trial by Bezwoda, et al. (*J Clin Oncol* 1995;13:2483-2489) in South Africa had shown a better survival in the BMT group than in the controls, I said, “the study of Bezwoda et al. was poorly designed and unconvincing.” (What neither Canellos nor I knew at the time was that the study by Bezwoda was fraudulent and he had fabricated some of the treated patient records and most of the controls and he was later fired by the University of Witswatersrand for scientific misconduct and the papers were withdrawn). I suggested, “Contrary to your characterization of all the third-party payers as the villains of this missed scientific opportunity, in my personal experience at least two of the largest private insurance companies in America tried to deal with the problem in good faith; they paid for many more BMTs than the evidence justified, they tried to do the right thing for their insured clients with what we then thought was a demonstrated need for a BMT without wasting \$150,000 per inappropriate BMT, and tried to advance medical therapy with sponsorship of evidence based scientific studies.”

Two years later, at the plenary session of the American Society of Clinical Oncology, four abstracts were presented that demonstrated no benefits for BMT for metastatic breast cancer and were followed by full peer-reviewed articles (Bergh J et al, *Lancet* 2000; 356:1384-1391; Hortobagyi GN et al, *J Natl Cancer Inst* 2000; 92:225-233; Hu WW et al, *Biol Bone Marrow Transplant* 2000; 6:58-69). The fourth peer-reviewed article appeared in the *New England Journal of Medicine* on April 13, 2000 (342:1069-1076) by Stadtmauer EA et al to set the record straight. In that same issue, Marc E. Lippman wrote an editorial that concluded, “Advocates of high-dose chemotherapy plus autologous bone marrow transplantation for metastatic breast cancer contend that since this treatment is unproven, its use is justified outside of a trial – that is, because they think it might be helpful, they should be allowed to use it. We should now acknowledge that, to a reasonable degree of probability, this form of treatment for women with metastatic breast cancer has been proved to be ineffective and should be abandoned in favor of well-justified alternative experimental approaches.” Lippman had the courage to say publically that the scientific evidence demonstrated that his earlier belief was incorrect and that we must treat our patients on the scientific evi-

dence. He is a true son of Yale and a credit to the medical profession. If the randomized clinical trials had not been done, we might still be doing useless stem cell transplantations with high-dose chemotherapy for women with metastatic breast cancer.

Are non-randomized clinical trials ever justified? Clearly the answer is yes, some are. One of the most famous occurred during World War II. Penicillin had just been shown to be highly effective in treating pneumococcal, staphylococcal and streptococcal infections, but was in very short supply and most was consigned to the military. To regulate civilian use, Chester Keefer, MD, chair of internal medicine at Boston University School of Medicine, was appointed “Penicillin Czar,” and the drug was to be used only for indications that he approved. He had tried it in sub-acute bacterial endocarditis (SBE), a 99% fatal disease, and it was NOT successful and hence banned for such use. In a classic paper, Loewe L, et al. (JAMA 1944; 124:144-149) reported combined penicillin and heparin therapy cured seven consecutive cases of SBE. No controls were needed. Keefer immediately released penicillin for treatment of SBE. Similarly, the NCI treatment of HD with MOPP needed no controls because the cure rate without therapy or with RT alone was so poor that MOPP needed no controlled trial. When it was to be used instead of another therapy, then it needed a randomized controlled trial comparing it (alone) “head-to-head” against the other therapy.

The Yale New Haven Hospital Tumor Registry (YNHH-TR) was established in 1926 and is the oldest registry in the United States. The Connecticut State Tumor Registry (CSTR) was established in 1935 and is the oldest State tumor registry in the U.S. After it began functioning, the YNHH-TR was under Connecticut’s Public Health Code, Section 19a-73, and was required to furnish to CSTR information concerning “diagnosis, stage of disease, medical history, laboratory data, tissue diagnosis, radiation, surgical or other methods of treatment and annual life-time follow-up for each cancer patient” in addition to occupational history. The CSTR is one of the 10 used by the NCI’s Surveillance Epidemiology and End Results program (SEER). More than 20% of the yearly incidence of new cases of cancer (excluding basal and squamous cell skin cancer) that are reported to CSTR are diagnosed or treated at Yale. All registry records were handled manually until the 1970s.

Diana Bradbury Fischer, Ph.D. (then married to Dr. James J. Fischer, chair of Radiation Therapy) computerized the records of the RT department in the 1970s and was hired to do the same for the YNHH-TR. The Registry was then put into the Department of Therapeutic Radiology administratively. She obtained the Yale records that had been computerized by the CSTR for the earlier years and then entered our data in her new computer files. Starting in December 2000, Yale data was entered into the ACoS National Cancer Data Base (NCDB). The registry also maintained supplementary information required for the Radiation Oncology Review Committee of the Accreditation Committee of Graduate Medical Education (ACOME). Annual statistics required by the NCI in support of the YCCC Core Grant are also supplied. For many years, the YNHH-TR was in the forefront of registries with its ability to gather computerized information rapidly, but newer and faster systems were developed elsewhere. As additional information was required, staffing had to be increased.

Teresita Vega, CTR (our first CTR) joined the registry in 2000 to increase the credentialed staff but the computerization remained accessible only to Diane Fischer. When she became ill in 2004 and resigned, access to the data became difficult. Ms. Vega was appointed Manager of the YNHH-TR in 2004 and enlisted the help of John Sinard, MD, PhD of the Department of Pathology and together, in 2004-2005, they converted the data from the old computer system to a new IMPAC management system called Medical

Registry System (MRS), but the registry had to re-abstract the 2004 data because that was the beginning of the collaborative staging system and the computer program of that year had not been set up to include that information. To make reports to the ACoS manageable, 1999 was established as the reference year and we now report to the Commission on Cancer (CoC) on all patients alive that year and all patients since then. We continue to report cancer incidence and follow-up to the Connecticut Tumor Registry on all cases since 1926. Under the excellent guidance of Ms. Vega, the YNHH-TR has grown in size, in personnel, in the amount of information it reports and has a perfect record with NCDB for accuracy of its reports. It is used for clinical research in a variety of ways by investigators of many departments. A cancer program without an outstanding registry will be mediocre or worse. Fortunately, we have a registry of which we can be very proud.

The Department of Pathology provides the diagnostic support upon which the cancer program relies. According to a review by Raymond Yesner, M.D., "A Century of Pathology at Yale: Personal Reflections", *Yale J Biol Med* 1998; 71:397-408, the modern department of pathology at YSM was established by Milton C. Winternitz, MD in 1917 (I have relied heavily on Yesner's article for much of this discussion, sometimes in quotes and sometimes without. We became good friends when we both served on the Medical Advisory Board of the Connecticut Division of the American Cancer Society as former presidents of the organization). I have already discussed the enormous influence of Winternitz as dean in transforming YSM into a first class medical and research institution and will not recapitulate it. During his deanship, much of the day-to-day activity of the department was carried by Raymond G. Hussey, MD, although Winternitz remained chair of the department and participated actively in its functions and direction. It is necessary to indicate that as chair of pathology, he set the pattern for his trainees and successors to follow, with a few exceptions.

Harry Zimmerman, MD was sent by Winternitz to Munich to study neuropathology under Walter Spielmeyer in Munich and when he returned in 1930, Zimmerman established the first neuropathology section in the U.S. at YSM. He established a friendship with Harvey Cushing when the great neurosurgeon came to Yale in 1933 as Professor of Neurology. When Cushing died, Zimmerman did the autopsy and found that Cushing had a thrombosis of the aorta below the renal arteries which was responsible for the partial paralysis of his legs. After Zimmerman returned from the Pacific Theatre of War, Winternitz wanted him to come to Yale but warned him that Yale was not yet ready for another Jewish full professor and he deserved that rank. Instead, he became Chairman of Pathology at Montefiore Hospital in the Bronx, NY and Professor of Pathology at Columbia's College of Physicians and Surgeons. Years later, the president of Yeshiva University asked Zimmerman to help establish a new medical school. Although the institution was Jewish sponsored, he accepted the assignment on condition that it would be non-sectarian and he became acting dean. He helped design the facility, recruited the original faculty and wanted to name it after Albert Einstein. He told me that when he went to Princeton to persuade Einstein to lend his name to the new institution, Einstein was reluctant and suggested that it be named for a famous Jewish physician. Zimmerman said, "We could name it after Bela Shick." Einstein said, "Who is he?" Zimmerman responded, "You make my case. No one will ask who is Albert Einstein?" Einstein said, "You have my permission to name it after me. Harry, are you sure that you are not a lawyer?" and they became friends. When Einstein died in 1955, Zimmerman autopsied his brain. Zimmerman became one of the most productive neuropathologists in the U.S., published extensively, and trained a large cadre of neuropathologists, including a large group of Japanese pathologists. He was honored in Japan with the Order of the Sacred Treasure in the Second Degree. When I asked Zimmerman why the honor was "Second Degree," he said that he was told that "First Degree" was reserved for members of the Royal family. He also

received the “Gold-Headed Cane” of the American Association of Pathology among many other honors. He is honored at Yale by the endowed Harry M. Zimmerman Chair in Neurology.

Averill Liebow, MD, was born in Austria in 1911 and came to the U.S. as a small boy. He was a 1935 YSM graduate and a protégé of Winternitz and became a faculty member and a researcher. After W.W. II, he returned as an assistant professor and was assigned to the Atomic Bomb Casualty Commission that entered Japan to survey the disasters of Hiroshima and Nagasaki. His recorded observations made significant contributions not only to science but also to history. His personal diary of those days entitled *Encounter with Disaster* is an accurate and sensitive history of the transition phase of government in postwar Japan. On his return to Yale, he rose rapidly in the pathology ranks to full professor. He ran the teaching program at YSM and the autopsy service and was a favorite of the students. He received the Francis Gilman Blake award for teaching excellence from the graduating class. Since Harry Greene did not obtain a Connecticut medical license, he appointed Liebow as chief of the pathology service at YNH. Liebow wrote the first Armed Forces Institute of Pathology Fascicle on Tumors of the Lower Respiratory Tract. He was soon recognized as the premier pulmonary pathologist in the U.S. With Gustaf Lindskog, he wrote a textbook on diseases of the lung that went through two editions. In 1948, Liebow published a study on the accuracy of cytologic diagnosis of sputum and bronchial secretions, controlled by surgical specimens. He was passed over as chairman after Winternitz's retirement in 1950 and left Yale in 1968 to accept a new challenge to go to a new medical school at the University of California in San Diego (UCSD) to be Professor and Chairman of its Department of Pathology, a position he held until 1975. At UCSD he received the teaching award for excellence from the graduating class in two of his active seven years. He served as an international leader in pathology. One of the great testimonies to his devotion to the field is evidenced by the activities of his students. More than 93% of his trainees went on to active academic careers and filled the ranks of professorships and department chairmen at different institutions in this country and around the world. At Yale, the pathology department makes an annual teaching award in his name.

Harry S.N. Greene, MD did not go into military service and Winternitz recruited him in 1941 because of his work on tissue transplantation in the anterior chamber of rabbits' eyes. There he was able to grow both embryonic and some malignant tissues. Yesner points out that “Since carcinoma in situ and occult carcinomas did not survive transfer, he (Greene) believed truly malignant cells were not present in these conditions. Also, since lymphomas, myelosarcomas and leukemia did not survive such transfers, he concluded that they, too, were not neoplastic disease. Greene succeeded Winternitz as chairman of pathology, despite the fact that he did not believe pathologists contributed anything, and would not bring them into his department...When I (Yesner) once asked him why he came to Yale, Greene said he liked to open the window and smell skunk...Greene took a position contrary to the mounting evidence that smoking was contributing to lung cancer. He had, he said, taken some of the “crud” from his pipe and put it in the subcutaneous tissue of a rabbit, along with some embryonic tissue. Since no cancer resulted, it indicated that the tobacco residue was not carcinogenic.” Several members of the department have indicated to me that they feel that Yesner's treatment of Greene was unduly harsh, possibly because they did not get along very well. Michael Kashgarian pointed out that Greene felt “that what was seen through the microscope did not necessarily reflect the biology of the malignancy and that the only biologic criterion was a tumor's ability to grow independently in the anterior chamber of the rabbit's eye. It is a shame that he did not recognize that the reason tumors survived in that location was that the tumor was sequestered from the immune system there. At the time, the only other successful model involved transplanting tumors into brains of Guinea pigs that were pretreated with corticoids. He actually was a good diagnostic patholo-

gist himself although he would never admit it in public. He enjoyed being controversial and publicly denigrated epidemiological evidence when he testified for the tobacco companies in court.” Kashgarian remembers one of Greene’s most famous arguments, “The front row of a burlesque house has bald men ergo naked women cause baldness.” Greene developed some fame or notoriety as a paid spokesperson for the tobacco industry. Greene felt that the department should be primarily a research department with minimal clinical responsibilities. In 1958, when YSM decided to consolidate its 27 scattered clinical laboratories into a single division under David Seligson, MD, Greene did not want them in the Department of Pathology and accordingly Paul Beeson accepted them into Internal Medicine and Seligson was appointed associate professor of medicine. He was a nationally respected pioneer in the field of laboratory medicine and was one of the earliest to mechanize and computerize tests to accelerate the reporting of results and reducing their costs. Others followed many of his procedures. Later, a Department of Laboratory Medicine was established at YNH of which he was appointed chairman and which included the Blood Bank. Joseph Bove, MD became the first full-time director of the Blood Bank. He served in that position with distinction for nearly 30 years and established most of the procedures and standards that are still used by it. He is honored with the annual Joseph Bove Lectureship in Laboratory Medicine.

Edward Snyder, MD, who was previously mentioned in connection with the stem cell transplantation program, was the second and is the current Blood Bank director. He was mentored by Bove and has continued the tradition of excellence and has expanded the role of the blood bank to include the monitoring of the tissue bank as well. I am proud that in 1996 he asked me to be chairman of the Transfusion and Tissue Bank Committee and we have worked together well and achieved such a level of excellence in both blood banking and control of tissue products that our inspections by credentialing bodies have all been highly rated. Snyder has gained national recognition for his many research publications, his energetic leadership in multi-institutional research, often with industry. He recently co-edited Hematopoietic Stem Cell Transplantation – A Handbook for Clinicians. For many years he was YCCC associate director of shared resources and recently succeeded me as chairman of the membership committee of the YCCC.

Dr, Greene would not allow his residents to rotate through the West Haven VAH when it was integrated into the YSM. It was not until 1961 that Seligson was granted a secondary appointment in pathology, and it was not until 1964 that Beeson declared the situation intolerable at the Dean’s Committee meeting and Greene was forced to integrate pathology at WHVAH and rotate residents there. Since Greene had little interest in surgical pathology, it developed a poor reputation at Yale until Wilhelm Albrink, MD was assigned to head it. When Albrink was passed over for promotion, he left to become chair at West Virginia University. Greene then offered the position to Robert Hutter, MD of MSKCC. In the meantime, Greene had a stroke and he died in 1969. A search committee headed by Philip Bondy, chair of internal medicine, recommended Baruj Benacerraf, MD, an internationally-known immunologist for the chair in pathology. Many members of the department opposed the appointment of an immunologist as chair and Benacerraf accepted a position at Harvard. In 1980 Benacerraf shared the Nobel Prize in Physiology and Medicine for “discoveries concerning genetically determined structures on the cell surface that regulate immunological reactions.”

Elias E. Manuelidis, MD was born in Constantinople and became a refugee in Athens at the age of 4. He graduated from the University of Munich with an MD in 1942 and from 1946 to 1949 he was director of anatomical pathology at the Max Planck Institute of Psychiatry in Munich. He worked as a civilian neuropathologist for the United States Army and was invited to join the YSM faculty in 1951 under the auspices of John Paul, MD in the Department of Preventive Medicine. He worked on the transmission

of poliomyelitis by blood, doing the neuropathology among other things and was given a joint appointment in pathology, where he taught and organized neuropathology after Harry Zimmerman left. He transferred fully to pathology in 1953 and rose from instructor to full professor of pathology by 1964. His work on viral brain infections, brain tumors, Alzheimer's disease, Creutzfeldt-Jacob disease (CJD) and how people could become infected by contaminated tissue transplants made him internationally famous. Other contributions included the first long-term culture of human brain tumors in 1959, and in 1964, the demonstration that a virus could be used selectively to kill a malignant tumor. When the neuropathologist, Louise Eisenhardt, MD, Harvey Cushing's coworker and the curator of the Brain Tumor Registry died in 1967, Manuelidis became the curator of that registry in the Brady Building basement of the pathology department. He also was curator of the extensive written archives, slides and many brain specimens stored in formalin. Numerous additional precious brains for teaching were subsequently collected from the many autopsies done by the neuropathology team at YNH, WHVAH and at outside mental hospitals. In 1979, Manuelidis transferred from a primary appointment in pathology to become Professor of Neuropathology (surgery) and Neurology at the request of William Collins, MD, who was then chair of neurosurgery (Collins later became chair of surgery in 1984). The transfer may have been related to the fact that the department of pathology wanted the Brady Building space and the Brain Tumor Registry was moved to the sub-basement of the Harkness dormitory where it languished until it was moved to the YSM library where it is now well displayed for all to see. Manuelidis trained many residents and many practicing neurosurgeons, like Davey and Robinson, and for 40 years was regarded as an outstanding teacher and researcher.

Laura Kirchman Manuelidis, MD (LKM) was a student of Elias E. Manuelidis (EEM) and later married him and became his colleague in neuropathology and after 1979, in neuropathology (surgery) and eventually his successor. In 1981, she became associate professor of surgery (neuro-pathology) and later professor. Together with EEM she questioned the prion concept of transmissible spongiform encephalopathies (TSEs) such as human CJD and endemic sheep scrapie. They established the first rodent models of human CJD in the 1970s and suggested that an infectious agent with many viral characteristics causes this progressive neurodegenerative disease. They reported that many "neurotropic" viruses like the TSE agent can spread through the blood to infect lymphoreticular tissues such as the spleen and lymph nodes before invading the brain. LKM has gone on to do much additional research on TSEs, scrapie and CJD.

Lewis Thomas, MD was recruited from New York University where he was chairman of internal medicine and dean of the medical school to be chairman of pathology in 1969. He was a prize-winning author, famous for his writings, first published in the *New England Journal of Medicine* and later in books. When he arrived, Hutter was running a first-rate surgical pathology service but insisted that Greene had appointed him to head anatomic pathology but he had no written proof. He left when that position was denied him. Lewis was fortunate to have inherited a group of first class pathologists including Levin L. Waters, MD, a Winternitz protégé, who was acting chair for the year after Greene died and until Lewis arrived. Waters received his MD from YSM in 1937 and climbed the academic ladder from assistant in pathology to full professor by 1957. He spent many years as Director of the Jane Coffin Childs Memorial Fund for Medical (especially cancer) Research, succeeding Winternitz in that role. Ironically, one of the many areas of his research was the pathogenesis of vascular disease, a disorder that was to later take his life. Others included Romeo A. Vidone, MD, a 1957 graduate of YSM (who later left to become chair of pathology at the Charlotte Hungerford Hospital in Torrington, CT and still later at the Hospital of St. Raphael partly as a result of my recommendation to their search committee), and William Barry McAllister, Jr., MD. McAllister had received his MD at Johns Hopkins School of Medicine (JHSM) and stayed

on to work with the famed pathologist Arnold Rich before coming to YSM. McAllister headed the Grace Community Hospital (GCH) pathology unit in the then new Memorial Unit built to consolidate GCH with NHH as GNHCH. He worked extensively with the part-time faculty and was a fine teacher. He had an office just inside the entrance from the physicians' parking lot and I used to stop there before seeing my patients and he showed me the new pathology on all my patients and interesting cancers of patients of other physicians. Essentially, he gave me a lesson in malignant pathology on his double headed microscope every weekday morning. He was honored with an endowed lectureship on his retirement for his service to the YSM (and not for reeducating me in pathology). After Hutter left, Thomas hired John L. Cornog, Jr., an early advocate of the use of electron microscopy in pathology. He also brought George E. Palade, MD and his wife Marilyn T. Farquhar, PhD, a cell biologist to the YSM. Palade shared a Nobel Prize in Physiology and Medicine in 1974, as previously mentioned. Lewis presided over the establishment of a new department of human genetics. He became dean of YSM in 1972, set in motion the application for YCCC but left in 1973 to become director of MSKCC.

Raymond Yesner, MD received his B.A. from Harvard and his M.D. from Tufts in 1941. After W.W. II, he was demobilized from the armed forces and took a job at the Newington VA Hospital which had opened in 1946. He became chief of laboratory services in March 1947 and was responsible for all anatomic and clinical pathology functions. When the "Dean's Committee Hospital System" was set up, Newington VAH became Yale's affiliate. Averill Liebow became the consultant and Yesner was appointed as an assistant clinical professor of pathology at Yale. When the West Haven VAH was completed in 1953, Yesner was assigned to be chief of the laboratory service. From 1969 to 1974 he was associate dean for the VA Hospital and developed a four-year training program in pathology, including anatomic and clinical pathology. Among his many achievements, he is perhaps best known as the author and editor of the WHO Histological Typing of Lung Tumors, 2<sup>nd</sup> ed., Geneva, 1981. He has had many honors. In May 2005 he received the Gold Medal from the U.S. and Canadian Academy of Pathology and a few months later, the Gold Medal of the International Academy of Pathology for excellence in teaching and research. In 2007 he received the Pulmonary Pathology Society Lifetime Achievement Award.

Other distinguished members of the pathology department that I personally recall include Juan Rosai, MD (who was the principle author and editor of a major textbook and characterized novel medical conditions such as Rosai-Dorfman disease and the desmoplastic small round cell tumor); Virginia A. LiVolsi, MD, Kenneth W. Barwick, MD, George Walker Smith, MD, David Rimm, MD, PhD (an outstanding researcher who has opened new areas of investigation by his technological advances), Maria-Luisa Carcangiu, MD and Richard Flavell, PhD, (head of section of immunology which subsequently became the first free-standing immunology section in the U.S.). Daryl Carter, MD (who co-authored the second edition of the AFIP Tumors of the Lower Respiratory Tract and Interpretation of Breast Cancer Biopsies, 1984, second edition 1990 and third edition 1996) was for many years the pathology representative on the Cancer Committee. Michael Kashgarian, M.D., a leading electron microscopist, graduated YSM in 1958 and did extensive studies in renal disease, and lung disease. He identified the spirochete in the microangiopathic lesions of Lyme disease, among many other studies. He is well known to YSM alumni as editor of the Alumni Bulletin for many years and is still active as an Emeritus Professor. For many years Stuart Flynn, MD, was the surgical pathologist for the melanoma tumor board and the pathologist who gave the introductory lecture for the oncology module for second year medical students and was repeatedly rated by the students as the best lecturer in the module.

Vincent T. Marchesi, MD, PhD was brought to Yale by Thomas because of his work on red cell mem-

branes and discovered spectrin, the main protein comprising the red cell cytoskeleton, genetic mutations of which appeared to account for hereditary elliptocytosis and spherocytosis. The pathology department became strongly committed to research in immunology which it had previously scorned. One of its earliest prominent research workers was Richard Gershon, MD (with whom I had collaborated and published, as previously mentioned). Gershon was a chain smoker and tragically died young of lung cancer while on the cusp of a brilliant career. As previously noted, for reasons not entirely clear to me, pathology lost part of the section of neuropathology to surgery and most of dermatopathology to dermatology, and Clinical Laboratories had become a separate department. Marchesi's career was interrupted when his wife, Sally, a clinical hematologist and a research pathologist, developed Alzheimer's disease and he took a six month sabbatical to care for her and begin a study of the disease. After the Boyer Center for Molecular Medicine was created in 1989, Marchesi became its first (and so far only) director and stepped down as chair of pathology. In 1990 Jon S. Morrow, MD, PhD was appointed the Raymond Yesner Professor of Pathology and of Molecular, Cellular, and Developmental Biology and Chair of the Department of Pathology and Chief of Pathology at YNH. He and his laboratory are involved in studies of hemolytic disease, degenerative brain diseases, spectrin and its role in cell contact mediated signaling and spatial organizations of specialized membrane-surface domains. Jose Costa, MD was Director of Anatomical Pathology and Translational Diagnostics, a prolific researcher particularly in the area of molecular diagnostics and molecular cancer genetics. He was also a very effective and knowledgeable Deputy Director of the YCCC for many years. A. Brian West, MB who took some of his training here is now Director of Anatomic Pathology, and a CC member.

The chairmen of the modern department of pathology were:

Milton C. Winternitz	1917-1950
Harry S.N. Greene	1950-1968
Levin L. Waters	1969-1969 (acting)
Lewis Thomas	1969-1973
Vincent T. Marchesi	1973-1989
Michael Kashgarian	1982-1983 (acting)
Jon S. Morrow	1990-

Pathology is a large department and its members are listed on the department's web site. The members of the pathology department who served on our tumor boards in 2008 included:

F. Tavassoli, V. Bossuyt, S. Sanati, K. Haines, C. Theoharis, D. Jain, M. Robert, Z. Walther, D. Braddock, P. Hui, D. Kowalski, C. Bifulco, A. Vortmeyer, J. Kim, A. Huttner, E. Zambrano and R. Homer. Interestingly, at Yale Dermatopathology is a section of the Department of Dermatology and most dermatopathologists have an appointment in dermatology with a secondary appointment in pathology. Only one has his primary appointment in pathology. The dermatopathologists who attended one or more of our melanoma tumor board meetings in 2008 include: Marcus Bosenberg, Shawn Cowper, Anjela Galan, Earl Glusac, Christine Ko, Rossitza Lazova, Jennifer McNiff and Antonio Subtil.

The Department of Dermatology at YSM is unique and internationally recognized as outstanding. Its history from 1955 to 1985 is described at some length in an article by Aaron B. Lerner (J Am Acad Dermatol 2000; 44:1030-1040). It all began with Aaron B. Lerner, MD, PhD, who was born and raised in Minneapolis and received his M.D. and Ph.D. from the University of Minnesota. He was recruited to YSM from the University of Oregon by Paul Beeson who wanted a full-time section chief of dermatology in the



department of internal medicine. Lerner came as an associate professor of internal medicine and brought with him Teh H. Lee, Ph.D., Yoshiyata Takahashi, M.D. and Marguerite R. Lerner, M.D. Lee and AB Lerner isolated melanocyte-stimulating hormone (MSH), the first neuro-hormone found in the intermediate lobe of the pituitary gland and determined most of the amino acid sequence of corticotrophin. Takahashi and AB Lerner started the melatonin project and found the agent in the pineal gland. Dermatology was made a separate department in 1972 and in 1982 dermatopathology was incorporated as a section of dermatology. Lerner's paper covers the period 1955 to 1985 and lists the Yale medical students who went into dermatology, the residents, the full-time clinical and research faculty, the research fellows and trainees and clinical personnel, and part-time clinical attendings. Lerner stepped down as chair in 1985, and one of his Yale students, Richard L. Edelson, MD became the second chair and remains so. Edelson's remarkable career has already been discussed in his role as the fourth director of the YCCC. The members of dermatology who participated in our melanoma tumor board in 2008 included: Jennifer Choi, MD, a general dermatologist with a special interest in melanoma and the effects of chemotherapy and radiation therapy; John Pawelek, Ph.D., a renowned basic research scientist; Ruth Halaban, PhD, is principle investigator of the Yale skin cancer SPORE grant in malignant skin disease, including melanoma, basal cell carcinoma, cutaneous T cell lymphoma and epithelial cancers. It is one of only 12 skin SORES in the U.S. and the only SPORE at YSM now. Halaban and her laboratory associate Antonella Bacchiocchi are engaged in a multitude of studies including the biochemistry and genetics of melanoma in our patients.

Nursing is fundamental to cancer care and nursing in general probably antedates formal medical care. In the U.S., nurses worked primarily in the home and few had any formal training. During the American Civil War, military hospitals were formed with good nursing staffs and this reduced the mortality of the wounded. After the war, it was recognized that creating training schools for nurses was worthwhile. The Connecticut Training School for Nurses was founded in 1873 and was the third such training school in the U.S. Although the school was independent, it started to provide student nurses to hospitals almost immediately. In April 1873, the Directors of the General Hospital Society of Connecticut (forerunner of NHH), and the Officers of the Training School signed an agreement to work together. Student nurses would provide nursing services on the wards in exchange for room and board and training by the visiting and consulting physicians of the hospital. The Superintendent of Nurses would be responsible to the physicians and in charge of the student nurses. The hospital soon came to depend heavily on the unpaid work of the students, but to some extent, the training school was independent of NHH until 1926. In that year, the first class of the newly formed Yale School of Nursing and the last class of the Connecticut Training School held a joint graduation ceremony.

Based on the Report of the Committee for the Study of Nursing Education, the Rockefeller Foundation decided in 1923 to fund an experiment in nursing education. This project was to establish a school of nursing as a part of the university. With the support of Winternitz, who became Dean of YSM in 1920, Yale President James R. Angell, and Chair of Public Health C.-E. A. Winslow, this experiment was initiated at Yale. With funding from the Rockefeller Foundation, the Yale School of Nursing (YSN) was founded in 1923 as the first independent University-based school for the education of nurses. It had its own Dean, faculty, and budget and awarded a degree meeting the standards of the University and on parity with the other schools and colleges of the University, rather than organized under another department or school. Annie Warburton Goodrich was appointed the first Dean of YSN and was the first woman Dean at Yale University. She hired Effie Jean Taylor, the last Dean of the Training School as an assistant professor and the first Superintendent of Nursing at the NHH. Eleven years later, Taylor became the second Dean of YSN (1934-1944). That year the school started to require a bachelor's degree for admission,

and the Yale Corporation authorized a Master of Nursing program and the award of a MN degree. This continued through the difficult war years. Elizabeth S. Bixler was the third Dean of YSN (1944-1959) and during her tenure, an Advanced Program in Psychiatric Nursing leading to a Master of Science degree in the Graduate School became available. Yale President A. Whitney Griswold (according to Yale Historian George Pierson) “wanted to eliminate all vocational programs from the undergraduate schools of Yale. He thought professional training should be conducted on a graduate level and be of graduate-caliber.” When the Yale Corporation decided in 1956 that the MN program was to be terminated, Bixler resigned effective June 30, 1959 (the end of her term, but in fact, asked to be relieved of all duties June 30, 1958). Florence Schorske Wald became the acting Dean 1958-1959 and the fourth Dean of the YSN (1959-1966). The Master of Science in Nursing (MSN) program began in 1956. The MSN required students to have a prior background in nursing to gain entry into the program. The Nurse Practitioner track was established in 1971 with the offering of the Pediatric Nurse Practitioner specialty. This was expanded in 1972, when the Family Nurse Practitioner specialty began. By 1975, YSN offered 10 specialty programs and tracks, and was in the vanguard of education of nurse practitioners at the graduate level along with clinical nurse specialists and nurse-midwives.

The Grace School of Nursing was established in 1895 (as previously mentioned) to provide training for nurses in general and especially for the Grace Hospital which had been chartered in 1889. When the Grace Community Hospital staff merged with the New Haven Hospital in 1945, it formed the Grace-New Haven Community Hospital. In 1953, the combined hospital built the Memorial Unit, which became the main building for care of community patients, and later for most patients. From 1953 to 1975, the Grace Education Building provided dormitory space and classroom space for the now combined Grace-New Haven School of Nursing under the hospital’s Director of Nursing. In 1972, the decision was made to close the GNHCH nursing school because of the growing preference among nursing students for a baccalaureate program rather than a diploma program. Meanwhile, the YSN had begun to require a bachelor’s degree for admission and had set up a Master of Nursing program and nurse practitioner programs. I will return to Dean Florence Wald and her very important role in cancer care later, but now it is time to list the Deans of the YSN and then to address the contributions to cancer care of a few of the nurses of whom I have personal knowledge.

The Deans of the Yale School of Nursing were:

Annie W. Goodrich	1923-1934
Effie Jane Taylor	1934-1944
Elizabeth Seelye Bixler Torrey	1944-1958
Florence Schorske Wald	1958-1959 (acting)
	1959-1966
Margaret Gene Arnstein	1967-1972
Donna Kaye Diers	1972-1984
Judith Belliveau Krauss	1985-1998
Catherine Gilliss	1998-2004
Margaret Grey	2005-

Oncology Nursing developed shortly after cancer programs became multidisciplinary and began to use toxic drugs 50 years ago in the therapeutic management of cancer and in the investigation of new modalities of cancer care. Generally trained nurses had to be trained to understand and administer cytotoxic

chemotherapy drugs, to start and monitor IVs and later to administer intra-cavitary therapeutic agents by a variety of modalities in the hospital (both in the inpatient and outpatient units) and in private oncology offices. (which I have discussed in other venues, Fischer, DS, *The Oncology Nurse* in Fischer, DS & Marsh, JC, *Cancer Therapy*, 1982, G.K. Hall Med Publ., pp. 87-90; and Fischer, DS, *The Office Practice of Oncology* in Calabresi, P & Schein, PS, *Medical Oncology: Basic Principles & Clinical Management of Cancer*, 2<sup>nd</sup> ed., 1993, McGraw-Hill, Inc., pp. 1231-1246). All of these new functions were in addition to their underlying role of the care of the patient. The hospital nurses also had to perform an educational role in teaching the patients how to care for themselves at home and what adverse effects to note and report. The office nurses had to do all these functions and in addition act as quasi-social workers and coordinate rehabilitation, respiratory, ostomy and prosthesis support functions which are generally assigned to specialized nurses in the hospital setting. We have been fortunate that we have maintained a high standard of hospital oncology nurses supported by oncology nurse specialists who I will mention later. I have been especially fortunate to have had many talented and dedicated oncology nurses (RNs) work with me in my private office over the years, including: Lorraine Almo, Rita Ahern, Laurie Leu Markham, Patricia Kono, Theresa Hellauer, Eileen Selkis and others. They did the nursing, administered the chemotherapy and served as patient advocates and quasi-social workers. Charlene Malard, while not an RN, helped me before I could train the first office oncology nurse. Gerald Cohen and Sally Stankye were certified laboratory technicians in my office over many years and were also quite effective as patient advocates and quasi-social workers in some cases. Finally, there is the research oncology nurse who must be proficient in all the areas mentioned and in addition must have familiarity with research technology and procedures, ranging from use of radioactive isotopes to an understanding of mechanisms of action of chemotherapy and biotherapy drugs and their interactions and where they fit into research protocols.

Susan M. Hubbard, RN, MPA was the first medical oncology research nurse at YNHH of whom I am aware. She worked with Joseph Bertino, Ronald DeConti and John Marsh in the chemotherapy clinic which was then on Farnam 5 and both attended to patient care and to clinical trials research with new drugs. She left Yale in 1972 to go to the NIH where she had a remarkable career. There she worked with Vincent DeVita, Dan L. Longo, Robert Young, Bruce Chabner and others in the Medical Oncology Branch. She wrote or co-authored about 70 peer-reviewed papers on topics ranging from Hodgkin's disease and non-Hodgkin's lymphoma, to treatment of breast cancer and ovarian cancer. She played an important role in the development of the Physician Data Query (PDQ) and sponsoring its widespread use. She wrote about the role of the oncology nurse and the research nurse and ended her career as the Director of the International Cancer Information Service at the NCI.

Bonnie L. Johnson, RN took Hubbard's research position in 1972 and Bonnie remained at Yale for two years until she caught hepatitis from a patient and was out for some time. She then followed Hubbard to the NCI and she too worked with DeVita, Chabner, Richard Fisher and Young and the group and published with them in the *Am J Med* 1980:69:667-674, among other articles. In 1985, she collaborated with Jody Gross, RN on the *Handbook of Oncology Nursing*, Boston, Jones & Bartlett, 1985, with a second edition in 1994 and a third in 1998, but on that book she spelled her name as Bonny. More recently she has been involved in clinical trials at the University of Connecticut, at a small pharmaceutical company and as an independent consultant. Jody Gross and Mary Ropka were research nurses with the Yale Gastroenterology Unit led by Howard Spiro, MD with Elliot Livstone, MD leading the oncology section of the unit. Mary Ropka, RN, PhD left Yale and is now Associate Professor, Division of Public Health at University of Virginia School of Medicine in Charlottesville. Jody Gross, RN left Yale and the last I heard was that she was the director of a hospice and palliative care unit in Key West, Florida.

Mary Katherine “Tish” Knobf, RN, MSN, PhD, AOCN, best known as Tish Knobf, shared with Johnson the research position that Hubbard had vacated. She had and continues to have a most distinguished career. She became nurse director of the oncology clinic for some years and in the late 1970s, she became concerned about the Yale Internship Program that made the intern the only one who could write orders on patients on the internal medicine service. While this may have been safe with many drugs, it was clearly dangerous with some of the oncology drugs because most interns were unfamiliar with their mechanisms of action, their considerable toxicities and their proper dosing. Wendy Schneider, RN and Debbie Welch, RN shared her concern and they decided to write an in-house manual for the interns and nurses with discussions of the drugs used for chemotherapy, their indications, mechanisms of action (when known), metabolism, dose, administration, toxicities, mixing, storage and for injectable drugs, dosage supplied. They asked Keith P. Lewis, RPh, an oncology pharmacist and me to join them as co-authors. Marion Morra edited the first volume and it was cosponsored by American Cancer Society (ACS) Connecticut Division, Connecticut Oncology Association (COA) and the YCCC. It was published February 1979 as an “in-house” manual.

**CANCER CHEMOTHERAPY:** treatment and care, as it was called, was actually printed by Yale Printing and Publishing Services as a private printing, although it is not so listed. It was distributed throughout the state by the ACS and shortly thereafter, we were approached by G.K. Hall Co. of Boston to update it and they printed a commercial version in 1980 (so called first edition). The book became the de facto source of most chemotherapy ordering at YNH and those who wanted to order drugs in excess of the usual amounts or in combinations not cited in the book, had to list, in the patient’s chart, the source in the literature for the protocol. The second edition was published in 1984 with just Knobf, Fischer and Welch-McCaffrey as authors and was again advertised primarily to the nurses and pharmacists. When Year Book Medical Publishers purchased the rights, they found that there was a large market for the book among physicians and suggested a change in emphasis that would make it suitable for physicians, nurses and pharmacists. The title was changed to The Cancer Chemotherapy Handbook for the third edition in 1989; we added a chapter entitled Ethical Considerations in Cancer, and authorship was by Fischer and Knobf. By the time we wrote the fourth edition in 1993, Mosby had acquired Year Book, but the volume was so well known that the title was retained and we invited Henry J. Durivage, PharmD, a pharmacologist, to join us. This was the first edition in which we added a chapter on biologic response modifiers. This edition was translated into Italian by Gianni Bonadonna, MD and his colleagues and published in 1993 by Masson in Milano and was also translated into Japanese and published by Igaku-Shoin MYW Ltd, Tokyo, in 1994. The fifth edition, by Fischer, Knobf and Durivage, came out in 1997 with a new chapter on High-dose Chemotherapy with Stem Cell Support and an invited chapter on Blood Transfusion Therapy for the Cancer Patient by Edward Snyder, MD, Director of the Yale Blood Bank and Professor of Laboratory Medicine, and a chapter on Principles of Pediatric Cancer Therapy by Diana Komp, MD, Professor of Pediatrics. For the sixth edition in 2003, Nancy J. Beaulieu, RPh, BCOP, an oncology clinical pharmacy specialist joined us as a fourth coauthor. One of the happy consequences of my participation in the Chemotherapy Handbook was the invitation to write the section on Cancer Chemotherapy Agents in the second edition of the Encyclopedia of Toxicity, published by Elsevier, Inc in 2005. In 2007, the four of us declined to do a seventh edition of the Cancer Chemotherapy Handbook because the internet had made all the information more easily available and more up-to-date than a printed volume could be.

Tish Knobf has continued to work at the YCCC and the YSN and somehow found the time to earn a PhD from the University of Pennsylvania, care for her household of one husband, two children and a dog. She was recognized by the Oncology Nursing Society (ONS) in 1993 with the Excellence in Scholar-

ship and Contribution to the Oncology Literature Award and by YSN with the Annie Goodrich Teaching Award in 2002. She is the American Cancer Society Professor of Oncology Nursing, a member of numerous nursing journals' editorial boards, a member of the first board of directors of the ONS in 1977, and a great many more distinguished positions. In 1995, when two patients tragically died at the Dana-Farber Cancer Institute, Dr. DeVita was asked by the NCI to review that situation, and he asked several of us to form a committee to evaluate the safety of our own chemotherapy process. We established a multi-disciplinary committee of medical oncologists, nurses, and pharmacists to study our chemotherapy program and suggest improvements. We found no evidence that any patient had died at YNHH from a chemotherapy dosage error since the publication of our book. We contacted 123 hospitals to ascertain their in-house process to prevent chemotherapy errors. We then published our findings and recommendations, Fischer DS, Alfano S, Knobf MT, Donovan C and Beaulieu N, Improving the Cancer Chemotherapy Use Process, *J Clin Onc* 1996; 14:3148-3155. It was the first thorough study with recommendations for chemotherapy error prevention. It became the seminal work on the subject and is cited by Womer RW et al in *J Clin Onc* 2002; 20:4705-4712, and by ASCO and ONS Chemotherapy Administration Safety Standards, *J Clin Onc* 2009;27:5469-5475. Although the YSN had an advanced practice degree in oncology and had granted a MSN to Clinical Nurse Specialists since 1970, Knobf created a curriculum for an Oncology Nurse Practitioner in 1998 and the first student entered in 1999. This was one of the first in the country. Now the healthcare market is demanding more "mid-level" practitioners and specialty nurse practitioners (NP), so the YSN was ahead of the curve.

Constance T. Donovan, RN, MSN, AOCN came to the YSN in the late 1970s and received an appointment at YNHH as a Cancer Clinical Nurse Specialist. For many years she assisted and taught nurses, interns and oncology fellows how to care for patients with cancer combining the best technology with tenderness and compassion. After she saw a chapter in Fischer and Marsh, *Cancer Therapy*, 1981 with a listing of all the chemotherapy drugs then in use with a list of their common toxicities that I had prepared for my patients, she asked if we could collaborate to keep it up-to-date as new drugs became FDA approved. We prepared a sheet for each drug and gave it to the patients who were placed on those drugs. Over the years, we did a fair job of keeping up with it, but a few years ago we fell behind and just before Connie retired, she asked Judith Grasso, RN, MSN, AOCN, Joan Moore, MN, APRN, AOCN, Lisa Barbarotta, MSN, RN, AOCN, Wendelin Nelson, PharmD and Desiree Sanchis, RN and me to update it with her. This was typical Connie--every task had to be completed and to the best of our collective abilities. She also took primary responsibility for writing the template orders for multi-drug regimens and standard order sets for all the agreed upon protocols. Connie was a member of YNHH Bioethics Committee and chairperson of the Nursing Ethics Special Interest Group of the Division of Nursing. She taught ethics and was on the advisory board of the Nursing Ethics Network. She was recognized for her work in the field and wrote about "Ethics and Human Rights Issues in Nursing Practice," "Nurse Participation in Decisions Regarding Limitations of Treatment," "Preventing Chemo Errors," and with M. Tish Knobf, "An Evidence-Based Project to Advance Oncology Nursing Practice" among many other publications. She was also part of the first group that developed standards of oncology nursing practice and educational standards for the ONS. She began the first Oncology Nursing Council at YNHH and initiated the first Oncology Nursing Conference, now an annual event. Most of all, she was consistently responsible for maintaining the high quality of nursing care on the inpatient units (medical oncology and gynecological oncology) in her role as the senior oncology clinical nurse and the "go-to person" when there was a problem.

Marion E. Morra, MA, SCD is not a nurse, but was associate professor in the YSN for many years. Marion was and is a superb communications expert. For many years she was Associate Director of the

YCCC where she was also responsible for the Cancer Information Service (CIS), patient education and support and community outreach. She originated the CIS (1-800-CANCER) at Yale in 1975, as one of the first offices to be funded by the NCI and directed it for over 20 years. When we started to write the in-house chemotherapy manual, Marion edited it for us. As an outgrowth of that, when John Marsh and I edited (and wrote about 50% of the text) of Cancer Therapy, Marion helped to edit it. She was always helpful and full of good ideas. As already mentioned, she was the one who put me in touch with Mr. Libassi at the Department of HEW. She was the chairperson of YCCC membership committee for many years, and when she retired from Yale, she arranged for me to be chairman. I was very fortunate to have the assistance of Ann Mattei as secretary for most of my tenure as chair of the membership committee. On the national scene, Morra was a founding member of the International Cancer Information Services Group and a member of its Board of Directors. She began assisting international partners in setting up CIS offices many years ago, first assisting in setting up the CIS office in Germany. Early in her career, she identified the need for and initiated and wrote four patient pamphlets (Chemotherapy and You, Radiation Therapy and You, Eating Hints and Dealing with Pain) and turned their publication rights over to the NCI. Over the years, millions of copies have been distributed free to patients and their families. She is also co-author (with her sister, Eve Potts) of four patient help books: CHOICES: A Sourcebook for Cancer Information, 1980, 1987, 1994, 2003, Avon Books, Harper Collins; The Prostate Cancer Answer Book, 1996; Triumph: Getting Back to Normal When You have Cancer, 1990; and Understanding Your Immune System, 1986. She serves as a Past Chair of the American Cancer Society National Board of Directors. She is the author of over 100 peer-reviewed publications.

Bonnie Indeck, LCSW, MSW, graduated from the City College of NY with a degree in sociology and received her MSW in social work from the State University of NY. She came to YNHH in 1981 as a social worker. Since 1992 she has been a member of the Cancer Committee and in 1993 she was appointed a clinical instructor in internal medicine. She has added immeasurably to the cancer program, participating in setting up a series of lectures by oncology-hematology faculty for patients; community symposia on cancer; an annual one-day head and neck cancer screening program with the section of ENT; support groups in a variety of cancers; and worked with me to set up the Patient Resource Facility with its computers and cancer literature from ACS and NCI. She is the Director of Patient and Family Services at YNHH and YCC and more recently was promoted to Supervisor of Oncology Social Services. She is also the coordinator of outreach programs and educational programs for the Cancer Committee and also served on the YNHH Medical Board Ethics Committee. She has been actively involved in the “Look Good...Feel Better” program which YCC sponsors in collaboration with the ACS and the Cosmetic, Toiletry and Fragrance Association Foundation. She also runs the “Look Your Best Basket at Yale” that helps to provide wigs for patients who lose their hair secondary to chemotherapy treatments. In addition to other publications, she has written or co-authored the chapter on Community Resources for multiple editions of the DeVita, Hellman and Rosenberg text, Cancer: Principles and Practice of Oncology. Her observations on social, informational, emotional and instrumental support have been particularly valuable in addition to the discussion of survivorship and internet resources. She has also shared this information in lectures and on Yale radio programs. She is a major asset to the Yale Cancer Program and has been for nearly 30 years.

Renee Gaudette, a graduate of George Washington University, joined the YCC in 1999. She is the Director of Public Affairs and Marketing at YCC and oversees all internal and external print, electronic, and media communications. She is the editor of the YCC Bulletin, Centerpoint, and coordinates the YCC Oncology Grand Rounds lecture program. She arranges for the guests' travel, lodging, meetings and is the

all around person for public relations, even managing the website. She is a board member and co-chair of the Communications Committee of the Connecticut Cancer Partnership. While not a nurse or social worker, she is a key participant in maintaining the excellence of the YCCC.

Ruth McCorkle, MSN, PhD, is the first Florence Schorske Professor at the YSN and the director of the Center for Excellence in Chronic Illness Care. She is also the program leader for Cancer Control at YCCC and a professor in the Department of Epidemiology and Public Health. She came to Yale from the University of Pennsylvania after having previously taught at the Universities of Washington and Iowa. She has a strong interest in improving psychosocial cancer care and stresses the importance of interdisciplinary cooperation to achieve this goal. Her interest in palliative and end-of-life care is longstanding. Over 20 years ago, she studied at St Christopher's Hospice in London, and participated in clinical studies to relieve distressing symptoms associated with dying. She has since been continuously funded by NIH for her studies on managing life with cancer. She was elected to the Institute of Medicine (IOM) in 1990 and is the recipient of numerous awards. Some of those honors include the Book of the Year Award for Cancer Nursing from the American Journal of Nursing, a Distinguished Merit Award from the International Society of Nurses in Cancer Care, and a Distinguished Research Award from the ONS. She was named the Nurse Scientist of the Year by the Council of Nurse Researchers of the American Nurses Association, one of the most coveted awards in nursing.

Florence Schorske Wald, RN, MN, MS was the fourth Dean of the Yale University School of Nursing 1959-1966. She introduced many new programs to the YSN particularly in the area of psychiatric nursing (she had been assistant professor of psychiatric nursing at YSN 1957-1958 and became acting dean in 1958 before she became dean in 1959). In 1963, Dr. Paul Beeson was caring for terminally ill A. Whitney Griswold, President of Yale, and having a difficult time with his management. Bernard Lytton, MB a young assistant professor of urology from England mentioned to Beeson that he had spent a year at St. Joseph's Hospice in east London and worked with Dr. Cicely Saunders there and thought that her management of the terminally ill might be instructive. Lytton was busy setting up a kidney transplant program at YSM and was too busy to work on the hospice program, but he and Beeson arranged for Saunders to come to New Haven later that year and she gave a lecture to about 40 people. She explained her methods of using palliative care for terminally ill cancer patients with the intention of allowing those in the latest stages of their disease to focus on their personal relationships and prepare themselves for death. Dr. Saunders made an indelible impression on Wald who attended that lecture. She then worked to update the YSN curriculum to encourage students to focus on the patient and the family, and to keep all of them involved in patient care. She invited Saunders to spend part of the Spring Term of 1965 as a visiting faculty member. She was so inspired by the concept of a hospice that she stepped down as dean in 1966 to devote herself to exploring the possibility of opening a hospice in New Haven. In fact, she presided over the opening of the first hospice home care program in the U.S. on Prospect Street in New Haven. Later, she became interested in healthcare problems in prisons and was instrumental in the creation of the first prison hospice program in the country. In the meantime, Saunders opened St. Christopher's Hospice in 1967, the world's first purpose-built hospice. Why call it a hospice? She said "the name hospice, 'a resting place for travelers or pilgrims,' was chosen because this will be something between a hospital and a home, with the skills of one and the hospitality, warmth, and time of the other."

Cicely Saunder, MB was initially trained as a nurse, then a social worker, and in 1979 was promoted to Dame Commander of the Order of the British Empire (DBE) so that she was generally referred to as Dame Cicely Saunders rather than as doctor. Later she was elected a Fellow of the Royal College of Physicians, the Royal College of Nursing and the Royal College of Surgeons. In 1967, Wald invited her to New Haven again and she spoke to packed audience of 200 of us and explained her methods. Wald arranged to spend a month with Saunders at St. Christopher's Hospice in 1969. Shortly thereafter, with strong encouragement from Wald, a group of us met, including Ira Goldenberg, MD (breast surgeon), Morris Wessel, MD (pediatrician), Reverend Edward Dobihal (hospital chaplain) and his wife, Shirley Dobihal, RN, and David Fischer, MD (medical oncologist). Dr. Lytton did not join us in spite of his experience because he was busy setting up the kidney transplant program at Yale. We agreed that we wanted to establish an inpatient hospice but that it was important to begin with a hospice home care program and we began raising funds for such a program. Wald spent two years conducting a research program studying how terminally ill patients fared at home or in a healthcare facility, and tracked how patients and their families felt throughout the process. While developing the outpatient service, Wald had kept her eye on developing an inpatient facility and her husband, Henry Julius Ward, left his engineering firm and enrolled in Columbia University in 1971 with a major in hospital planning. It was his master's degree thesis that provided the framework for the structure that would later be built.

The New Haven Hospice (TNHH), a non-profit organization, was established in 1974 as a home-care organization based on the work of Florence Wald. Dennis Rezendes was its first president and it operated out of a headquarters on Prospect Street in New Haven. This was the first hospice program in the U.S. It was funded initially by charitable contributions and then by the NCI for 3 years to develop a demonstration center for home care for the terminally ill and their families. I referred many patients to the home care program and continued to care for them as the physician of record with the help of the home-care nurses. We started thinking about an inpatient facility in 1976 just as soon as the home care program was successful and we had NIH financial support. I was anxious to see continuity of care and I met with Mr. C. Thomas Smith when he became president of YNHH in 1977 to suggest that the hospice inpatient facility be on the property of YNHH or immediately adjacent to it. He saw it as a money loser and did not feel that YNHH could absorb more than it was already losing on the emergency service and other unreimbursed or inadequately reimbursed services. I spoke to Sister Louise Anthony, president of the Hospital of St. Raphael and she did not even wish to consider it, probably for the same reason. Contrary to my suggestion, the other members of the committee never had any intention of having the inpatient facility anywhere near either hospital. Their idea was to have it at least 5 miles out of town so that the hospice could not be conveniently visited by the patients' medical oncologist lest he (there were only four medical oncologists in New Haven by then and we were all male) continue to give the patient active therapy. They preferred to have a cadre of hired physicians who would be employed by the hospice who would provide only palliative care and follow hospice principles as determined by the director and the Board of Directors. At that time, IV fluid therapy and feeding tubes were not employed and the emphasis was on pain control. I agreed that this was the proper palliative care for the hospice and routinely sent my terminally ill patients to the hospice three to four weeks before I anticipated their death and I ceased all anti-cancer drugs. Although I would have preferred to continue to care for my patients and supervise the palliative care at the hospice, the board had firmly decided that it wanted its own hired physicians. Thus, I visited my hospice patients once a week, but it was a social visit to keep in touch. Since a cadre of hospice trained physicians had to be trained and the public had to be educated to understand the nature and purpose of hospices, the Connecticut Hospice Institute (later renamed the John D. Thompson Hospice Institute in 1993) was opened in 1979 to serve as an educational center and to spread the Principles of Hospice Care.



Ten Principles of Hospice Care have been developed over many years and listed in a variety of places. Below, I have listed those published by Thomson GE, Hurzeler, RJ, Fraunhar, G and Howe, K ([http://www.hospice.com/Hospice Institute/775.htm](http://www.hospice.com/Hospice%20Institute/775.htm)). They are not much different than other listings, but they are enumerated by the authors as part of their new initiative called Connecticut Physician Assisted Living (PAL):

1. Patient and family are regarded as the unit of care.
2. Services are physician-directed and nurse-coordinated.
3. Emphasis is on control of symptoms (physical, sociological, spiritual & psychological).
4. Care is provided by an interdisciplinary team.
5. Trained volunteers are an integral part of the team.
6. Services are available on a 24-hours-a-day, seven day-a-week basis.
7. Family members receive bereavement follow-up.
8. Home care and inpatient care are coordinated.
9. Patients are accepted on the basis of health needs, not on ability to pay.
10. There are structured systems for staff support.

The Connecticut Hospice (TCH) (note name change) was built pretty much as Henry Wald suggested. It opened and was licensed as a 44 bed hospital in 1980 on Burban Drive in Branford, and it was the first free standing hospice built specifically for that purpose. Rosemary Johnson Hurzeler, RN became the president (and still is) and Sylvia Lach was the first medical director. I was on the medical advisory board and remained on it for 13 years under medical directors including Drs. Robert Zanes, Lawrence Solomon and Fred Flatow and others until I went out of practice. There have been several medical directors since. I am now on the Hospice Home Care Professional Advisory Committee. Dr. Flatow is currently a member of our YNHH-YCC ACoS Cancer Committee. When the Dana Corporation decided to move its headquarters out of Branford, the building at 100 Double Beach Road was acquired by TCH and remodeled into a hospital of modern design with 52 beds. It is located on a rocky prominence overlooking Branford's Homeport Cove with its own adjoining sandy beach and its own offshore island and nestled amidst tall oaks and maples which dot the landscape. In 1980, TCH was designated as the statewide referral center for inpatient hospice care. In 1985, it was the only hospice accredited by the Accreditation Council for Continuing Medical Education (ACCME). In 1986, medical oncology fellows at YCCC were offered the opportunity to rotate through TCH and many chose to do so. As a result of hospice activities, in 1982, Congress included a provision to create a Medicare hospice benefit in the Tax Equity and Fiscal Responsibility Act with a 1986 sunset provision. In 1986, the Medicare Hospice Benefit was made permanent by Congress and states were given the option of including it in their Medicaid programs. There are now over 3,000 hospice and palliative care programs in the U.S. The rest of the story is national history.

Ethics has a long history dating back to biblical times, and probably to pre-historical times. At Yale, it dates back to its earliest years as a school for training of clergy and permeating several of the schools and departments. However, I will restrict my history to its role in medicine and more particularly as it relates to cancer. After World War II, the extent of the horror of Nazi physicians' experiments on human subjects became widely known from the Nuremberg Trials of 1946-47. Although they were tried under preexisting international law, the Nuremberg Code was developed for the Military Tribunal as standards to guide and by which to judge the morality of research involving human subject in the future. The Code's provisions specified that "the voluntary consent of the human subject is absolutely essential." Other provisions included a capacity to consent, freedom from coercion and comprehension of the risks and benefits involved, the minimization of risk and harm, a favorable risk/benefit ratio, qualified investigators using

appropriate research designs, and freedom for the subject to withdraw at any time. Some German doctors argued in their defense that what they had done differed little from previous studies on malaria (for which Sir Ronald Ross was awarded the Nobel Prize in 1902), and some ethically questionable studies on plague and cholera. Although it was not known to them then, the Tuskegee Syphilis Study which was begun by the U.S. Public Health Service in 1932 was tainted by several serious unethical components including the fact that when penicillin became more widely available for civilian use in 1946, it was not given to the subjects so that the natural history of syphilis could be followed until 1972. The U.S. government has formally apologized for this ethical aberration. To try to prevent unethical human experimentation in the future, the NIH Clinical Center formed a committee in 1953 to establish guidelines based largely on the principles of the Nuremberg Code. It was also given the responsibility for prior review of proposals to do studies on “normal volunteers: and studies to introduce novel modes of therapy. The committee had jurisdiction only over studies done in the Clinical Center. There was no requirement for committee review generally until 1966 when the Surgeon General issued his famous memorandum. Then review by a “committee of institutional associates” was required for all research conducted or supported by the USPHS.

In 1962, the Clinical Investigation Committee (CIC) was formed at YSM and the chairmen were Louis Welt, then William Hollingsworth and then Stuart Finch. In 1964, the World Medical Association established recommendations guiding physicians in biomedical research involving human subjects, The Declaration of Helsinki. The Declaration governs international research ethics and defines rules for “research combined with clinical care” and “non-therapeutic research.” In a talk in 1965, later published (*N Engl J Med* 1966; 274:1354-1360), Henry K. Beecher, MD, an anesthesiologist at the Massachusetts General Hospital called attention to published “examples of unethical or questionably ethical studies” performed on patients without their consent or procedures that had substantial risk with little or no therapeutic benefit to the subject. This increased the general perception that there had to be more formal protection for human subjects. In 1966, Robert Levine became a member of the CIC and in 1969 he became chair and the committee was renamed the Human Investigation Committee (HIC). At other institutions, it is known as the Institutional Review Board (IRB). (Actually, “IRB” is the generic name established by federal statute in 1974 and most institutions have local “brand names”. This is because, particularly in the early years, the Institutional Review Board conveyed no meaning to the faculty and students of most institutions while Human Investigation Committee did). At Yale, the brand name is HIC but in correspondence with the federal government, it is called IRB. Its mandate is to review, approve, and monitor biomedical and behavioral research involving humans with the aim to protect the rights and welfare of the research subjects. A U.S. Public Health Services (USPHS) memo in 1966 issued by the Research Grants Division specified that no new, renewal or continuation research would be supported unless there was an independent assurance “by a committee of institutional associates” of the rights and welfare of the individual, the appropriateness of the methods used to secure informed consent, and the risk and potential medical benefits of the investigation.

In July of 1974, the passage of the National Research Act established the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research (NCPHSBBR) which met for the next four years. Between 1975 and 1978 it developed definitions of basic ethical principles, and an account of the distinctions between research and the practice of medicine and behavioral therapy. (The definitions and distinctions described in the preceding sentence are found in one of its reports, the Belmont Report). It also provided multiple other reports which included recommendations for guidelines covering all research involving human subjects with special reports on such populations as children, the fetus and IVF, prisoners and “those institutionalized as mentally infirm.” With one exception (those institutional-

ized as mentally infirm), these recommendations were promptly converted into regulations and remain the central core of the regulations to this day. The Belmont Report (BR) rapidly became the standard on such matters around the world, cited in most national and international ethical codes, regulations and guidelines. The BR was co-authored by Tom Beauchamp of Georgetown University and Robert J. Levine of Yale. It came to be known as the Belmont Report (because it was developed at Belmont House in the Washington, D.C. area) was published in 1978 and was reprinted in the Federal Register in 1979, and that date is frequently cited as the BR date of publication. Regulations first published in 1974 as the Code of Federal Regulations Title 45-Part 46 Protection of Human Subjects (45 CFR 46) [the regulations published in 1974 were replaced by new regulations] that were based on the recommendations of the National Commission. These new regulations were promulgated in 1975 (for fetuses, pregnant women and IVF, most other categories in 1981 and children in 1983) originally applied only to the Department of Health, Education and Welfare (DHEW) and later to its successor, the Department of Health and Human Services (DHHS), specifically the Office for Human Research Protections (OHRP). The regulations did not “apply” to the OHRP, rather, OHRP was the name of the office within DHHS given the assignment to ensure compliance with the regulations. A later iteration in 1991, known as the Common Rule is applicable to all Executive Branch agencies other than the FDA whose regulations contain only minor variations from the Common Rule. These regulations empower IRBs to approve human experiments, or require modifications in planned research prior to approval, or to disapprove some research projects entirely.

Robert J. Levine, MD graduated from the George Washington University School of Medicine; internship and residency at the Peter Bent Brigham Hospital; Clinical Associate at the National Heart Institute (NHLBI) from which he was recruited to become Chief Resident on the medical service at the West Haven VA Hospital, was chairman of the HIC from 1969 to 2000. He is Professor of Medicine and a Lecturer in Pharmacology and is Director of the Law, Policy and Ethics Core of the Yale University (YU) Center for Interdisciplinary Research on AIDS; founding Co-Director of the YU Interdisciplinary Center for Bioethics (currently Senior Fellow and Chair of the Executive Committee); and formerly Chief of the Section of Clinical Pharmacology. Levine convinced me to serve on the HIC for five years, which was a heavy burden but gratifying and educational. He was deeply committed to patient safety and empowerment and emphasized the importance of the patient’s informed consent, if such is possible. He was the Founding Editor of *IRB: A Review of Human Subjects Research* [now *IRB: Ethics & Human Research*] (Editor 1979-2000 and is current Chair of the editorial board); Associate Editor of *Biochemical Pharmacology* and Editor of *Clinical Research* (now *Journal of Investigative Medicine*). He has served as a consultant to several federal and international agencies. He was a ‘Special Consultant’ to the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research which established the basic guidelines for human clinical research in the U.S. and he wrote a significant portion of its several reports; he also coauthored the Belmont Report, a highly influential publication in the development of national and international regulations and ethical codes.

Levine has published two editions of his highly regarded *Ethics and Regulation of Clinical Research*. Most of his research, teaching and publications in the past 35 years have been in the field of medical ethics, with particular concentration on the ethics of research involving human subjects. Earlier publications, as suggested above, were in medicine and pharmacology. He was Chairperson of the Council for International Organizations of Medical Science’s Steering Committee for Revision of International Ethical Guidelines for Biomedical Research; Chair of the World Medical Association’s Working Group for Revision of the Declaration of Helsinki; consultant with the Joint United Nations Program on HIV/AIDS, Project on Ethics in HIV Vaccine Trials (assigned to draft the Guidance Documents for trials of preventive HIV

vaccines). He has been honored by organizations all over the world and Yale has recently established the annual Robert J. Levine Lectureship in Bioethics in his honor.

After Levine stepped down as chair of the HIC, it was divided into two committees named HIC-I and HIC-II with Maurice Jeremiah Mahoney, MD, JD and Robert Lange, PhD each serving as chairs of one of them. After Lange's death, Sandra Alfano, PharmD replaced him as Chair of one of the HICs. Now there are four HICs with a complex bureaucracy running the overall program. Alfano had been director of the investigational drug pharmacy for some years and was co-chair of the committee that surveyed the safety of chemotherapy administration at YNHH; she was also the second author of the 1996 paper Improving the Cancer Chemotherapy Use Process along with Fischer, Knobf, Donovan and Beaulieu. The Yale New Haven Medical Center Bioethics Committee, for which Levine wrote the charter and served as a founding member, was chaired by Howard V. Zonana, MD. He is a psychiatrist and also an adjunct professor of law and was able to merge the two perspectives. Thomas Duffy and later Mark Siegel, MD succeeded him as chairmen. There is also a Pediatrics Ethics Committee first chaired by Melvin Lewis (Levine was a member) and is now chaired by Mark Mercurio, MD. Its origin, responsive to the Baby Doe incident, antedated that of the Bioethics Committee.

Howard M. Spiro, MD established the Program for Humanities in Medicine (PHIM) in 1983 in collaboration with the late Enid R. Peschel, PhD. Its mission is to bring attention to the links between the arts and humanities and the practice of medicine. I have had the honor and great opportunity to be on its advisory board for almost two decades and was the proud sponsor of six lectures. Spiro has been a friend and mentor for almost four decades. He is a graduate of Harvard College and HMS, took postgraduate training at the Peter Bent Brigham Hospital and the MGH before he was invited to YSM by Beeson in 1955 to establish a program in gastro-intestinal disease (GI). He was eminently successful in creating the section of GI which he chaired for 25 years. He also started the Yale Digestive Disease Program which trained a large cadre of GI physicians who populated Connecticut and many other states and universities with well trained GI practitioners and researchers. In 1965, he established the Yale Affiliated Gastroenterology Program, a unique educational collaboration between fellowship training programs in south-central Connecticut. As Dr. Spiro traveled to these institutions with fellows from Yale, his trainees observed a master clinician and diagnostician eliciting a complicated history from a patient and synthesizing it into a coherent picture. I interacted with him professionally when he and Elliot Livstone were involved in the Gastrointestinal Tumor Study Group (GITSG) which did many of the early studies in GI tumors with drugs and multidisciplinary studies, including RT. He has published extensively. His *Clinical Gastroenterology* was a classic in the field, and he wrote the first three editions entirely by himself and edited the book for 20 additional years. He wrote *The Optimist: Meditation on Medicine*, and *The Power of Hope: a Doctor's Perspective*. With Harvey Mandell he edited *When Doctors Get Sick* and with Mary G. McCrea Curnen, Enid Peschel and Deborah St. James, *Empathy and the Practice of Medicine: Beyond Pills and the Scalpel*, and with Curnen and St. James, *Doctors Afield*. With Curnen and Lee Palmer Wandel, he also edited *Facing Death: Where Culture, Religion and Medicine Meet*. When he became emeritus in 1999, Spiro founded, with George Trone, the *Yale Journal for Humanities in Medicine (YJHM)* as a clearing house for manuscripts treating the humanities and medicine. The YJHM accepts submissions of prose and poetry from doctors, nurses, patients and others. Spiro also founded the "Geezers," an organization of senior physicians of the greater New Haven area who were either retired or were practicing part-time, and invited them to meet at his New Haven apartment monthly to discuss their interests, medical or otherwise, over a glass of wine, some pizza.

Thomas P. Duffy, MD graduated from Johns Hopkins Medical School and had his internship, residency and fellowship in hematology there. After six years as an assistant professor there, he came to YSM as an associate professor of medicine to run the clinical program, which he did with distinction. He became professor in 1981 and in 1982 was chosen as chair of the Clinical Education Committee in the DIM. For 10 years he was chief of the Klatskin Medical Firm and since 1985, he has been Director of the Hematology Fellowship Program. He was a founding member of the Ethics Committee of YNHH and beginning in 1995, he was chairman for many years. When Spiro became emeritus, Duffy became Director of the PHIM. In 2008, he was appointed Ethicist Scholar in the Interdisciplinary Center for Bioethics (IDCBE) and the chairperson of the Jerome Medalie sponsored End-of-Life Issues Study Group (ELISG) within that center. The co-directors of the IDCBE were Margaret A. Farley, Ph.D. and Robert J. Levine, M.D. I attend the ELISG regularly for the past decade and was invited in 2005 to present a paper there entitled Medical Futility and Inadvisability in Cancer: the Oncologist's Role. It was subsequently published as part of a symposium (What's The Point? Clinical Reflections on Care that Seems Futile, edited by D H Smith, C McKhann, CZ Peppard, T P Duffy and S Rosenbaum. 6 Nov. 2007, [Http://www.yale.edu/bioethics/publications/Medical%Futility.pdf](http://www.yale.edu/bioethics/publications/Medical%Futility.pdf) In 2008, David H. Smith became director. Duffy has been very active in meeting with house staff and fellows for ethics conferences. His publications are numerous and particularly in the areas of medical ethics. He and I co-chaired a symposium on Ethical Issues in Hematology-Oncology which was expanded to a full issue of the Yale J Biol Med 1992; 65:63-142. In the mid-1990s, he did a series called Clinical Problem Solving for the New England Journal of Medicine that was very favorably received.

Summing Up: Cancer was not a major problem when Yale College decided to collaborate with the Connecticut State Medical Society to establish a medical institution. The new school started with a strong base in science and that has been its strength over the years. It did not have a fully committed hospital partner for 100 years and hence its emphasis on clinical medicine was not as strong as some other institutions. In 1913, Dean George Blumer forged an agreement with the New Haven Hospital to allow the medical school to train its students on the hospital's wards and to have a full time clinical chief in medicine, surgery and obstetrics/gynecology. He had hoped to move the YSM to the vicinity of the NHH but World War I left both institutions with heavy debts. When Milton C. Winternitz, became Dean in 1920, he began a rapid transformation of the medical school from a mediocre institution to a first rate one with the help of Abraham Flexner, who directed a large amount of resources from Rockefeller's General Education Board to YSM and the NHH, where Col. Isaac Ullman supported and enhanced his efforts. It allowed Winternitz to build a full-time faculty, clinical laboratories, and a professional school of nursing and helped to secure funds to move the medical school to a site across the street from the NHH. After he stepped down as Dean and World War II began, he secured a federal contract for YSM to study the health effects of poison gases. As a result of these studies, in 1942, Goodman, Gilman and Lindskog at Yale were the first to use nitrogen mustard for the treatment of lymphoma and pioneered cancer chemotherapy. Unfortunately, that research was not pursued at Yale until after WW II, which itself left a legacy of financial problems for the University and YSM that almost led to the demise of YSM. However, that catastrophe was averted and YSM started to grow again.

It was not until Arnold Welch became chair of pharmacology in 1953 that a major department devoted most of its resources to studies of cancer and its therapy. That established part of the basis for the selection of YSM as one of the first 15 NCI CCCs in 1974. Although the first, third and fourth directors were nationally known for their cancer research contributions, the YCCC grew slowly because of a lack of adequate financing and a weak hospital commitment to the CCC mission and insufficient clinical trials

accrual. This led it to the brink of losing its NCI designation. For the past ten years, YNHH-YCCC has had an excellent cancer committee (and its current members are listed in this year's annual report). They have worked hard to insure that we not only meet the standards of the CoC of ACoS, but that we exceed them and have a better clinical program. The basic science program and its faculty (which I have not mentioned at length because of my lack of personal and intimate familiarity with their work) have continued to be extraordinarily productive and YSM is fifth in overall NIH grants behind JHSM, University of California at San Francisco, University of Pennsylvania and Washington University. Yale is second in grants per full-time faculty member. With the current YSM Dean Robert Alpern and the current YNHH President Marna P. Borgstrom strongly committed and working together, the YCCC and YNHH should prosper. YSM is usually listed in the top 10 U.S. medical schools. YNHH is usually listed in the top 20 U.S. hospitals. Norman G. Roth, YNHH vice president for administration who guided the construction of the Smilow Cancer Hospital at Yale New Haven to completion on budget and on time, laid out the goal: "We plan to be one of the 10 best cancer hospitals in the U.S. in the next few years." (Roth was later recruited to be COO of Bridgeport Hospital, which is part of the Yale New Haven Consortium). With the team of Thomas Lynch, MD, Director of YCCC and Physician-in-Chief of Smilow, Mr. Abe Lopman as Executive Director of Smilow, Arthur Lemay, RPh, Executive Director of the Oncology Network, Catherine Lyons, RN, MS as Clinical Program Director and Director of Oncology Nursing at Smilow, and Peter W. Marks, MD, PhD as Chief Clinical Officer at Smilow, and with the recent acquisition of a large new and well equipped West Campus for Yale University and YSM, I have every confidence that our cancer program will prosper and that Roth's goal will happen, and I hope, soon. It is my good fortune to have been and to be a part of it for more than 48 years.

Note: After this history was completed, an excellent biography, Dean Winternitz: Yale Medical School's Passionate Humanist authored by Priscilla Waters Norton and Howard Spiro, was published by the Program for Humanities in Medicine/Yale University, 2010, New Haven, CT, 480 pp, \$25. A review by Basil Riggs, MD, DSc was published in the JAMA 2011; 306 (15):1711-1713. Howard M. Spiro, MD died on March 11, 2012.

Final completion and submission for publication: May 10, 2012

APPENDIX 1A  
Compilation of Yale Medical Oncology Fellows, 1964 to 2010 (Alphabetical)

**Compilation of Physician Services Fellows listing and Medical Oncology Fellowship office records - ALPHA ORDER**

Last Name	First Name	Mid/Initi	Degree	Current status	Status	Department	Section	From	To
Abou-Alfa	Ghassan		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/98	6/30/01
Abu-Khalaf	Maysa	M.	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/02	6/30/05
<b>Acevedo-Gadea</b> (Aggarwal) Dhanjal	<b>Carlos</b> Sandhya	<b>M.D.</b>	<b>M.D.</b>	<b>Active</b>	<b>Fellow</b>	<b>Internal Medicine</b>	<b>Oncology</b>	<b>7/1/11</b>	
Anmad	Yusef Haroon		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/04	6/30/07
Alfano	Francis		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/81	6/30/83
Alpdogan	Seyfettin	Onder	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/06	6/30/09
<b>Alsamarai</b>	<b>Susan</b>		<b>M.D.</b>	<b>Active</b>	<b>Fellow</b>	<b>Internal Medicine</b>	<b>Oncology</b>	<b>6/23/09</b>	
Andersen	Nicolaj		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/02	6/30/05
Antonia	Scott	J.	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/91	6/30/94
Arcasoy	Murat		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/97	6/30/98
Argiris	Athanasios		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/97	6/30/00
Austin	Mariette		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/89	6/30/93
<b>Baumgart</b>	<b>Megan</b>		<b>M.D.</b>	<b>Active</b>	<b>Fellow</b>	<b>Internal Medicine</b>	<b>Oncology</b>	<b>7/1/11</b>	
Behal	Amita		M.D.	Inactive	Fellow	Internal Medicine	Oncology	9/27/93	3/31/94
Benz	Christopher		M.D.	Inactive	Fellow	Internal Medicine	Oncology	10/1/78	12/31/80
Berd	David		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/72	6/30/75
Berger	Anne	Maxine	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/91	6/30/93
Bleickhardt	Eric		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/99	6/30/02
Blunk	Karen	L.	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/90	6/30/92
Bober-Sorcinelli	Kathleen		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/84	6/30/86
Bobrow	Samuel		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/72	6/30/74
Bodden	William	L.	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/84	6/30/86
Boston	Barry		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/73	6/30/76
Brandt	Debra	Schwab	D.O.	Inactive	Fellow	Internal Medicine	Oncology	7/1/95	6/30/98
Brescia	Thomas		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/73	7/31/74
Brewer	Yvelise	Paule	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/88	6/30/91
Brown	Suzanne	J.	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/96	6/30/00
Bruckner	Howard		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/70	7/31/73
Brus	Christina		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/08	6/30/11
Cadman	Edward		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/72	6/30/74
Canova	Andres	Eduardo	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/96	6/30/99
Capizzi	Robert	Lawrenc	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/67	7/31/69
Carr	Francis		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/81	11/1/81
Castillo	Elquis	M.	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/90	6/30/92
Chang	Victor		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/98	6/30/01
Chao	Herta	Huey-An	M.D., Ph.D	Inactive	Fellow	Internal Medicine	Oncology	7/1/03	6/30/06
Chaves	Jorge	Mario	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/08	6/30/11
Choromanska	Olga	D.	D.O.	Inactive	Fellow	Internal Medicine	Oncology	7/1/04	6/30/07
Chung	Gina		M.D.	Inactive	Fellow	Internal Medicine	Oncology	1/1/98	12/30/01
Cohenuram	Michael		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/05	6/30/08
Cooper	Dennis		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/76	6/30/79
Danhauser	Lynn		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/81	6/30/83
Daniel	Lambert		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/83	6/30/87
Davis	Lynn	Keyes	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/76	6/30/78
DeConti	Ronald		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/64	6/30/66
DeLap	Robert	J.	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/81	9/30/83
DeRosa	William	T.	D.O.	Inactive	Fellow	Internal Medicine	Oncology	7/1/85	6/30/88



Last Name	First Name	Mid/Initial	Degree	Current status	Status	Department	Section	From	To
DiGiovanna	Michael		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/94	6/30/97
Dine	Max	Eliot	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/71	6/30/72
DiPasquale	Albert		M.D.	Inactive	Fellow	Internal Medicine	Oncology	8/1/72	6/30/73
Doria	Raul		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/92	6/30/95
Dubowy	Ronald		M.D.	Inactive	Fellow	Internal Medicine	Oncology	8/1/79	6/30/81
Edwards	Andrea		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/00	6/30/03
Elifky	Aymen		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/05	6/30/08
Ennever	Peter	R.	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/92	6/30/95
Ernstoff	Marc		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/81	6/30/84
Ersontrala-Mao	Maria	C.	M.D.	Inactive	Fellow	Internal Medicine	Oncology	11/11/86	10/31/87
Farber	Leonard		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/69	6/30/71
Fairrell	Michael		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/00	6/30/03
Fernandes	Daniel		M.D.	Inactive	Fellow	Internal Medicine	Oncology	9/1/77	9/30/80
<b>Flanigan</b>	<b>Jaelyn</b>	<b>Christin</b>	<b>M.D.</b>	<b>Active</b>	<b>Fellow</b>	<b>Internal Medicine</b>	<b>Oncology</b>	<b>7/1/09</b>	
Fogarasi	Miklos	C.	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/98	6/30/01
Friedman	Neil	S.	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/89	6/30/91
Fynan	Thomas		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/89	6/30/92
Gallardo	Rafael		M.D.	Inactive	Fellow	Internal Medicine	Oncology	3/1/80	5/31/81
Ganpule	Sanjay	Ramcha	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/86	6/30/88
Germino	F	George	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/90	6/30/91
Gibney	Geoffrey	Thomas	M.D.	Active	Fellow	Internal Medicine	Oncology	7/1/08	6/30/11
Ginsberg	Steven		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/88	6/30/92
Goldberg	David		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/81	6/30/84
Gollerkeri	Ashwin		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/95	11/19/02
Graham	Michael		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/80	6/30/82
Grant	Steven		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/78	6/30/80
Grosch	Eric		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/82	6/14/84
<b>Gunturu</b>	<b>Krishna</b>	<b>Soujanya</b>	<b>M.D.</b>	<b>Active</b>	<b>Fellow</b>	<b>Internal Medicine</b>	<b>Oncology</b>	<b>6/23/09</b>	
Haedicke	Kay		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/85	6/30/88
Hait	William		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/82	6/30/83
Harrold	Laurie		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/94	6/30/97
Hassinger	Dawn		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/80	6/30/82
Henderson-Bakas	Marie	P.	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/92	6/30/95
Hobby	Erole	Mae	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/01	6/30/04
Hoffman	Howard		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/78	6/30/79
Hoimes	Christopher	James	D.O.	Active	Fellow	Internal Medicine	Oncology	7/1/06	6/30/10
Hsieh	Frank (Hsieh)	Tze	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/97	6/30/00
Hu	Triefeng		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/90	6/30/93
Hwu	Wen Jen Poo		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/86	6/30/89
Idriss	Jean		M.D.	Inactive	Fellow	Internal Medicine	Oncology	1/14/74	2/28/75
Isufi	Iris		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/08	6/30/11
Jillella	Anand	P.	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/93	6/30/96
Juneja	Vinni		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/03	6/30/06
Kamen	Barton		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/78	6/30/79
Kang	Soonmo	Peter	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/05	6/30/08
Kass	Frederic	Charles	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/86	12/31/86
Katz	Andrea		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/08	6/30/11
Keiser	Leroy	Wayne	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/75	6/30/77
Kelley	Susan		M.D.	Inactive	Fellow	Internal Medicine	Oncology	9/1/85	6/30/86
Kelly	Kathleen		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/80	6/30/81

Last Name	First Name	Mid/Initi	Degree	Current status	Status	Department	Section	From	To
Kennealey	Gerard		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/75	6/30/77
Khan	Kalsom	K.	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/95	6/30/98
Khitrik-Palchuk	Marina	A.	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/05	6/30/08
Kim	Tracy		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/99	6/30/02
Kim	Richard		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/03	6/30/06
Kirkwood	John	M	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/76	6/30/78
Klimant	Eiko		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/00	11/19/02
Kluger	Harriet		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/99	6/30/02
Koletsky	Alan	J.	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/83	6/30/86
<b>Kournioti</b>	<b>Chryssanthi</b>		<b>M.D.</b>	<b>Active</b>	<b>Fellow</b>	<b>Internal Medicine</b>	<b>Oncology</b>	<b>7/1/11</b>	
Kowal	Charles		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/78	6/30/81
Kritsi	Zaphiroula		M.D.	Inactive	Fellow	Internal Medicine	Oncology	1/1/80	6/30/80
Kutcher	Jacqueline		M.D.	Inactive	Fellow	Internal Medicine	Oncology	?????	6/30/74
Kwong	Myron	S.	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/01	6/30/04
Lacy	Jill		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/82	6/30/85
Lansigan	Frederick		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/06	6/30/09
Lee	Gary		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/82	6/30/84
Lefkowitz	Estelle		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/65	6/30/67
Lekakis	Lazaros		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/02	6/30/05
Leopold	Clayton	Edward	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/78	6/30/80
Lerro	Keith	Andrew	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/00	6/30/03
Levitt	Martin		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/68	6/30/70
Levy	Arthur		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/70	6/30/73
Li	Jia		M.D./PhD	Inactive	Fellow	Internal Medicine	Oncology	7/1/07	6/30/10
Lin	James		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/83	6/30/86
Lok	Warren		M.D.	Active	Fellow	Internal Medicine	Oncology	7/1/07	6/30/10
Luikhart	Sharon		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/79	6/30/81
Lundberg	W	Bruce	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/74	6/30/78
Lutzker	Stuart	G.	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/92	6/30/93
Magnifico	Michael		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/79	6/30/82
Mani	Sridhar		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/92	6/30/95
Marshall	Natalie		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/97	6/30/00
Mayer	Tina	M.	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/06	6/30/09
Mazur	Eric		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/80	6/30/81
McGowan	Margit		D.O.	Inactive	Fellow	Internal Medicine	Oncology	7/1/04	6/30/08
<b>McLaughlin</b>	<b>Joseph</b>		<b>M.D.</b>	<b>Active</b>	<b>Fellow</b>	<b>Internal Medicine</b>	<b>Oncology</b>	<b>7/1/11</b>	
Medina	William	D.	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/79	6/30/82
Medina	Daniel		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/92	6/30/94
Mehnert	Janice		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/04	6/30/07
Mehra	Ranee		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/03	6/30/06
<b>Mercer-Falkoff</b>	<b>Aleagia</b>	<b>Maryn</b>	<b>M.D.</b>	<b>Active</b>	<b>Fellow</b>	<b>Internal Medicine</b>	<b>Oncology</b>	<b>6/23/09</b>	
Mineiro	Luiz		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/69	6/30/70
Mini	Enrico		M.D.	Inactive	Fellow	Internal Medicine	Oncology	2/1/82	2/29/84
Minor	David		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/76	6/30/78
Mitchell	Malcolm	Stuart	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/66	6/30/68
Morris	Stephan	W.	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/84	6/30/87
Mosher	Michael	Bennett	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/70	6/30/72
Mota	Augusto	C.A.	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/98	6/30/00
Mukhopadhyay	Madan		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/71	6/30/72
Murphy	Gerard	J.	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/88	6/30/89

Last Name	First Name	Mid/Initi	Degree	Current status	Status	Department	Section	From	To
Murray	Ethelann		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/70	6/30/71
Murren	John		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/88	6/30/91
Nabbout	Nassim		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/98	6/30/01
Nair	Balagopalan A.		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/93	12/31/94
Nathan	Carl		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/76	6/30/77
Nelson	Kristine	A.	M.D.	Inactive	Fellow	Internal Medicine	Oncology	11/1/87	11/30/90
Newcomer	Lee		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/79	6/30/81
Nishihori	Taiga		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/06	6/30/09
Noronha	Vanita		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/02	6/30/05
O'Brien	Paul	Edward	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/01	6/30/04
Oladele-Bankole	David		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/78	6/30/79
Oluwole	Odujinrin		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/71	6/30/72
Openshaw	Thomas		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/85	6/30/88
Patel	Bimal	J.	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/89	6/30/92
Pavlovic	Mirjana		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/92	6/30/93
Paz-Combes	Guillermo		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/77	6/30/79
Podolitsev	Nikolai	A.	M.D., Ph.D	Active	Fellow	Internal Medicine	Oncology	7/1/07	6/30/10
Psyrry	Diamanda		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/99	6/30/02
Radin	Arthur		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/85	6/30/87
Rafi	Rezvandokht		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/90	6/30/93
Rajani	Nadkarni	P.	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/94	6/30/97
Razzkowski	Ronald		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/73	6/30/74
<b>Raza</b>	<b>Mohammad Ali</b>		<b>M.D.</b>	<b>Active</b>	<b>Fellow</b>	<b>Internal Medicine</b>	<b>Oncology</b>	<b>7/1/10</b>	
Reale	Michael	A.	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/91	6/30/94
Reiss	Michael		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/82	6/30/85
Reuben	Dan		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/01	6/30/04
Rich	Randy	S.	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/98	6/30/01
Rivest	Rachel	S	M.D.	Inactive	Fellow	Internal Medicine	Oncology	11/16/81	10/31/84
Rosales	Marguerite		M.D.	Inactive	Fellow	Internal Medicine	Oncology	2/8/93	6/30/94
Rosman	Martin		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/72	6/30/74
Roszkowski	Ronald		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/73	6/30/74
Roy	Shailja		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/03	6/30/06
Rudnick	Seth	Allen	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/76	6/30/78
<b>Saadati</b>	<b>Hamid</b>		<b>M.D.</b>	<b>Active</b>	<b>Fellow</b>	<b>Internal Medicine</b>	<b>Oncology</b>	<b>7/1/10</b>	
Saidman	Bruce		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/87	6/30/89
Salloum	Emile		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/93	6/30/95
Sandler	Alan	B.	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/89	6/30/92
Sarid	Rami		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/96	6/30/99
Sarkar	Rita		M.D.	Inactive	Fellow	Internal Medicine	Oncology	2/1/93	3/31/93
Sarris	Andreas	H.	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/85	6/30/87
Scanlon	Kevin	Joseph	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/74	6/30/76
Schertz	Gerald		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/75	6/30/77
Schiffman	Fred		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/78	6/30/81
Schnall	Sandra		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/83	6/30/86
Schultz	Michelle	Z.	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/91	6/30/94
Scott	William	L.	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/86	6/30/90
Seropian	Stuart		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/94	6/30/97
Shiba	David		M.D.	Inactive	Fellow	Internal Medicine	Oncology	11/1/88	12/30/90
Sigurdsson	Fridbjorn		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/92	6/30/95
Silber	Andrea		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/85	6/30/87

Last Name	First Name	Mid/Initial	Degree	Current status	Status	Department	Section	From	To
Simon	Miklos		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/00	6/30/03
Skeel	Roland	Thor	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/69	6/30/71
Smaldone	Laurie		M.D.	Inactive	Fellow	Internal Medicine	Oncology	9/1/82	6/30/84
Sobrero	Alberto	F	M.D.	Inactive	Fellow	Internal Medicine	Oncology	11/1/80	11/30/83
Spaulding	Monica		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/69	6/30/72
Spieker	Paul		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/77	6/30/79
Stebbins	Robert		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/75	1/31/76
Tansino	Gary		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/87	6/30/89
Tara	Harold		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/99	6/30/02
<b>Thumar</b>	<b>Jaykumar</b>		<b>M.D.</b>	<b>Active</b>	<b>Fellow</b>	<b>Internal Medicine</b>	<b>Oncology</b>	<b>6/23/09</b>	
<b>Tian</b>	<b>Ligeng</b>		<b>M.D.</b>	<b>Active</b>	<b>Fellow</b>	<b>Internal Medicine</b>	<b>Oncology</b>	<b>7/1/10</b>	
Todd	MaryBeth		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/81	6/30/84
Tomita	Megumi		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/04	6/30/06
Tonkonow	Barry	Lee	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/78	12/31/80
Trautmann	Thomas	G.	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/84	6/30/86
Triano	Laura	R.	M.D.	Active	Fellow	Internal Medicine	Oncology	7/1/07	6/30/10
<b>Velcheti</b>	<b>Vamsidhar</b>		<b>M.D.</b>	<b>Active</b>	<b>Fellow</b>	<b>Internal Medicine</b>	<b>Oncology</b>	<b>7/1/10</b>	
Vera	Raul		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/80	6/30/83
Vlock	Daniel		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/82	6/30/84
Waldron-Lynch	Maeve	Geraldin	M.D.	Active	Fellow	Internal Medicine	Oncology	10/1/08	9/30/11
Wang	Hao		MD, PhD	Active	Fellow	Internal Medicine	Oncology	7/1/07	6/30/10
Weisberg	Tracey		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/86	6/30/88
Weiss	Steven		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/87	6/30/90
Wheler	Jennifer		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/02	6/30/04
White	Charles	F	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/79	6/30/81
Whorf	Robert		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/01	6/30/03
Williams	Marcia		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/86	6/30/88
Windsor	Stephen	J.	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/95	6/30/98
Witman	Gary		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/78	6/30/80
Wiznitzer	Israel		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/81	6/30/84
Wolnak	Kenneth		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/83	6/30/84
Wizesinski	Stephen	Henry	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/05	6/30/08
Yen	Yun		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/91	6/30/93
Zaman	Aamir		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/94	6/30/97
<b>Zheng</b>	<b>Hong</b>		<b>M.D.</b>	<b>Active</b>	<b>Fellow</b>	<b>Internal Medicine</b>	<b>Oncology</b>	<b>7/1/10</b>	
Marin	Alberto		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/92	???
Chopyk	Ricki		M.D.	Inactive	Fellow	Internal Medicine	Oncology	NO Records	NO Records
Bennett	James		M.D.	Inactive	Fellow	Internal Medicine	Oncology	NO Records	NO Records
Kaplan	Stephen		M.D.	Inactive	Fellow	Internal Medicine	Oncology	NO Records	NO Records

APPENDIX 1B  
Compilation of Yale Medical Oncology Fellows, 1964 to 2010 (Chronological)  
Compiled by Savannah Woods

**Compilation of Physician Services Fellows listing and Medical Oncology Fellowship office records - CHRON ORDER**

Last Name	First Name	Mid/Initial	Degree	Current status	Status	Department	Section	Status from date	Status thru date
DeConti	Ronald		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/64	6/30/66
Lefkowitz	Estelle		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/65	6/30/67
Mitchell	Malcolm	Stuart	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/66	6/30/68
Capizzi	Robert	Lawrence	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/67	7/31/69
Levitt	Martin		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/68	6/30/70
Mineiro	Luiz		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/69	6/30/70
Ferber	Leonard		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/69	6/30/71
Murray	Ethelann		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/70	6/30/71
Skeel	Roland	Thor	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/69	6/30/71
Dine	Max	Eliot	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/71	6/30/72
Mosher	Michael	Bennett	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/70	6/30/72
Mukhopadhyay	Madan		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/71	6/30/72
Oluwole	Odujinrin		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/71	6/30/72
Spaulding	Monica		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/69	6/30/72
DiPasquale	Albert		M.D.	Inactive	Fellow	Internal Medicine	Oncology	8/1/72	6/30/72
Bruckner	Howard		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/70	6/30/73
Levy	Arthur		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/70	7/31/73
Bobrow	Samuel		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/70	6/31/1973
Cadman	Edward		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/72	6/30/74
Kutcher	Jacqueline		M.D.	Inactive	Fellow	Internal Medicine	Oncology	?????	6/30/74
Raskowski	Ronald		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/73	6/30/74
Rosman	Martin		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/72	6/30/74
Roszkowski	Ronald		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/73	6/30/74
Brescia	Thomas		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/73	7/31/74
Idriss	Jean		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/74	2/28/75
Berd	David		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/72	6/30/75
Stebbins	Robert		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/75	1/31/76
Boston	Barry		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/73	6/30/76
Scanlon	Kevin	Joseph	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/74	6/30/76
Keiser	Leroy	Wayne	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/75	6/30/77
Kennealey	Gerald		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/75	6/30/77
Nathan	Carl		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/76	6/30/77
Schertz	Gerald		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/75	6/30/77
Davis	Lynn	Keyes	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/76	6/30/78
Kirkwood	John	M	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/76	6/30/78
Lundberg	W	Bruce	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/74	6/30/78
Minor	David		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/76	6/30/78
Rudnick	Seth	Allen	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/76	6/30/78
Cooper	Dennis		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/76	6/30/79
Hoffman	Howard		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/78	6/30/79
Kamen	Barton		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/78	6/30/79
Oladele-Bankole	David		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/78	6/30/79
Paz-Combes	Guillermo		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/77	6/30/79
Spieler	Paul		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/77	6/30/79
Grant	Steven		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/78	6/30/80
Kritsi	Zaphiroula		M.D.	Inactive	Fellow	Internal Medicine	Oncology	1/1/80	6/30/80
Leopold	Clayton	Edward	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/78	6/30/80
Witman	Gary		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/78	6/30/80
Fernandes	Daniel		M.D.	Inactive	Fellow	Internal Medicine	Oncology	9/1/77	9/30/80
Benz	Christopher		M.D.	Inactive	Fellow	Internal Medicine	Oncology	10/1/78	12/31/80
Tonkonow	Barry		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/78	12/31/80
Gallardo	Rafael	Lee	M.D.	Inactive	Fellow	Internal Medicine	Oncology	3/1/80	5/31/81
Dubowy	Ronald		M.D.	Inactive	Fellow	Internal Medicine	Oncology	8/1/79	6/30/81
Kelly	Kathleen		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/80	6/30/81
Kowal	Charles		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/78	6/30/81
Luikhart	Sharon		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/79	6/30/81

Last Name	First Name	Mid/Initial	Degree	Current status	Status	Department	Section	Status_from_date	Status_thru_date
Mazur	Eric		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/80	6/30/81
Newcomer	Lee		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/79	6/30/81
Schiffman	Fred		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/78	6/30/81
White	Charles	F	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/79	6/30/81
Carr	Francis		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/81	11/1/81
Graham	Michael		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/80	6/30/82
Hassinger	Dawn		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/80	6/30/82
Magnifico	Michael		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/79	6/30/82
Medina	William	D.	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/79	6/30/82
Alfano	Francis		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/81	6/30/83
Danhauser	Lynn		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/81	6/30/83
Halt	William		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/82	6/30/83
Vera	Raul		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/80	6/30/83
Delap	Robert	J.	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/81	9/30/83
Sobrero	Alberto	F	M.D.	Inactive	Fellow	Internal Medicine	Oncology	11/1/80	11/30/83
Mini	Enrico		M.D.	Inactive	Fellow	Internal Medicine	Oncology	2/1/82	2/29/84
Grosch	Eric		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/82	6/14/84
Ernststoff	Marc		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/81	6/30/84
Goldberg	David		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/81	6/30/84
Lee	Gary		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/82	6/30/84
Smaldone	Laurie		M.D.	Inactive	Fellow	Internal Medicine	Oncology	9/1/82	6/30/84
Todd	MaryBeth		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/81	6/30/84
Vlock	Daniel		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/82	6/30/84
Wiznitzer	Israel		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/81	6/30/84
Wolnak	Kenneth		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/83	6/30/84
Rivest	Rachel	S	M.D.	Inactive	Fellow	Internal Medicine	Oncology	11/16/81	10/31/84
Lacy	Jill		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/82	6/30/85
Reiss	Michael		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/82	6/30/85
Bober-Sorcinelli	Kathleen		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/84	6/30/86
Bodden	William	L.	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/84	6/30/86
Kelley	Susan		M.D.	Inactive	Fellow	Internal Medicine	Oncology	9/1/85	6/30/86
Koletsky	Alan	J.	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/83	6/30/86
Lin	James		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/83	6/30/86
Schnall	Sandra		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/83	6/30/86
Trautmann	Thomas	G.	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/84	6/30/86
Kass	Frederic	Charles	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/86	12/31/86
Daniel	Lambert		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/83	6/30/87
Morris	Stephan	W.	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/84	6/30/87
Radin	Arthur		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/85	6/30/87
Sarris	Andreas	H.	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/85	6/30/87
Silber	Andrea		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/85	6/30/87
Escontrela-Mao	Maria	C.	M.D.	Inactive	Fellow	Internal Medicine	Oncology	11/11/86	10/31/87
DeRosa	William	T.	D.O.	Inactive	Fellow	Internal Medicine	Oncology	7/1/85	6/30/88
Garpute	Sanjay	Ramchandra	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/86	6/30/88
Haedicke	Kay		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/85	6/30/88
Openshaw	Thomas		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/85	6/30/88
Weisberg	Tracey		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/86	6/30/88
Williams	Marcia		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/86	6/30/88
Hwu	Wen Jen Poo		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/86	6/30/89
Murphy	Gerard	J.	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/88	6/30/89
Saidman	Bruce		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/87	6/30/89
Tansino	Gary		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/87	6/30/89
Scott	William	L.	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/86	6/30/90
Weiss	Steven		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/87	6/30/90
Nelson	Kristine	A.	M.D.	Inactive	Fellow	Internal Medicine	Oncology	11/1/87	11/30/90
Shiba	David		M.D.	Inactive	Fellow	Internal Medicine	Oncology	11/1/88	12/30/90
Brewer	Yvelise	Paule	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/88	6/30/91

Last Name	First Name	Mid/Initial	Degree	Current status	Status	Department	Section	Status_from_date	Status_thru_date
Friedman	Neil	S.	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/89	6/30/91
Germino	F	George	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/90	6/30/91
Murren	John		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/88	6/30/91
Ahmad	Yusef Haroon		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/90	6/30/92
Blunk	Karen	L.	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/90	6/30/92
Castillo	Elquis	M.	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/90	6/30/92
Fynan	Thomas		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/89	6/30/92
Ginsberg	Steven		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/88	6/30/92
Patel	Bimal	J.	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/89	6/30/92
Sandler	Alan	B.	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/89	6/30/92
Sarkar	Rita		M.D.	Inactive	Fellow	Internal Medicine	Oncology	2/1/93	3/31/93
Austin	Mariette		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/89	6/30/93
Berger	Anne	Maxine	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/91	6/30/93
Hu	Triefeng		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/90	6/30/93
Lutzker	Stuart	G.	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/92	6/30/93
Pavlovic	Mirjana		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/92	6/30/93
Rafi	Rezvandokht		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/90	6/30/93
Yen	Yun		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/91	6/30/93
Behal	Amita		M.D.	Inactive	Fellow	Internal Medicine	Oncology	9/27/93	3/31/94
Antonia	Scott	J.	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/91	6/30/94
Medina	Daniel		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/92	6/30/94
Rosales	Marguerite		M.D.	Inactive	Fellow	Internal Medicine	Oncology	2/8/93	6/30/94
Schultz	Michelle	Z.	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/91	6/30/94
Nair	Balagopalalan	A.	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/93	12/31/94
Doria	Raul		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/92	6/30/95
Ennever	Peter	R.	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/92	6/30/95
Henderson-Bakas	Marie	P.	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/92	6/30/95
Mani	Sridhar		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/92	6/30/95
Salloum	Emile		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/93	6/30/95
Sigurdsson	Fridbjorn		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/92	6/30/95
Jillella	Anand	P.	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/93	6/30/96
DiGiovanna	Michael		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/94	6/30/97
Harold	Laurie		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/94	6/30/97
Rajani	Nackarni	P.	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/94	6/30/97
Seropian	Stuart		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/94	6/30/97
Zaman	Aamir		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/94	6/30/97
Arcasoy	Murat		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/97	6/30/98
Brandt	Debra		D.O.	Inactive	Fellow	Internal Medicine	Oncology	7/1/95	6/30/98
Khan	Kalsoom	K.	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/95	6/30/98
Windsor	Stephen	J.	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/95	6/30/98
Canova	Andres	Eduardo	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/96	6/30/99
Sarif	Rami		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/96	6/30/99
Argiris	Athanassios		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/97	6/30/00
Brown	Suzanne	J.	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/96	6/30/00
Hsieh	Frank (Hsieh)	Tze	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/97	6/30/00
Marshall	Natalie		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/97	6/30/00
Mota	Augusto	C.A.	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/98	6/30/00
Abou-Alfa	Ghassan		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/98	6/30/01
Chang	Victor		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/98	6/30/01
Fogarasi	Miklos	C.	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/98	6/30/01
Nabbout	Nassim		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/98	6/30/01
Rich	Randy	S.	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/98	6/30/01
Chung	Gina		M.D.	Inactive	Fellow	Internal Medicine	Oncology	1/1/98	12/30/01
Bleickhardt	Eric		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/99	6/30/02
Kim	Tracy		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/99	6/30/02
Kluger	Harriet		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/99	6/30/02
Psyrti	Diamanda		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/99	6/30/02



Last Name	First Name	Mid/Initial	Degree	Current status	Status	Department	Section	Status_from_date	Status_thru_date
Tara	Harold		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/99	6/30/02
Gollerkeri	Ashwin		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/95	11/19/02
Klimant	Eiko		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/00	11/19/02
Edwards	Michael		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/00	6/30/03
Farrell	Michael		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/00	6/30/03
Lerro	Keith	Andrew	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/00	6/30/03
Simon	Miklos		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/00	6/30/03
Whorf	Robert		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/01	6/30/03
Hobby	Erole	Mae	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/01	6/30/04
Kwong	Myron	S.	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/01	6/30/04
O'Brien	Paul	Edward	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/01	6/30/04
Reuben	Dan		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/01	6/30/04
Wheeler	Jennifer		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/02	6/30/04
Abu-Khalaf	Maysa	M.	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/02	6/30/05
Andersen	Nicolaj		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/02	6/30/05
Lekakis	Lazaros		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/02	6/30/05
Noronha	Vanita		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/02	6/30/05
Chao	Herta	Huey-An	M.D., Ph.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/03	6/30/06
Juneja	Vinni		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/03	6/30/06
Kim	Richard		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/03	6/30/06
Mehra	Ranee		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/03	6/30/06
Roy	Shailja		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/03	6/30/06
Tomita	Megumi		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/04	6/30/07
Aggarwal	Sandhya		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/04	6/30/07
Choromanska	Olga	D.	D.O.	Inactive	Fellow	Internal Medicine	Oncology	7/1/04	6/30/07
Mehner	Janice		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/04	6/30/07
Cohenuram	Michael		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/05	6/30/08
Elfky	Aymen		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/05	6/30/08
Kang	Soonmo	Peter	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/05	6/30/08
Khatrik-Palchuk	Marina	A.	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/05	6/30/08
McGowan	Margit		D.O.	Inactive	Fellow	Internal Medicine	Oncology	7/1/04	6/30/08
Wrzesinski	Stephen	Henry	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/05	6/30/08
Alpdogan	Seyfettin	Onder	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/06	6/30/09
Lansigan	Frederick		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/06	6/30/09
Mayer	Tina	M.	M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/06	6/30/09
Nishihori	Taiga		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/06	6/30/09
Hoimes	Christopher	James	D.O.	Active	Fellow	Internal Medicine	Oncology	7/1/06	6/30/10
Li	Jia		M.D./PhD	Inactive	Fellow	Internal Medicine	Oncology	7/1/07	6/30/10
Lok	Warren		M.D.	Active	Fellow	Internal Medicine	Oncology	7/1/07	6/30/10
Podoltsev	Nikolai	A.	M.D., Ph.D.	Active	Fellow	Internal Medicine	Oncology	7/1/07	6/30/10
Triano	Laura	R.	M.D.	Active	Fellow	Internal Medicine	Oncology	7/1/07	6/30/10
Wang	Hao		M.D., Ph.D.	Active	Fellow	Internal Medicine	Oncology	7/1/07	6/30/10
Brus	Christina		M.D.	Active	Fellow	Internal Medicine	Oncology	7/1/08	6/30/11
Chaves	Jorge	Mario	M.D.	Active	Fellow	Internal Medicine	Oncology	7/1/08	6/30/11
Gibney	Geoffrey	Thomas	M.D.	Active	Fellow	Internal Medicine	Oncology	7/1/08	6/30/11
Isufi	Iris		M.D.	Active	Fellow	Internal Medicine	Oncology	7/1/08	6/30/11
Katz	Andrea		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/08	6/30/11
Waldron-Lynch	Maeve	Geraldine	M.D.	Active	Fellow	Internal Medicine	Oncology	10/1/08	9/30/11
Alsamrai	Susan		M.D.	Active	Fellow	Internal Medicine	Oncology	7/1/09	6/30/12
Flanigan	Jaclyn	Christine	M.D.	Active	Fellow	Internal Medicine	Oncology	7/1/09	6/30/12
Gunturu	Krishna	Soujanya	M.D.	Active	Fellow	Internal Medicine	Oncology	7/1/09	6/30/12
Mercer-Falkoff	Aleagia	Maryn	M.D.	Active	Fellow	Internal Medicine	Oncology	7/1/09	6/30/12
Thumar	Jaykumar		M.D.	Active	Fellow	Internal Medicine	Oncology	7/1/09	6/30/12
Raza	Mohammad	Ali	M.D.	Active	Fellow	Internal Medicine	Oncology	7/1/10	6/30/13

Last Name	First Name	Mid/Initial	Degree	Current status	Status	Department	Section	Status_from_date	Status_thru_date
Saadati	Hamid		M.D.	Active	Fellow	Internal Medicine	Oncology	7/1/10	6/30/13
Tian	Ligeng		M.D.	Active	Fellow	Internal Medicine	Oncology	7/1/10	6/30/13
Veicheti	Vamsidhar		M.D.	Active	Fellow	Internal Medicine	Oncology	7/1/10	6/30/13
Zheng	Hong		M.D.	Active	Fellow	Internal Medicine	Oncology	7/1/11	6/30/14
Acevedo-Gadea	Carlos		M.D.	Active	Fellow	Internal Medicine	Oncology	7/1/11	6/30/14
Baumgart	Megan		M.D.	Active	Fellow	Internal Medicine	Oncology	7/1/11	6/30/14
Kourmotti	Chryssanthi		M.D.	Active	Fellow	Internal Medicine	Oncology	7/1/11	6/30/14
McLaughlin	Joseph		M.D.	Active	Fellow	Internal Medicine	Oncology	7/1/11	6/30/14
Wadia	Roxanne		M.D.	Active	Fellow	Internal Medicine	Oncology	7/1/11	6/30/14
Marin	Alberto		M.D.	Inactive	Fellow	Internal Medicine	Oncology	7/1/92	???
Chopyk	Ricki		M.D.	Inactive	Fellow	Internal Medicine	Oncology	NO Records found	NO Records found
Bennett	James		M.D.	Inactive	Fellow	Internal Medicine	Oncology	NO Records found	NO Records found
Kaplan	Stephen		M.D.	Inactive	Fellow	Internal Medicine	Oncology	NO Records found	NO Records found

APPENDIX 2A  
Compilation of Yale Hematology Fellows, 1955 to 2010 (Alphabetical)

Compilation of Physician Services Fellows listing and Hematology Fellowship office records - ALPHA ORDER									
Last Name	First Name	Mid/Initial	Degree	Current status	Status	Department	Section	Start date	Finish date
Ahmad	Yusuf	H	MD	Inactive	Fellow	Internal Medicine	Heme & Onc	7/1/93	6/30/94
Aleali	Syed		MD	Inactive	Fellow	Internal Medicine	Heme w/ St. V	5/27/05	5/28/05
			MD	Inactive	Fellow	Internal Medicine	Heme & Onc	7/1/92	6/30/1993
Arcasoy	Murat	O	MD	Inactive	Fellow	Internal Medicine	Hematology	1970	1971
Arronson	Robert		MD	Inactive	Fellow	Internal Medicine	Hematology	7/1/85	12/31/85
Arrow	A		MD	Inactive	Fellow	Internal Medicine	Heme w/St. M	5/27/05	5/29/05
Azikiwe	Abiodun		MD	Inactive	Fellow	Internal Medicine	Hematology	7/1/1988	6/30/1989
Becker	Pamela		MD/PhD	Inactive	Fellow	Internal Medicine	Hematology	7/1/1990	6/30/1991
Benz, Jr.	Edward	J.	MD	Inactive	Fellow	Internal Medicine	Hematology	7/1/78	6/30/80
Bering	Harriet	A.	MD	Inactive	Fellow	Internal Medicine	Hematology	7/1/80	6/30/81
Bering	Harriet	A.	MD	Inactive	Fellow	Internal Medicine	Hematology	7/1/82	6/30/84
Bodemann	Heinz		MD	Inactive	Fellow	Internal Medicine	Hematology	5/25/05	5/26/05
Boldato	Helen		MD	Inactive	Fellow	Internal Medicine	Heme w/ St. V	5/25/05	5/27/05
Bolkens	Jacques		MD	Inactive	Fellow	Internal Medicine	Hematology	2/1/88	1/31/91
Bromberg	Michael	E.	MD	Inactive	Fellow	Internal Medicine	Heme & Onc	7/1/91	6/30/95
Cadwell	Anne	B	MD	Inactive	Fellow	Internal Medicine	Hematology	7/1/82	6/30/85
Cai	Ji-Lian		MD/PhD	Inactive	Fellow	Internal Medicine	Hematology	6/30/02	6/29/04
Castro	Oswaldo		MD	Inactive	Fellow	Internal Medicine	Hematology	5/20/05	5/22/05
Chang	Victor		MD	Inactive	Fellow	Internal Medicine	Heme & Onc	6/30/98	6/29/00
Chasis	Joel	A.	MD	Inactive	Fellow	Internal Medicine	Hematology	7/1/75	6/30/78
Chen	Wendy		DO	Inactive	Fellow	Internal Medicine	Heme & Onc	7/1/06	6/30/09
Chopyk	Ricki		MD/PhD	Inactive	Fellow	Internal Medicine	Heme & Onc	1984 ?/7/1985	1985 ?/7/1987
Chowdhury	Saeeda		M.D.	Inactive	Fellow	Internal Medicine	Heme & Onc	10/1/06	9/30/09
Clark	Bruce	C.	MD	Inactive	Fellow	Internal Medicine	Hematology	7/1/82	6/30/84
Clark	J	M	MD	Inactive	Fellow	Internal Medicine	Hematology	6/23/86	6/22/87
Covey	William		MD	Inactive	Fellow	Internal Medicine	Hematology	1967	1969
Dainiak	Nicholas		MD	Inactive	Fellow	Internal Medicine	Hematology	7/1/76	6/30/79
DeCastro	Laura		MD	Inactive	Fellow	Internal Medicine	Heme & Onc	7/1/95	6/30/98
Desai	Haren		MD	Inactive	Fellow	Internal Medicine	Heme w/ St. M	5/26/05	5/27/05
Donadio	Joseph	A	MD	Inactive	Fellow	Internal Medicine	Hematology	5/23/05	5/25/05
Donohue	Susan	E.	MD	Inactive	Fellow	Internal Medicine	Hematology	10/1/94	9/30/95
Ernever	Peter		MD	Inactive	Fellow	Internal Medicine	Heme & Onc	7/1/93	6/30/95
Firshain	Stephen	I.	MD	Inactive	Fellow	Internal Medicine	Hematology	7/1/76	6/30/78
Gauwerky	Charlotte	E.	MD	Inactive	Fellow	Internal Medicine	Hematology	5/1/84	6/30/87
Gewirtz	Alan	M	MD	Inactive	Fellow	Internal Medicine	Hematology	7/1/81	6/30/82
Ginsberg	Steven	S.	MD	Inactive	Fellow	Internal Medicine	Heme & Onc	7/1/1988 1989(Onc.) 7/1/1991	6/30/1989 1991(Onc.) 6/30/1992
Goldenfarb	Paul	B	MD	Inactive	Fellow	Internal Medicine	Hematology	5/24/05	5/26/05
Gorsky	Mila		MD	Inactive	Fellow	Internal Medicine	Heme & Onc	6/30/04	6/29/07
Halene	Stephanie		MD	Inactive	Fellow	Internal Medicine	Hematology	6/30/02	2/28/06
Hall	Shaynn	D	MD/PhD	Inactive	Fellow	Internal Medicine	Hematology	7/1/00	6/30/03
High	Katherine	A.	MD	Inactive	Fellow	Internal Medicine	Hematology	7/1/81	6/30/84
Horowitz	Rivka	S.	MD	Inactive	Fellow	Internal Medicine	Hematology	7/1/81	6/30/82
James	Edward	Samuel	MD	Active	Fellow	Internal Medicine	Hematology	7/1/11	6/30/13
Kahlon	Kanwarpal		M.D.	Active	Fellow	Internal Medicine	Heme & Onc	7/1/10	6/30/14
Kaplan	Sandra	S	MD	Inactive	Fellow	Internal Medicine	Hematology	5/16/05	5/18/05

Last Name	First Name	Mid/Initial	Degree	Current status	Status	Department	Section	Start date	Finish date
Kaplan	Moreson	H	MD	Inactive	Fellow	Internal Medicine	Hematology	5/21/05	5/22/05
Kathuna	Navneet			Inactive	Fellow	Internal Medicine	Hematology	6/16/86	6/15/87
Kiehl	Ralph	K	MD	Inactive	Fellow	Internal Medicine	Heme & Onc	7/1/1989	6/30/1990
								7/1/1991	6/30/1992
Klein	Michael	E.	MD	Inactive	Fellow	Internal Medicine	Hematology	7/1/77	6/30/79
<b>Kocoglu</b>	<b>Mehmet</b>	<b>Hakan</b>	<b>M.D.</b>	<b>Active</b>	<b>Fellow</b>	<b>Internal Medicine</b>	<b>Heme &amp; Onc</b>	<b>7/1/10</b>	<b>6/30/13</b>
Krishnadadan	Ravi		MD	Inactive	Fellow	Internal Medicine	Heme & Onc	7/1/03	6/30/06
<b>Landau</b>	<b>Dan-Avi</b>		<b>M.D.</b>	<b>Active</b>	<b>Fellow</b>	<b>Internal Medicine</b>	<b>Heme &amp; Onc</b>	<b>7/1/09</b>	<b>6/30/12</b>
Lebowitz	Paul		MD	Inactive	Fellow	Internal Medicine	Hematology	5/20/05	5/23/05
Lindquist	Susan	T.	MD	Inactive	Fellow	Internal Medicine	Hematology	7/1/78	6/30/79
Lockridge	Leslie		MD	Inactive	Fellow	Internal Medicine	Hematology	6/30/99	6/29/02
Lomax	K.			Inactive	Fellow	Internal Medicine	Hematology	6/1/83	5/30/86
Maggiore	Ronald	J	M.D.	Inactive	Fellow	Internal Medicine	Hematology	7/1/07	6/30/10
Magnifico	Michael	C.	MD	Inactive	Fellow	Internal Medicine	Hematology	7/1/79	6/30/81
Maun	Noel		MD/PhD	Inactive	Fellow	Internal Medicine	Hematology	x/xx/1997	x/xx/2000
Mazur	Eric	M.	MD	Inactive	Fellow	Internal Medicine	Hematology	7/1/79	6/30/81
McHugh	Colleen	M	MD	Inactive	Fellow	Internal Medicine	Hematology	6/30/95	12/31/96
McPhedran	Peter		MD	Inactive	Fellow	Internal Medicine	Hematology	1965;	1965
								1969	1970
Meichinger	David	B	MD	Inactive	Fellow	Internal Medicine	Hematology	5/25/05	5/26/05
Melnick	D.	A.		Inactive	Fellow	Internal Medicine	Hematology	7/1/81	6/30/84
Morris	Stephen	W	MD	Inactive	Fellow	Internal Medicine	Heme & Onc	6/25/86	6/24/87
Mugnaini	Emiliano		MD/PhD	Inactive	Fellow	Internal Medicine	Heme & Onc	07/01/2004	6/30/07
Murray	Ethlyann		MD	Inactive	Fellow	Internal Medicine	Hematology	5/22/05	5/23/05
Nash	Inwin		MD	Inactive	Fellow	Internal Medicine	Hematology	1973	1975
Neparidze	Natalia		M.D.	Inactive	Fellow	Internal Medicine	Heme & Onc	7/1/07	6/30/10
Odujirin	Oluwole		MD	Inactive	Fellow	Internal Medicine	Hematology	1971	1973
Okam	Maureen	M	MD	Inactive	Fellow	Internal Medicine	Hematology	7/1/01	6/30/04
Openshaw	Thomas	H	MD	Inactive	Fellow	Internal Medicine	Heme & Onc	6/29/87	6/28/88
Oren	Mark	E	MD	Inactive	Fellow	Internal Medicine	Hematology	5/24/05	5/25/05
O'Shea	James		MD	Inactive	Fellow	Internal Medicine	Heme & Onc	7/1/94	6/30/95
<b>Parker</b>	<b>Terri</b>		<b>M.D.</b>	<b>Active</b>	<b>Fellow</b>	<b>Internal Medicine</b>	<b>Heme &amp; Onc</b>	<b>7/1/09</b>	<b>6/30/12</b>
Parnes	Aric		MD	Inactive	Fellow	Internal Medicine	Heme & Onc	6/30/05	6/29/08
Perez	Lia		MD	Inactive	Fellow	Internal Medicine	Heme & Onc	6/30/97	6/29/00
Prosnitz	Leonard	R	MD	Inactive	Fellow	Internal Medicine	Hematology	7/1/65	6/30/67
Perillie	Pasquale	E	MD	Inactive	Fellow	Internal Medicine	Hematology	1955	1956
Radin	Arthur	I.	MD	Inactive	Fellow	Internal Medicine	Hematology	7/1/83	6/30/89
Rado	Thomas	A.	MD	Inactive	Fellow	Internal Medicine	Hematology	7/1/80	6/30/83
Richter	Joshua		M.D.	Inactive	Fellow	Internal Medicine	Heme & Onc	7/1/08	6/30/11
Rinder	Henry	M	MD	Inactive	Fellow	Internal Medicine	Hematology	7/1/88	x/xx/1991
Rogers	Elois		MD	Inactive	Fellow	Internal Medicine	Hematology	5/25/05	5/26/05
Rose	Michal		MD	Inactive	Fellow	Internal Medicine	Heme & Onc	9/13/93	9/12/96
Rosen	Michael	W	MD	Inactive	Fellow	Internal Medicine	Hematology	5/25/05	5/27/05
Ross	Stephen	A	MD	Inactive	Fellow	Internal Medicine	Hematology	1969	1970
Rudolph	Priya		MD/PhD	Inactive	Fellow	Internal Medicine	Hematology	6/30/01	6/29/04
Sawada	Unihiko		MD	Inactive	Fellow	Internal Medicine	Hematology	1975	1976
Schiffman	Fred	J.	MD	Inactive	Fellow	Internal Medicine	Hematology	7/1/79	6/30/81
Schnall	Sandra	<b>F</b>	<b>MD</b>	<b>Inactive</b>	<b>Fellow</b>	<b>Internal Medicine</b>	<b>Hematology</b>	<b>7/7/1983</b>	<b>7/7/1985</b>
Shreim	Ali		MD	Inactive	Fellow	Internal Medicine	Heme.w/ St. V	5/25/05	5/26/05
Simmonds	John		MD	Inactive	Fellow	Internal Medicine	Hematology	1967	1968

Last Name	First Name	Mid/Initial	Degree	Current status	Status	Department	Section	Start date	Finish date
Sinning	Joseph		MD	Inactive	Fellow	Internal Medicine	Heme & Onc	1/1/97	12/31/00
Spaulding	Monica	M	MD	Inactive	Fellow	Internal Medicine	Hematology	5/23/05	5/24/05
Stier	Stanley	D	MD	Inactive	Fellow	Internal Medicine	Hematology	5/20/05	5/21/05
Stolle	C.	A.		Inactive	Fellow	Internal Medicine	Hematology	4/1/85	3/31/86
Strout	Matthew		MD/PhD	Inactive	Fellow	Internal Medicine	Hematology	7/1/04	6/30/07
Todd	M.		DO	Inactive	Fellow	Internal Medicine	Hematology	7/1/82	6/30/84
Vietzke	Wesley	M	MD	Inactive	Fellow	Internal Medicine	Hematology	5/21/05	5/22/05
Weissmann	Lisa		MD	Inactive	Fellow	Internal Medicine	Hematology	?/7/1984	?/7/1985
Winkelmann	John	C.	MD	Inactive	Fellow	Internal Medicine	Hematology	7/1/84	6/30/87
Wong	Ellice		M.D.	Inactive	Fellow	Internal Medicine	Heme & Onc	7/1/08	6/30/11
Yen	Yun		MD/PhD	Inactive	Fellow	Internal Medicine	Heme & Onc	7/1/1990 - 1991	6/30/1991
Zhang	Paul (Xuejun)		MD/PhD	Inactive	Fellow	Internal Medicine	Hematology	7/1/98	6/30/01
Zhang	Yue		MD/PhD	Active	Fellow	Internal Medicine	Hematology	7/1/11	6/30/14
Zhou	Ming		MD/PhD	Inactive	Fellow	Internal Medicine	Hematology	6/30/00	6/29/03

APPENDIX 2B

Compilation of Yale Hematology Fellows, 1955 to 2010 (Chronological)  
Compiled by Savannah Woods, Richard Carr and Bernard Forget, MD

**Compilation of Physician Services Fellows listing and Hematology Fellowship office records - CHRON ORDER**

Last Name	First Name	Mid/Initial	Degree	Current status	Status	Department	Section	Start date	Finish date
Perillie	Pasquale	E	MD	Inactive	Fellow	Internal Medicine	Hematology	1955	1956
Prosnitz	Leonard	R	MD	Inactive	Fellow	Internal Medicine	Hematology	23924	24653
Kaplan	Sandra	S	MD	Inactive	Fellow	Internal Medicine	Hematology	1963	1965
McPhedran	Peter		MD	Inactive	Fellow	Internal Medicine	Hematology	1965; 1968	1965; 1970
Ster	Stanley	D	MD	Inactive	Fellow	Internal Medicine	Hematology	1967	1968
Simmonds	John		MD	Inactive	Fellow	Internal Medicine	Hematology	1967	1968
Castro	Oswaldo		MD	Inactive	Fellow	Internal Medicine	Hematology	1967	1969
Covey	William		MD	Inactive	Fellow	Internal Medicine	Hematology	1967	1969
Lebowitz	Paul		MD	Inactive	Fellow	Internal Medicine	Hematology	1967	1970
Kaplan	Moreson	H	MD	Inactive	Fellow	Internal Medicine	Hematology	1968	1969
Vietzke	Wesley	M	MD	Inactive	Fellow	Internal Medicine	Hematology	1968	1969
Murray	Ethylann		MD	Inactive	Fellow	Internal Medicine	Hematology	1969	1970
Ross	Stephen	A	MD	Inactive	Fellow	Internal Medicine	Hematology	1969	1970
Arronson	Robert		MD	Inactive	Fellow	Internal Medicine	Hematology	1970	1971
Spaulding	Monica	M	MD	Inactive	Fellow	Internal Medicine	Hematology	1970	1971
Donadio	Joseph	A	MD	Inactive	Fellow	Internal Medicine	Hematology	1970	1972
Oren	Mark	E	MD	Inactive	Fellow	Internal Medicine	Hematology	1971	1972
Goldenfarb	Paul	B	MD	Inactive	Fellow	Internal Medicine	Hematology	1971	1973
Odujirin	Oluwole		MD	Inactive	Fellow	Internal Medicine	Hematology	1971	1973
Bodemann	Heinz		MD	Inactive	Fellow	Internal Medicine	Hematology	1972	1973
Melchinger	David	B	MD	Inactive	Fellow	Internal Medicine	Hematology	1972	1973
Rogers	Elois		MD	Inactive	Fellow	Internal Medicine	Hematology	1972	1973
Shreim	Ali		MD	Inactive	Fellow	Internal Medicine	Heme w/ St. V	1972	1973
Rosen	Michael	W	MD	Inactive	Fellow	Internal Medicine	Hematology	1972	1974
Boldiatio	Helen		MD	Inactive	Fellow	Internal Medicine	Heme w/ St. V	1972	1974
Desai	Haren		MD	Inactive	Fellow	Internal Medicine	Heme w/ St. M	1973	1974
Nash	Irwin		MD	Inactive	Fellow	Internal Medicine	Hematology	1973	1975
Aleali	Syed		MD	Inactive	Fellow	Internal Medicine	Heme w/ St. V	1974	1975
Azikiwe	Abiodun		MD	Inactive	Fellow	Internal Medicine	Heme w/ St. M	1974	1976
Sawada	Unihiko		MD	Inactive	Fellow	Internal Medicine	Hematology	1975	1976
Chasis	Joel	A.	MD	Inactive	Fellow	Internal Medicine	Hematology	7/1/75	6/30/78
Firshein	Stephen	I.	MD	Inactive	Fellow	Internal Medicine	Hematology	7/1/76	6/30/78
Dainiak	Nicholas		MD	Inactive	Fellow	Internal Medicine	Hematology	7/1/76	6/30/79
Klein	Michael	E.	MD	Inactive	Fellow	Internal Medicine	Hematology	7/1/77	6/30/79
Lindquist	Susan	T.	MD	Inactive	Fellow	Internal Medicine	Hematology	7/1/78	6/30/79
Benz, Jr.	Edward	J.	MD	Inactive	Fellow	Internal Medicine	Hematology	7/1/78	6/30/80
Schiffman	Fred	J.	MD	Inactive	Fellow	Internal Medicine	Hematology	7/1/79	6/30/81
Mazar	Eric	M.	MD	Inactive	Fellow	Internal Medicine	Hematology	7/1/79	6/30/81
Magnifico	Michael	C.	MD	Inactive	Fellow	Internal Medicine	Hematology	7/1/79	6/30/81
Rado	Thomas	A.	MD	Inactive	Fellow	Internal Medicine	Hematology	7/1/80	6/30/83
Bering	Harriet	A.	MD	Inactive	Fellow	Internal Medicine	Hematology	7/1/80	6/30/81
Horowitz	Rivka	S.	MD	Inactive	Fellow	Internal Medicine	Hematology	7/1/81	6/30/82
High	Katherine	A.	MD	Inactive	Fellow	Internal Medicine	Hematology	7/1/81	6/30/84
Gewirtz	Alan	M	MD	Inactive	Fellow	Internal Medicine	Hematology	7/1/81	6/30/82
Bering	Harriet	A.	MD	Inactive	Fellow	Internal Medicine	Hematology	7/1/82	6/30/84
Melnick	D.	A.		Inactive	Fellow	Internal Medicine	Hematology	7/1/81	6/30/84
Todd	M.		DO	Inactive	Fellow	Internal Medicine	Hematology	7/1/82	6/30/84
Cadwell	Anne	B	MD	Inactive	Fellow	Internal Medicine	Hematology	7/1/82	6/30/85
Clark	Bruce	C.	MD	Inactive	Fellow	Internal Medicine	Hematology	7/1/82	6/30/84



Last Name	First Name	Mid/Initial	Degree	Current status	Status	Department	Section	Start date	Finish date
Lomax	K.			Inactive	Fellow	Internal Medicine	Hematology	6/1/83	5/30/84
Schnall	Sandra	F	MD	Inactive	Fellow	Internal Medicine	Hematology	?/?.1983	?/?.1985
Radin	Arthur	I.	MD	Inactive	Fellow	Internal Medicine	Hematology	7/1/83	6/30/89
Lomax	K.			Inactive	Fellow	Internal Medicine	Hematology	6/1/84	5/31/86
Weissmann	Lisa		MD	Inactive	Fellow	Internal Medicine	Hematology	?/?.1984	?/?.1985
Gauwerky	Charlotte	E.	MD	Inactive	Fellow	Internal Medicine	Hematology	5/1/84	6/30/87
Winkelmann	John	C.	MD	Inactive	Fellow	Internal Medicine	Hematology	7/1/84	6/30/87
Stolle	C.	A.	MD	Inactive	Fellow	Internal Medicine	Hematology	4/1/85	3/31/86
Arrow	A			Inactive	Fellow	Internal Medicine	Hematology	7/1/85	12/31/85
Chopyk	Ricki		MD/PhD	Inactive	Fellow	Internal Medicine	Heme & Onc	1984	1985
								?/?.1985	?/?.1987
Kathuria	Navneet			Inactive	Fellow	Internal Medicine	Hematology	6/16/86	6/15/87
Clark	J	M		Inactive	Fellow	Internal Medicine	Hematology	6/23/86	6/22/87
Morris	Stephen	W	MD	Inactive	Fellow	Internal Medicine	Heme & Onc	6/25/86	6/24/87
Openshaw	Thomas	H	MD	Inactive	Fellow	Internal Medicine	Heme & Onc	6/29/87	6/28/88
Bolkens	Jacques		MD	Inactive	Fellow	Internal Medicine	Hematology	2/1/88	1/31/91
Becker	Pamela		MD/PhD	Inactive	Fellow	Internal Medicine	Hematology	7/1/1988	6/30/1989
								7/1/1990	6/30/1991
Rinder	Henry	M	MD	Inactive	Fellow	Internal Medicine	Hematology	7/1/88	x/xx/1991
Ginsberg	Steven	S.	MD	Inactive	Fellow	Internal Medicine	Heme & Onc	7/1/1988	6/30/1989
								1989(Onc.)	1991(Onc.)
								7/1/1991	6/30/1992
Kiehl	Ralph	K	MD	Inactive	Fellow	Internal Medicine	Heme & Onc	7/1/1989	6/30/1990
								7/1/1991	6/30/1992
Yen	Yun		MD/PhD	Inactive	Fellow	Internal Medicine	Heme & Onc	7/1/1990	6/30/1991
								1991	1993
Bromberg	Michael	E.	MD	Inactive	Fellow	Internal Medicine	Heme & Onc	7/1/91	6/30/95
Ahmad	Yusuf	H	MD	Inactive	Fellow	Internal Medicine	Heme & Onc	7/1/93	6/30/94
Arcasoy	Murat	O	MD	Inactive	Fellow	Internal Medicine	Heme & Onc	7/1/92	6/30/1993
Ernever	Peter		MD	Inactive	Fellow	Internal Medicine	Heme & Onc	7/1/93	6/30/95
Rose	Michal		MD	Inactive	Fellow	Internal Medicine	Heme & Onc	9/13/93	9/12/96
O'Shea	James		MD	Inactive	Fellow	Internal Medicine	Heme & Onc	7/1/94	6/30/95
Donohue	Susan	E.	MD	Inactive	Fellow	Internal Medicine	Hematology	10/1/94	9/30/95
McHugh	Colleen	M	MD	Inactive	Fellow	Internal Medicine	Hematology	6/30/95	12/31/96
DeCastro	Laura		MD	Inactive	Fellow	Internal Medicine	Heme & Onc	7/1/95	6/30/98
Sinning	Joseph		MD	Inactive	Fellow	Internal Medicine	Heme & Onc	1/1/97	12/31/00
Perez	Lia		MD	Inactive	Fellow	Internal Medicine	Heme & Onc	6/30/97	6/29/00
Maun	Noel		MD/PhD	Inactive	Fellow	Internal Medicine	Hematology	x/xx/1997	x/xx/2000
Chang	Victor		MD	Inactive	Fellow	Internal Medicine	Heme & Onc	6/30/98	6/29/00
Zhang	Paul (Xuejun)		MD/PhD	Inactive	Fellow	Internal Medicine	Hematology	7/1/98	6/30/01
Lockridge	Leslie		MD	Inactive	Fellow	Internal Medicine	Hematology	6/30/99	6/29/02
Zhou	Ming		MD/PhD	Inactive	Fellow	Internal Medicine	Hematology	6/30/00	6/29/03
Hall	Sharynn	D	MD/PhD	Inactive	Fellow	Internal Medicine	Hematology	7/1/00	6/30/03
Rudolph	Priya		MD/PhD	Inactive	Fellow	Internal Medicine	Hematology	6/30/01	6/29/04
Okam	Maureen	M	MD	Inactive	Fellow	Internal Medicine	Hematology	7/1/01	6/30/04
Halene	Stephanie		MD	Inactive	Fellow	Internal Medicine	Hematology	6/30/02	2/28/06
Cai	Ji-Lian		MD/PhD	Inactive	Fellow	Internal Medicine	Hematology	6/30/02	6/29/04
Krishnadadan	Ravi		MD	Inactive	Fellow	Internal Medicine	Heme & Onc	7/1/03	6/30/06
Gorsky	Mila		MD	Inactive	Fellow	Internal Medicine	Heme & Onc	6/30/04	6/29/07
Mugnaini	Emiliano		MD/PhD	Inactive	Fellow	Internal Medicine	Heme & Onc	07/01/2004	6/30/07

Last Name	First Name	Mid/Initial	Degree	Current status	Status	Department	Section	Start date	Finish date
Strout	Matthew		MD/PhD	Inactive	Fellow	Internal Medicine	Hematology	7/1/04	6/30/07
Parnes	Aric		MD	Inactive	Fellow	Internal Medicine	Heme & Onc	6/30/05	6/29/08
Chowdhury	Saeeda		M.D.	Inactive	Fellow	Internal Medicine	Heme & Onc	10/1/06	9/30/09
Chen	Wendy		DO	Inactive	Fellow	Internal Medicine	Heme & Onc	7/1/06	6/30/09
Maggiore	Ronald	J	M.D.	Inactive	Fellow	Internal Medicine	Hematology	7/1/07	6/30/10
Neparidze	Natalia		M.D.	Inactive	Fellow	Internal Medicine	Heme & Onc	7/1/07	6/30/10
Richter	Joshua		M.D.	Inactive	Fellow	Internal Medicine	Heme & Onc	7/1/08	6/30/11
Wong	Ellice		M.D.	Inactive	Fellow	Internal Medicine	Heme & Onc	7/1/08	6/30/11
Landau	Dan-Avi		M.D.	Active	Fellow	Internal Medicine	Heme & Onc	7/1/09	6/30/12
Parker	Terri		M.D.	Active	Fellow	Internal Medicine	Heme & Onc	7/1/09	6/30/12
Kahlon	Kanwarpal		M.D.	Active	Fellow	Internal Medicine	Heme & Onc	7/1/10	6/30/13
Kocoglu	Mehmet	Hakan	M.D.	Active	Fellow	Internal Medicine	Heme & Onc	7/1/10	6/30/13
James	Edward	Samuel	MD	Active	Fellow	Internal Medicine	Hematology	7/1/11	6/30/14
Zhang	Yue		MD/PhD	Active	Fellow	Internal Medicine	Hematology	7/1/11	6/30/14

## APPENDIX 3

The careful and knowledgeable reader will note that although I said this history would end with December 2008; there is some information from later years. Due to a variety of problems, I was not able to complete this for publication in 2009 and was unable to do an adequate history beyond that date. On April 1, 2009, Dr. Thomas Lynch became the new Director of the Yale Cancer Center and Physician in Chief of the Smilow Cancer Hospital at Yale New Haven. Since then the Smilow has become fully operational and its inpatient census runs in excess of 90% occupancy. There has been a very significant increase of YCC professional staff which I list alphabetically, for the record, from May 1, 2009 to April 30, 2012: Alexander Au, Plastic Surgery; Anees Chagpar, Surgical Oncology; Sandy Chang, Lab Medicine; Anne Chiang, Medical Oncology; Lieping Chen, Immunobiology; Deborah Chirnomas, Pediatric Oncology; Joseph Contessa, Therapeutic Radiology; Shari Damast, Therapeutic Radiology; Suzanne Evans, Therapeutic Radiology; Leonard Farber, Medical Oncology; Bonnie Gould Rothberg, Medical Oncology; Valentina Greco, Genetics; Stephanie Halene, Hematology; Roy Herbst, Medical Oncology; Howard Hochster, Medical Oncology; Erin Hofstatter, Medical Oncology; Nina Horowitz, Surgical Oncology; Michael Hurwitz, Medical Oncology; Iris Isufi, Hematology; Benjamin Judson, Otolaryngology; Jennifer Kapo, Geriatrics; Peter Koo, Medical Oncology; Alfred Lee, Medical Oncology; Arthur Levy, Medical Oncology; Miguel Materin, Ophthalmology; Daniel Morgensztern, Medical Oncology; Don Nguyen, Pathology; Nikolai Podoltsev, Hematology; Katie Politi, Pathology; Lajos Pusztal, Medical Oncology; John Roberts, Medical Oncology; Tara Sanft, Medical Oncology; Peter Schulam, Urology; Fatma Shebl, Epidemiology; Stacey Stein, Medical Oncology; Mathew Strout, Hematology; Theodore Tsangaris, Surgical Oncology; Narendra Wajap-eyee, Pathology; Qin Yan, Pathology. In addition a few members of the YCC have left for other positions and a few have died. I do not list those changes.

Illustrations of some individuals and structures mentioned in the narrative are roughly in order of reference in the narrative. The pictures have been gathered from many sources but the vast majority is from Google Images and I believe that they are all in the public domain. Some were small and with limited pixels, do not enlarge well. Some were from photographs given to me by individuals with the understanding that they could be reproduced here. Other sources include, Yale Historical Library online photographic resource; YCC publications and websites and pictures sent to me; YSM publications and websites; Yale Alumni Association publications and pictures; YNH archive, publications and websites; Google; Wikipedia, and some pictures taken by me. I hope to make available copies of this history on the Internet. I hope to publish a few copies for the Yale Historical Library, the Yale Cancer Center Archive, the Yale-New Haven Hospital Archive and a few additional copies.

## APPENDIX 4

A Photographic History of the  
Clinical Cancer Program at  
Yale-New Haven Hospital &  
Yale Comprehensive Cancer  
Center

By David S. Fischer, MD, FACP

David S. Fischer, MD, Author



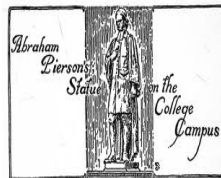
Rev. John Davenport  
Theophilus Eaton



Donation of Books Plaque



Rev. James Pierpont  
Rev. Abraham Pierson



Original Yale College Building



Elihu Yale



Rev. Cotton Mather



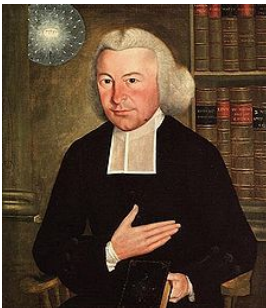
Pres. Thomas Clap



Connecticut Hall



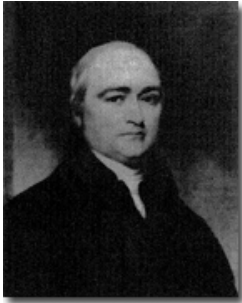
Rev. Ezra Stiles



CT State Medical Society Logo



Pres. Timothy Dwight, IV



Nathan Smith, MD



Eneas Munson, MD



Eli Ives, MD



Jonathan Knight, MD



Prof. Benjamin Silliman, Sr.





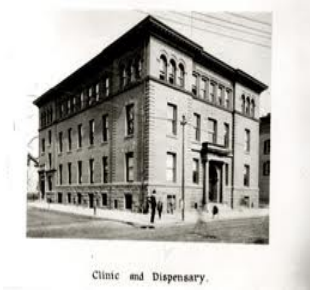
Grove Street Medical Building



York Street Medical Building



New Haven Dispensary  
(now Hope Building)



Harvey Cushing, MD



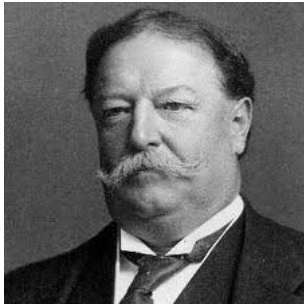
Prof. George Wilson Pierson



Abraham Flexner



Pres. William Howard Taft



George Blumer, MD



Brady Memorial Building



William Henry Welch, MD



Pres. Arthur Twining Hadley



Milton C. Winternitz, MD



Col. Isaac Ullman



Sterling Hall of Medicine



Lafayette. B. Mendel, PhD



Pres. James R. Angell



Louis S. Goodman, MD, PhD



Alfred Gilman, PhD



Gustaf E. Lindskog, MD



John E. Fenn, MD



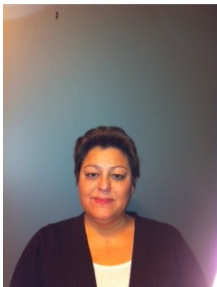
Robert Udelsman, MD



Michael Kashgarian, MD



Teresita Vega, CTR



Pres. Charles Seymour



Pres. Alfred Whitney Griswold



New Haven Hospital



Grace Hospital



William F. Verdi, MD



Hospital of St. Raphael



West Haven Veteran's Hospital



Arthur Lemay, RPh



Rose Papac, MD



John C. Marsh, MD



Edward Chu, MD



Yale New Haven Memorial Unit



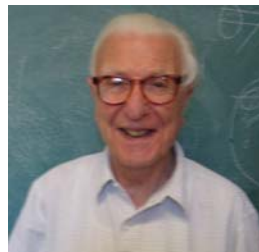
Vincent T. DeVita, Jr., MD



Arnold D. Welch, MD,PhD



William H. Prusoff, PhD



Robert Handschumacher, PhD



Alan C. Sartorelli, PhD



Pres. A. Bartlett Giamatti



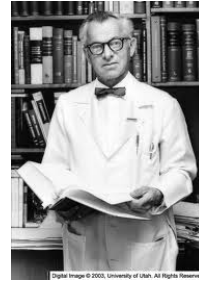
Joseph Bertino, MD



Joseph Schlessinger, PhD



Maxwell M. Wintrobe, MD, PhD



Paul B. Beeson, MD



Robert J. Levine, MD



Paul Calabresi, MD



Philip K. Bondy, MD





Ronald C. DeConti, MD



Malcolm S. Mitchell, MD



Sherwin Nuland, MD



Mary Lasker



Sidney Farber, MD



Lewis Thomas, MD



## Yale Comprehensive Cancer Center

- Received National Cancer Institute Designation as the 11th NCI designated Cancer Center in 1974 and the first Director: Joseph Bertino, MD 1974-75
- 2nd, Jack W. Cole, MD 1975-1984
- 3rd, Alan C. Sartorelli, PhD 1984-93
- 4th, Vincent T. DeVita, MD 1993-2004
- 5th, Richard Edelson, MD 2004-09

## Yale Cancer Center 1979



Jack Wesley Cole, MD



Samuel O. Their, MD



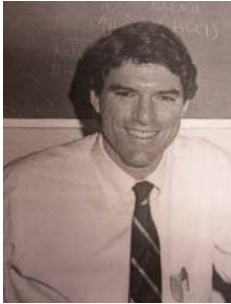
Edwin Cadman, MD



Leon C. Rosenberg, MD



William Hait, MD, PhD



T.F. Gilroy Daly, Esq



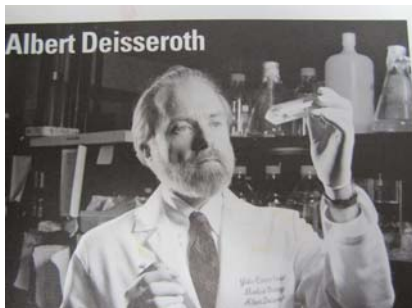
Marion Morra, BA, SCD



Gerard Noel Burrow, MD



Albert Deisseroth, MD, PhD



Bernard G. Forget, MD



Dennis L. Cooper, MD



Edward L. Snyder, MD



Pres. Richard C. Levin



Pres. Joseph Zaccagnino



Ralph I. Horwitz, MD



Peter N. Herbert, MD



Richard L. Edelson, MD



Aaron B. Lerner, MD, PhD



Dennis D. Spencer, MD



Stephen Ariyan, MD



Robert Alpern, MD



Pres. Marna P. Borgstrom



Yale Nemerson, MD



Peter McPhedran, MD



Thomas P. Duffy, MD



Joel M. Rapoport, MD



Peter W. Marks, MD, PhD



Madhav V. Dhodapkar, MBBS



Howard A. Pearson, MD



Frank Detterbeck, MD



William F. Collins, Jr., MD



Joseph M. Piepmeir, MD



Dr. John McLean Morris



Ernest I. Kohorn, MChir



Peter E. Schwartz, MD



Morton M. Kligerman, MD



James E. Fischer, MD, PhD



Peter M. Glazer, MD, PhD



Lynn D. Wilson, MD



Leonard R. Prosnitz, MD





Leonard R. Farber, MD



Kenneth B. Roberts, MD



Raymond Yesner, MD



Harry Zimmerman, MD



figure. 2

Averill Liebow, MD



Harry S.N. Greene, MD



David Seligson, MD



Elias E. Manuelidis, MD



Laura Manuelidis, MD



Florence Schorske Wald, RN



M. Tish Knobf, RN, PhD



Constance T. Donovan, RN



Ruth McCorkle, RN, PhD



Bonnie Indeck, LCSW



Renee Gaudette



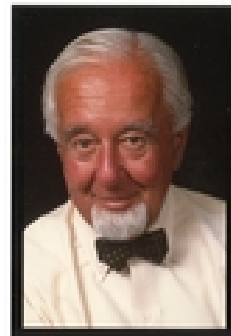
Bernard Lytton, MB



Dame Cecile Saunders, RN, MB



Howard Spiro, MD



Thomas Lynch, MD



Abe Lopman



Norman Roth



Joe Smilow



Smilow Cancer Hospital



APPENDIX 5  
Medical Oncology and Hematology Faculty for  
Academic Year 2011–2012  
(Compiled July 2011)

**MEDICAL ONCOLOGY FACULTY 2011-2012**



Maysa Abu-Khalaf, MBBS, M.D.



Anne Chiang, M.D., PhD



Gina Chung, M.D.



Hari Deshpande, M.D.



Michael DiGiovanna, M.D., PhD



Leonard Farber, M.D.



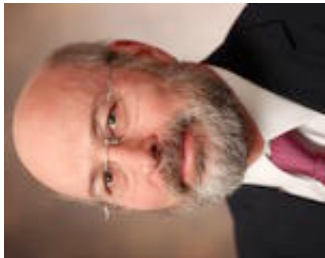
Scott Gettinger, M.D.



Lyndsay Harris, M.D.



Roy Herbst, M.D., PhD



Howard Hochster, M.D.



Erin Wysong Hofstatter, M.D.



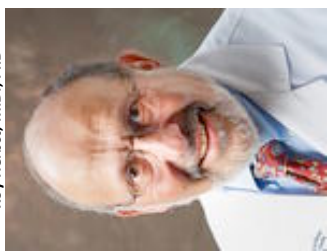
Michael Hurwitz, M.D.



Harriet Kluger, M.D.



Jill Lacy, M.D.



Arthur Levy, M.D.



Thomas Lynch, M.D.



Daniel Morgensztern, M.D.



Tara Sanft, M.D.

**MEDICAL ONCOLOGY FACULTY 2011-2012 (continued)**



Stacey Stein, M.D.



Mario Sznol, M.D.

**HEMATOLOGY FACULTY 2011-2012**



Madhav Dhodapkar, MBBS



Thomas Duffy, M.D.



Bernard Forget, M.D.



Stephanie Halene, M.D., PhD



Alfred I. Lee, M.D., PhD



Peter Marks, M.D., PhD



Peter McPhedran, M.D.



Nikolai Podoltsev, M.D., PhD.



Lawrence Solomon, M.D.  
Palliative Care



Matthew Strout, M.D., PhD

**BONE MARROW TRANSPLANT FACULTY 2011-2012**



**Dennis Cooper, M.D.**



**Francine Foss, M.D.**



**Iris Isufi, M.D.**



**Stuart Seropian, M.D.**



**Warren Shlomchik, M.D., PhD**



APPENDIX 6  
Photographs of the melanoma unit.



**Stephan Ariyan**  
Surgery



**Danielle Bonadies**  
Genetics



**Marcus Bosenberg**  
Pathology



**Jean Bologna**  
Dermatology



**Demetrios Braddock**  
Pathology



**David Cheng**  
Nuclear Medicine



**Veronica Chiang**  
Neuro Surgery



**Jennifer Choi**  
Dermatology



**Roy Decker**  
Radiation Therapy



**Leonard Farber**  
Medical Oncology



**Dwain Fehon**  
Psychiatry



**David Fischer**  
Medical Oncology



**Anjela Galan**  
Dermatopathology



**Kay Haedick**  
Medical Oncology



**Ruth Hataban**  
Basic Science Research



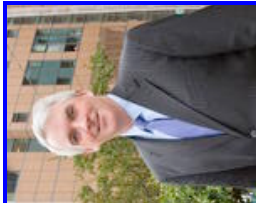
**Harriet Kluger**  
Medical Oncology



**Rossitza Lazova**  
Dermatopathology



**David Leffell**  
Dermatology



**Thomas Lynch**  
Medical Oncology



**Miguel Materin**  
Ophthalmologic Surg



**Deepak Narayan**  
Surgery



**Mario Szno**  
Medical Oncology



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by the National Cancer Institute



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