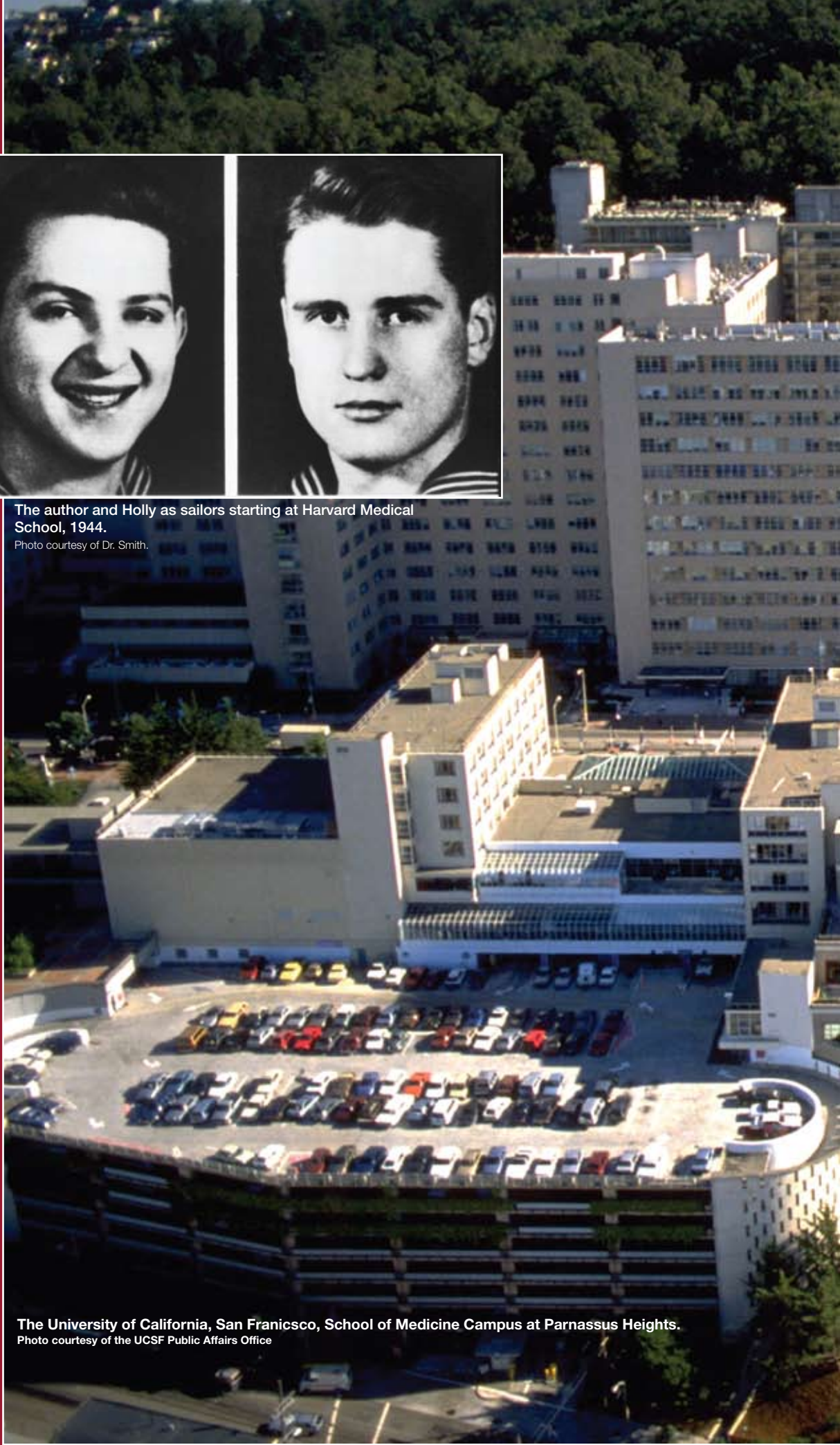


Lloyd H. (“Holly”) Smith, Jr., MD




The author and Holly as sailors starting at Harvard Medical School, 1944.

Photo courtesy of Dr. Smith.



The University of California, San Francisco, School of Medicine Campus at Parnassus Heights.
Photo courtesy of the UCSF Public Affairs Office



Marvin H. Sleisenger, MD

The author (AQA, University of California, San Francisco, 1972) is a graduate of Harvard Medical School's Class of 1947 and classmate of Holly Smith. In 1967 he became vice chair of UCSF's Department of Medicine and chief of Medicine at the San Francisco VA Medical Center, rejoining his lifelong friend in San Francisco. The two will return to Harvard Medical School in June 2007 to celebrate their 60th class reunion.

Lloyd H. ("Holly") Smith, Jr., was born in Easley, South Carolina, a town of about five thousand people in the red, rolling Piedmont countryside where cotton was once king. His mother, Phyllis Page, was a Virginian. Her parents' families were early settlers of Virginia—planters, lawyers, and teachers in the Charlottesville area. Holly's father descended from Job Smith, a settler in the old Cherokee Territory of South Carolina. Two of Job's sons were physicians, as was Holly's grandfather, Dr. Rufus Franklin Smith. Holly's father, Lloyd H. Smith, was an attorney and cotton farmer. An uncle, Dr. Hugh H. Smith, was a graduate of Johns Hopkins

who became a noted medical researcher at the Rockefeller Institute. Holly's older brother, Frank, also a graduate of Harvard Medical School, was chief of Medicine at the Gorgas Hospital in the Panama Canal Zone. As my mother once told me, "You know, Marvin, some genes are inherited!"

People in Easley in the 1920s drew strength from devotion to family and community, and from strict Calvinist precepts that Holly later characterized as "an odd admixture of residue of the Civil War and fundamental Protestantism . . . but life had its charms, and I never regretted this Southern childhood."

Holly attended Washington and Lee, a venerable, conservative all-male Virginia college, the alma mater of four other distinguished professors of medicine: Robert H. Williams (University of Washington), A. McGehee Harvey (Johns Hopkins), Edward W. Holmes (Duke, the University of Pennsylvania, and the University of California at San Diego), and Joseph L. Goldstein (the University of Texas Southwestern, Nobel Laureate). Holly was an A student and, in addition, became a skilled politician, achieving the trifecta of the presidency of both his class and fraternity, and the

editorship of the school annual, the *Calyx*. He also wrestled in the heavyweight division. His nickname, unfortunately, was "Canvasback Smith."



In the spring of 1943 Holly was accepted without interview to Harvard Medical School, joining his older brother, Frank, who was transferring into the third-year class at Harvard from the two-year school at the University of North Carolina.

When Holly and Frank left by train in January 1944 for Boston and Harvard Medical School, neither had ever been north of New York City. With about a third of the class, Holly and I entered medical school in the Navy's V-12 program. Most of the others were in the Army's corresponding ASTP program. His age of nineteen was average for this youngest class ever to enter Harvard Medical School. Two members of the class were only seventeen at the time of matriculation. Because of the war, the Class of 1947 had very limited premedical education and endured an accelerated curriculum. Academic failure in wartime could land us in the Fleet Marines or the Army Infantry, which was a great stimulus to scholarship.

During those years Harvard's outstanding teachers in the basic sciences included Eugene Landis, the newly-appointed successor to Walter Cannon in Physiology, A. Baird Hastings in Biochemistry, Otto Kroyer in Pharmacology, and John Enders in Microbiology (later a Nobel Laureate for his work with the polio virus). The curriculum included only passing reference to DNA and RNA since Oswald Avery and his colleagues' discovery of DNA's function as a "transforming principle" had only recently been published. We all struggled that year. Fifty percent of the class got D's or E's on the mid-year Physiology exam. One distraught student wrote on the posted announcement of the grades: "Lord, avenge thy slaughtered saints," to which Eugene Landis appended: "The Lord helps those who help themselves!" Holly took this advice, doing an elective research project in his second year with classmate John Stoeckle on the effects of atabrine on cardiac function. After his third year he worked in Landis's laboratory for a year on pain thresholds and blood flow in small vessels during reactive hyperemia.

Holly's interest in research was further stimulated by an elective in his fourth year at the Peter Bent Brigham Hospital with Drs. George W. Thorn and John P. Merrill, working on

the new artificial kidney. Based on the large dialysis machine devised by Dr. Willem Kolff in Holland during World War II, this early primitive machine proved to be highly effective. One of Holly's responsibilities on the team was to purchase each Monday morning a gross of condoms at Joe Sparr's drug store on Longwood Avenue. These were used to prevent coagulation of the dialyzed blood in the pump that returned it to the patient. Needless to say, Joe Sparr and his staff held Holly in awe as Casanova reincarnated.



Holly's honors in medical school included election to Alpha Omega Alpha and presidency of the chapter, presidency of the Boylston Medical Society, where selected senior students drank brandy and smoked cigars while listening to a colleague present an original paper, and the Henry A. Christian Prize. He and the late Sidney Ingbar graduated *magna cum laude*.

Holly did his internship and his residency in Medicine at the Massachusetts General Hospital (MGH), the "Grand Old Lady of Fruit Street," historically the first, and in 1948 the reigning queen of the Harvard teaching hospitals. There he was the beneficiary of a small but notable cadre of full-time teachers: thyroidologist James H. Means; Fuller Albright, the brilliantly imaginative founder of modern endocrinology; famed clinical cardiologist Paul D. White; eminent clinical gastroenterologist Chester M. Jones; Joseph Aub, the undisputed complete internist; and Walter Bauer, the academically forward-looking and mercurial rheumatologist.

During his two years on the MGH house staff, Holly and most other residents lived in the hospital since the salary of twenty-five dollars per month permitted little else. The work provided intensive experience with the serious illnesses common to those hospitalized in the late 1940s: congestive heart failure, cirrhosis of the liver, fevers of unknown origin, chronic lung disease, acute nephritis and chronic renal failure, peptic ulcer and gastrointestinal bleeding, poliomyelitis, severe rheumatoid arthritis, myocardial infarction, thyrotoxicosis, and the emerging so-called collagen vascular diseases. Holly learned that long hours of duty and low pay are more than compensated for by the exhilaration of acquiring the skills of internal medicine, the satisfaction of continuity of care, and the *esprit de corps* present on the wards. One of his fellow interns was James B. Wyngaarden, later chair of the Department of Medicine at Duke, director of the NIH, and co-editor with

Holly of the *Cecil Textbook of Medicine*. During this period Holly also continued his work on the artificial kidney, having been put in charge of setting up and running a Kolff machine purchased by the hospital at his suggestion.



Joining many other physicians, called into the Navy

After two years at MGH, Holly became a Junior Fellow in the elite Harvard Society of Fellows, an award that supported work by the recipient in the field of his choice. However, before settling into residence in Winthrop House, he was suddenly called to military service and assigned by the Navy to the Army for duty in the Korean War. During part of his service he studied viral hepatitis and glucose and fructose metabolism in liver disease at the Walter Reed Army Institute, and with George Schreiner reported the first patients with familial renal tubular acidosis. Sent to the Eleventh Evacuation Hospital in Wonju, Korea, Holly noticed the numbers of cases of acute renal failure due either to crush injuries or to epidemic hemorrhagic fever. His request for a Kolff-like artificial kidney was granted and he thus extended his experience with dialysis for acute renal failure during his last year in Korea. This was the first use of the artificial kidney in military medicine.



Holly and the artificial kidney in Korea, 1952.
Photo courtesy of Dr. Smith.

Holly's pursuit of an academic career began in earnest on his return from Korea, when he assumed the postponed Junior Fellowship at Harvard. He spent his first year studying organic chemistry and biochemistry at Cambridge, and later took an intensive course in the use of radioisotopes at Oak Ridge (for which he earned a diploma as "Master of Unclear Studies"). He subsequently joined the late DeWitt Stetten at the Public Health Research Institute of New York City in the study of purine and pyrimidine metabolism. Later, at the MGH, he began studies to quantify pyrimidine metabolism in man. He demonstrated the double enzyme defect (pyrimidine auxotropism) in the rare genetic disorder hereditary orotic aciduria. In association with Hibbard E. Williams, he helped to describe and define the enzyme defects of two distinct forms of primary hyperoxaluria. This state-of-the-art work was chosen in four successive years for presentation on the plenary sessions of the American Society of Clinical Investigation or the Association of American Physicians annual meetings in Atlantic City.



Chief of Endocrinology at the MGH—a ticket to greater callings

As a new faculty member at Harvard and the MGH following his chief residency, Holly was named the assistant chief of Medicine, and soon thereafter was also made chief of the Endocrine Unit at MGH. At this time Walter Bauer, the innovative, chain-smoking chair of Medicine, was creatively appointing bright young faculty with little previous experience to chiefships of various specialty units, including Cardiology (Edgar Haber); Rheumatology (Stephen Krane); Infectious Disease (Morton N. Swartz) and Gastroenterology (Kurt Isselbacher). It was a revolutionary and successful strategy by Bauer, initially resisted unsuccessfully by some of the old guard.

The Endocrine Unit prospered, continuing the tradition of its world-famous previous chief,

Fuller Albright, who was incapacitated by Parkinson's Disease. Among other notable members of the unit were Daniel D. Federman, Andrew G. Frantz, Donald B. Martin, T. D. R. Hockaday, and Jorgen Jacobsen, all of whom became professors of Medicine at distinguished institutions. In 1963, the seventh year of this appointment, Holly took a sabbatical leave to work on oxalate metabolism in the Department of Biochemistry at Oxford, directed by Nobel Laureate Hans Krebs.

During that year, Walter Bauer died from pulmonary failure. Alfred Kranes, a distinguished community faculty internist, was named as the acting chair. Holly returned from Oxford in the spring of 1964 to present a paper at the AAP meeting in Atlantic City. At that time (age forty) he was invited to look at the chairs of Medicine at both UCSF and the newly-established medical school at the University of California at San Diego (UCSD). On the day of his first meeting with Dean William O. Reinhardt and the search committee, he was offered the position at UCSF. He immediately accepted and telegraphed his wife Margaret: "Pack." Harvard's faculty and deans could not believe that anyone so promising would leave its hallowed halls. Interestingly, HMS's last written communication to him was: "Your salary next year will remain at \$18,000, but we plan to reduce our contribution from \$5,000 to \$3,000. Please inform us from what source you plan to receive the difference." His reply was tactful, courteous, and appropriately remorseful.

Established during the raffish, post-Gold Rush days of 1864, the UCSF School of Medicine (founded as the Toland Medical College) is the oldest medical school in continuous operation west of the Mississippi. Unfortunately, UCSF's centennial celebration in 1964 did not reflect an eminent institution, as President Clark Kerr's memoirs emphatically note. In sharp contrast to the University of California at Berkeley's broad achievements and successes, especially in the chemical and physical sciences, UCSF in 1964 was undistinguished, but it was poised for change. The components for its future growth were:

- The basic science departments had recently returned to San Francisco from Berkeley, where they had moved after the earthquake of 1906.
- In 1959 Stanford Medical School moved from San Francisco to Palo Alto, allowing control of San Francisco's major teaching hospitals to be unified.
- The NIH was sharply increasing its support of biomedical research. To exploit this opportunity, new laboratory towers were nearing completion on the Parnassus Avenue campus.
- Regular jet travel greatly diminished the sense of isolation of western institutions from the major eastern centers, including the NIH.

Newly-appointed Dean William O. Reinhardt, strongly supported by key members of the faculty, was determined to seize on these opportunities to create national status for his school. He began by instituting rigorous searches for new

leaders of the key clinical departments. In the first wave, Alexander R. Margulis was appointed chair of Radiology; J. Englebert Dunphy, chair of Surgery; and Holly Smith, chair of Medicine.



The department in 1964 had only fifty fulltime members (it now numbers 552), but among these were some who later attained national recognition. At the time there was only one member of the Association of American Physicians. The house staff training program was disjointed, with separate residences at San Francisco General Hospital (SFGH) and the San Francisco Veterans Affairs (SFVA) Medical Center (the latter desperately driven to advertising to fill its positions). The program was also marked by laxity. Grand Rounds, for example, were discontinued during the summer and attending rounds on the wards were held only three times a week.

Change for the Department of Medicine and UCSF began somewhat dramatically shortly after Holly's arrival in 1964. He found himself a key member of an insurgent cabal determined to replace Chancellor John B. de C. M. Saunders, who was perceived to personify and tolerate complacency and inertia. The struggle even found its way onto the front page of the *San Francisco Chronicle*, "Bitter Power Struggle at UC Medical Center." The San Francisco Medical Society and many UCSF alumni weighed in against the upstarts perturbing the tranquility of a venerable institution. Fortunately, President Clark Kerr unequivocally backed the insurgents. His bold action demonstrated clearly that the lax standards of the past were no longer acceptable. Holly quickly set about raising standards in the three basic functions of an academic medical department: patient care, teaching, and research.

Patient care at UCSF had always been excellent, although in those pre-Medicare and Medicaid days separate services existed for private and "staff patients." Oversight of patient care at the SFGH and the SFVA was seriously restricted by the limited number of full-time faculty (only four at each institution). Changes in the teaching program inevitably improved patient care.

The teaching program was greatly strengthened by consolidating the services at the Moffitt Hospital, the SFVA and the SFGH. Members of the house staff soon began serving equal time at each institution. The concept of three university hospitals, partners with equal academic status, fueled

growth in the number and quality of the faculty at both the SFVA and the SFGH. The chiefs of these services, I at SFVA and Hibbard Williams followed by Merle Sande at SFGH, were given major responsibilities as vice chairmen, sharing the leadership of the department. The number of teaching rounds, including weekly "Chiefs' rounds" were quickly increased. Oversight of undergraduate and graduate students was greatly improved as faculty were appointed or promoted using stricter academic criteria. Beginning in 1964, ambulatory care and teaching received greater emphasis under the direction of Robert Crede and later Steven Schroeder.

The new objective of the research program was to bring modern science into each specialty area of internal medicine, with vigorous recruiting of investigators with demonstrable promise. The results of these efforts at all three hospitals resulted in a rapid increase in research activity that was soon reflected in a steady increase in federal funding and memberships of the UCSF faculty elected to the honor societies of internal medicine.



After half a century of quietude, UCSF, in only a few years, was dramatically transformed into a dynamic and vibrant university. This represented the collective vision and enthusiastic partnership of many leaders at UCSF. Beginning in 1964 a continuous and rigorous focus was identifying the best possible candidates, weighed nationally, for faculty or house staff recruitment. The effect of this sustained policy underlies all subsequent progress and success. UCSF now ranks among the leaders in NIH funding for research. Numerous faculty have filled leadership positions in other academic centers, foundations, and federal agencies. Thirty-two of its faculty are members of the National Academy of Sciences.

Leadership is like itching, difficult to define but easy to recognize. Recently, Holly Smith somewhat facetiously, but basically seriously, summarized his approach to departmental administration in a series of pithy aphorisms:

Never attribute to malice what you can attribute to incompetence.



With fellow Washington and Lee graduates A. McGehee Harvey and Robert H. Williams.

Photo courtesy of Dr. Smith.

A thing not worth doing is not worth doing well—the tyranny of trivia.

Experiment. Take some chances. Remember the Peter Pan Principle, "most things peter out but some will pan out."

Avoid administrative sequestration. Show the flag. Remote virtue is rarely appreciated.

Don't speak unless you can improve over silence. When you are in power, others actually listen to you, often selectively.

Plan ahead. Always be concerned about the danger of mural dyslexia, the inability to read the handwriting on the wall.

Accept graciously your surrogate status. Although you may have been selected for past scholarship, it is highly unlikely that you will remain as a hero of the helix or any other domain of modern medical science.

Remember the central tragedy of leadership: Generally by the time you've made it, you've had it. Know when to let go.

Dress British; think Yiddish. [Holly admits that this aphorism is somewhat occult.]

In July 1985, after twenty-one years as chair, Holly was appointed "Associate Dean for Admissions and Special Projects." As chair of the Admissions Committee he organized and presided over the annual challenge of selecting 141 students from a pool of approximately five thousand applicants. He said, "I believe this is the most important committee in the School of Medicine. It actually has a product! The quality of our graduates is more dependent on those we admit than what we offer them during four years of captivity."



As associate dean he was also asked to oversee the assignments of space in the medical school. At the time Holly became “space tsar,” growth of physical space on the campus was severely limited by neighborhood opposition, which restricted the start of new programs and the expansion of those already established. Yet he managed somehow to alter and to shift space assignments as an “equitable distribution of poverty,” gently making the unhappy supplicants understand Tallyrand’s definition of the purpose of diplomacy: “To reach an equality of dissatisfaction.”

Other activities as associate dean included fund raising, chairing committees, giving advice to student organizations, working with the alumni office, liaison with the VA, and occasionally serving as acting dean. No longer chair, a job he described as an exercise in “high output failure,” he had more time to give to the important outside activities noted below.

- Member of the President’s Science Advisory Committee (1970 to 1973)—In 1973 Richard Nixon summarily abolished the PSAC because it did not support, among other things, his plan to build a nuclear powered aircraft. Holly took flak from colleagues (all, of course, liberal Democrats) who felt a Democrat was out of place as a Nixon appointee;

- The Board of Overseers of Harvard University for six years (1974–1980)—During this time he was chair of the Visiting Committees of the Department of Biochemistry and for the Program in Biomedical Sciences. (He rightly said, “For Harvard, the Overseers were clearly the House of Lords and not the House of Commons.”)

- The Howard Hughes Medical Institute’s Medical Advisory Board, of which he was a member for twenty-one years (1974–1995)—During the last nine of these years he was its chair, succeeding George W. Thorn, one of his mentors. During this era, HHMI became the largest sponsor of academic medical research besides the NIH.

- Presidency of national and regional societies—These include the Association of American Physicians, the American Society for Clinical Investigation, the Western Association of Physicians, and the Association of American Professors of Medicine.

- Holly also served on a committee that advised the Shah of Iran on the establishment of an academic medical center in Tehran. He has been known to muse over the fact that he has served “three of the most ambiguous and even sinister figures

of our time—Howard Hughes, Richard Nixon, and the Shah!”

- Editorships—Holly’s research papers, four of which were presented at the plenary sessions of the ASCI or AAP, earned him a place on the editorial boards of the *Journal of Clinical Investigation* and the *American Journal of Medicine*. For twenty-seven years he was Associate Editor of the *Western Journal of Medicine*. Most importantly, he served as co-editor with his close friend, James B. Wyngaarden, for the sixteenth through the nineteenth editions of the *Cecil Textbook of Medicine*, as well as four editions of the *Cecil Review of General Internal Medicine*.

Honors for his contributions to medical education and research abound, including honorary degrees from Washington and Lee University (his alma mater), the Medical College of Ohio, and the Medical University of South Carolina. Other distinguished awards are the John Phillips Memorial Award from the American College of Physicians, the George M. Kober Medal of the Association of American Physicians, the Golden Apple Award of the California Medical Association, the Abraham Flexner Award of the Association of American Medical Colleges, and the UCSF University Medal, perhaps the most personally meaningful of all. He always emphasizes his debt to his colleagues and to UCSF for his successes.

Few men go through professional careers with apparent ease, moving ahead with innovative ideas, demonstrating unwavering determination to succeed, and gaining achievements that reflect innate skills of leadership and the capacity to work easily with all. Even fewer enjoy simultaneous success in their personal lives. Holly Smith is one of these fortunate.



While at Harvard Medical School he was introduced by classmate John Avery to his younger sister at Wellesley, Margaret. Although they were separated for several years while Margaret served in the State Department in Beirut and Holly was busy with the Society of Fellows at Harvard and then served in the Korean war, they finally were reunited and married in 1954.

Their marriage has resulted in six children and seventeen grandchildren. The eldest, Virginia (Broudy) is professor and vice chair of the Department of Medicine at the University of Washington. Chris is a computologist, Rebecca an architect, Charlotte an ophthalmologist, Elizabeth a teacher, and Jeffrey runs an arborist company. This large and close family has had



Marriage to Margaret Avery, 1954.

Photo courtesy of Dr. Smith.

many good times together in some of the globe's more exotic venues—beaches on Martha's Vineyard, ski slopes in the Alps, sailboats in the Caribbean, Aegean, or the South Seas, or trout streams in Canada. And there always has been Margaret and Holly's love of tennis. They are still at it, although her backhand and his serve are not what they used to be. Well, what is at their age? What matters is the love and devotion of this large family, which gathers often either in Kentfield or their country place in Inverness.

In semi-retirement, Holly still functions as an emeritus associate dean, offering his "unsolicited advice" to the boards of two foundations and several research institutes.

Clearly, the man is enjoying this "retirement." A highlight for him is the Department of Medicine's annual Holly Smith Visiting Professor Week capped by a banquet. In both lighter exercises as well as more serious addresses to learned societies, he is known for lacing his presentations with pungent, often raunchy, humor, self deprecation, and incisive observations. He still has the dramatic phrase, the pregnant pauses, and the ever-apt quotations, all delivered with his residual soft Southern accent.

The Greek concept of happiness was "the exercise of vital powers along lines of excellence in a life affording them scope." Holly and Margaret Smith have attained together that priceless kind of happiness. In the process they have enhanced their environment at UCSF and among their many friends, and throughout the medical profession.

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The Smith biomass: Chris, Betsey, Rebecca, Charlotte, Virginia, and Jeff.

Photo courtesy of Dr. Smith.