In 1959, when president of The American Society for Pharmacology and Experimental Therapeutics, and president-elect of The American Association for the Advancement of Science

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HOW I AM

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Although I am primarily a pharmacologist, I have a great diversity of related interests. This is natural. Pharmacology and toxicology are diverse disciplines, related to all the life sciences (including psychology and sociology); to the various clinical specialties of the expanding health professions; to agriculture, agronomy, ecology, forestry, oceanography, and even meteorology; to law, politics, and public policy, and to the arts and humanities, even to philosophy, especially the ethics, the logics, and the esthetics.

My entrance into pharmacology came by chance. During World War I, I was full of adolescent idealism to "save the world for democracy," and I was in service in March 1917. Universities were generous in those days: Princeton gave me a bachelor's degree (with a major in chemistry, biology, and philosophy), even though I missed half of the last semester of my senior year and did not turn in a thesis expected of me.

A top sergeant in a machine gun outfit training in Anniston, Alabama, I was transferred to the newly organized Chemical Warfare Service and sent to the Medical Defense Division, operating under Majors J. A. E. Eyster (1881–1955) and Walter J. Meek (1878–1963), in the physiology and pharmacology laboratories of the University of Wisconsin. The pharmacologist of the group was Arthur S. Loevenhart (1878–1929). He was in Washington. So was the biochemist, Harold C. Bradley (1878–1975).

Harold Bradley was a personnel officer for the Chemical Warfare Service, and it was he who spotted my chemistry-biology background. After the war, he taught me physiological chemistry, and we became close friends. His Madison home was a happy gathering place for his pupils. When he retired, he moved back to his father's home in Berkeley, California and became a leader in conservation. We enjoyed many pleasant evenings together at the Chit Chat Club meetings in San Francisco.

My job in the Chemical Warfare Service, in the basement of old Science Hall on the Madison Campus, was to study the effects of toxic war gases on the acid-base balance of blood. We used morphinized dogs. Samuel Amberg (1874–1966), who had come from the Mayo Clinic to work with us, and Walter Meek taught me well. We studied chlorine, chlorpicrin, mustard gas, and lewisite. When the war was over,

I was asked to stay on and run the necessary controls: what does morphine do to blood reaction in mammals?

In dogs, morphine causes first an increase in respiration, usually with vomiting, followed by respiratory depression, lassitude, and analgesia. I interpreted this as an initial decrease in cellular oxidative mechanisms in the medulla oblongata with subsequent increase of oxidative processes, in accordance with ideas expressed by Arthur Loevenhart and his pupil, Herbert Gasser (1888–1963). I showed that initial stimulation of the vomiting center by morphine is followed by depression, when vomiting cannot be induced either centrally by apomorphine or peripherally by stomach irritants. A ketosis develops after morphine, with a mild acidosis.

These findings (*J. Pharmacol.* 20:359–64, 1922; *Arch. Int. Pharmacodyn. Ther.* 27:221–27, 1922) suggested that it might be worthwhile to see what anesthetic agents do to blood reaction. So with my ever patient wife, Elizabeth, whom I was fortunate enough to marry in 1921, and with Alfred Koehler, a graduate student, we studied blood reaction in dogs under anesthesia with ether, chloroform, and nitrous oxide oxygen. We found an acidosis under ether and chloroform, with an initial alkalosis going into an acidosis under nitrous oxide and oxygen. The latter involves oxygen want if real anesthesia is to be obtained.

Meanwhile, Arno Luckhardt (1885–1957) in Chicago had introduced ethylene anesthesia. This has an advantage over nitrous oxide in that it can be successful with 15% oxygen (at sea level), instead of the 10% with nitrous oxide. Twelve percent is needed for satisfactory blood oxygenation. With Alrick Hertzman, I found that there is relatively little change in blood reaction with ethylene oxygen, and I thought this could be correlated with the generally superior clinical condition of patients under ethylene and oxygen.

This set me thinking about combining the chemical unsaturation of the carbon atoms in ethylene into the ether configuration. Long discussions were held on this, especially with my toxicology associate, Clarence Muehlberger (1896–1966). The compound in question, divinyl ether, was not in existence, but I determined to try to get it.

Meanwhile I had become engaged in many other search and research efforts. I reported a summary of our work on anesthesia and blood reaction at the Third Congress of Anesthetists in 1924 (*Br. J. Anaesth.* 2:1–20, 1924). With Frank G. Hall, I showed that alkalosis gives vascular constriction, while acidosis brings vascular relaxation. With Thomas K. Brown I found that infections, such as in experimental pneumonia, when there is respiratory involvement, are accompanied by an acidosis, due to an anoxic anoxemia.

With my wife, I became interested in blood regulation in anemias. Figuring that there might be some kind of a hormonal regulation, with red blood cell production geared to red cell destruction, we studied the effects of giving saline extracts of mammalian spleen and bone marrow to dogs. Stupidly we used healthy dogs, instead of trying to make them anemic. We found that spleen extracts give equivocal effects on erythrocyte counts, while bone marrow causes some increase. When we combined spleen and bone marrow we found a considerable rise in the red cell count. Liver, kidney, and heart extracts had no effect in our healthy dogs. So we introduced combined desiccated spleen and bone marrow for the treatment of secondary

anemias. Clinically it seemed to be helpful. It had no effect in pernicious anemia. Years later, it seemed that spleen and bone marrow might give a kick to the reticuloendothelial system. My clinical balance was maintained by William S. Middleton, the sharp professor of medicine, who later became dean.

Those were busy years and happy ones, although we lived on a pittance. We canoed on Lake Mendota, picnicked on Picnic Point, and even got a secondhand auto for a trip to the East Coast. The university generously gave me a doctoral degree with publications in lieu of a thesis. My patient wife coached me in passing French in a qualifying exam. Walter Meek arranged for me to go to the Cleveland meeting of the Federated Societies in 1922, where Frederick Banting (1891–1941) thrilled us with his report on insulin. Meek got me into the American Physiology Society in 1923, but Torald Sollmann (1874–1962) kept me out of the Pharmacology Society until the following year, because as he said I was too young. Later he was a good friend.

I had become interested in historical and philosophical affairs, as a result of the stimulus of the William Snow Miller (1858–1939) seminar in medical history. One of my contributions was on the history of anesthesia (*Sci. Mon.* 20:304–28, 1925). This was later put into cadence, with a huge bibliographical chronology, and published by the University of Texas Press in 1947. I had written an account of Thomas Percival (1740–1804) and his misnamed "Medical Ethics" (*J. Am. Med. Assoc.* 81:366–71, 1923). This attracted the attention of Harvey Cushing (1869–1939), who asked me to come to Boston to present it there. He became one of my best friends and mentors. In 1927, this effort resulted in a book, *Percival's Medical Ethics,* which was published by Williams and Wilkins in Baltimore, under the direction of Charles C. Thomas, who later became his own distinguished publisher. This book fell flat as a mud pie. Amazingly, now, with much excitement over medical ethics, it is appearing in a second edition, nearly half a century after the first.

I became interested in William Harvey (1578–1657) and his great classic, *De Motu Cordis,* first issued in 1628. With coaxing from Charles Thomas, I undertook a new English translation to appear as a tercentennial tribute. Charles Thomas published it in fine format, and soon issued it in paperback, the first such in USA medical publishing. This has gone through five editions, the most recent in 1970. Harvey was probably the first to suggest giving drugs by injection into the blood circulation.

Meanwhile, Ralph Waters, the great anesthetist, came to Madison to develop anesthesia in the new Wisconsin General Hospital, the main clinical facility for the university. He came, in part, he said to have a chance to work with pharmacologists. He established a great residency training program in anesthesia, and we started a long work effort. In 1828, Henry Hill Hickman (1800–1830), in England, had used carbon dioxide as an anesthetic in dogs. No one had studied it since from that standpoint. Ralph Waters and I decided to try it out. We found that carbon dioxide, 30% with 70% oxygen, is indeed anesthetic, with no asphyxia involved. This we reported at the Seventh Congress of Anesthetists held at the University of Wisconsin in 1928, a century after Hickman.

Although I had started as a physiologist, Arthur Loevenhart persuaded me to move alone with him in pharmacology, and I soon was an associate professor, with major teaching responsibilities. In reality at Wisconsin, physiology, pharmacology,

and physiological chemistry worked together. We had a joint weekly seminar in Arthur Loevenhart's pleasant laboratory; the large graduate student laboratory, under the calm, efficient eye of William Young, our English "diener," was a center of experimentation, with its big kymograph, and I had a convenient office-laboratory of 300 square feet, with a chemical bench and hood on one side, a microscope bench along the windows, and desks along the other side. I had graduate students with me: Peter K. Knoefel, later professor of pharmacology at the University of Louisville; George Wakerlin, later professor of physiology at Louisville and director of the American Heart Association, and Warren Stratman-Thomas, who worked so well on African sleeping sickness and its chemotherapy. The chemotherapy of trypanosomiasis was one of Arthur Loevenhart's major contributions.

From the way the four of us worked together in one office-lab came the idea for "The Student's Unit Medical Laboratory" (*J. Am. Med. Assoc.* 82:114–17, 1924). This attracted the interest of Abraham Flexner (1866–1959) and was the beginning of the now popular multidiscipline medical laboratories. Lathan Crandall, later director of research for Miles Laboratories, also worked with us on a broad study of the pharmacology of nitrites and nitrates, initiated by Arthur Loevenhart at the request of the DuPont interests to see whether or not it would be possible to get the headache out of dynamite. It is not, unless one has a nonnitroglycerine dynamite.

I was fortunate in having many keen colleagues at Wisconsin. K. K. Chen, who introduced ephedrine and later became research director for Eli Lilly, was one. Elmer Sevringhaus, who later was research director for Hoffman-LaRoche, was another. Another was Fred Jenner Hodges, later professor of radiology at the University of Michigan, and one of our greatest leaders in the field. We had some great graduate students: Samuel Lepkovsky, distinguished in vitamin nutrition and my colleague in Berkeley; Karl Link, who developed the coumarin anticoagulants, and Conrad Elvehjem (1901–1962), who isolated niacin, and later was president of the University of Wisconsin. These students came over from the College of Agriculture, where they had been trained by the vitamin pioneers, Edwin B. Hart (1874–1953) and Harry Steenbock (1886–1967).

When I arrived at the University of Wisconsin, I roomed with Edwin and Mrs. Fred, on Mendota Court, close to the lake with its swimming and boating. Edwin Fred was a kind mentor; he later became dean of the College of Agriculture and president of the university. He was a distinguished bacteriologist. My Wisconsin experiences have been a continuing inspiration to me.

In July 1927, I had a telegram from Carl L. A. Schmidt, professor of biochemistry at the University of California in Berkeley, asking me to come out in August for four months to teach pharmacology to the second-year medical students, then studying in Berkeley. Out we went, full of excitement, leaving the hot Midwest, and arriving in foggy, cool Berkeley, where the palms waved over fur-coated coeds. My office was in old Budd Hall, and the class met in the redwood Spreckles Laboratory where Jacques Loeb (1859–1924) had taught. The class was an alert one. I had time to do a bit of work on the effect of anesthetics on the osmotic resistance of erythrocytes. It was a stimulating atmosphere, with Karl F. Meyer (1884–1974) as professor of microbiology, and Herbert M. Evans (1882–1971), the neurotic discov-

erer of vitamin E, and pioneer on the estrus cycle and anterior pituitary hormones, as professor of anatomy.

The Medical School of the University of California was being reorganized, and President William Wallace Campbell (1862–1938), the great astronomer, asked me to come back in July 1928 as professor of pharmacology. We did so, but found that a laboratory had been provided on the top floor of the old medical school building in San Francisco. I had an office, and arranged a small laboratory under a mezzanine which was built for graduate students at the front of the large high general laboratory. It was a great place. With William Gilmore as an efficient "diener," we soon had the place humming.

Peter Knoefel came as a National Research Council fellow; Eric Reynolds (who later was president of the California Medical Society) lent us clinical guidance, and Hamilton H. Anderson, with Norman A. David and Anderson Peoples, worked with us while getting their medical degrees. Peter Knoefel and I began work on divinyl ether, which had been prepared for us, along with other unsaturated ethers, by Randolph Major at Princeton. Major later became director of research for Merck. With Mei-Yu Chen, a remarkably able worker, whom I had met at the Boston Physiology Congress, we found that divinyl ether has the anesthetic properties we had predicted for it. We had the good, practical help of Arthur E. Guedel of Los Angeles, who had been an associate of Ralph Waters. Our experimental study was summarized in 1933 (*J. Pharmacol.* 47:5–16), and the agent soon went into clinical use. But it is flammable, very powerful, and likely to injure livers if anesthesia with it is too long maintained.

We experimented with various halogenated hydrocarbons and both saturated and unsaturated ethers, but found nothing safe or useful. It remained for John Krantz, the keen pharmacologist at the University of Maryland, to study fluorinized compounds, which became available after World War II. These led to halothane, now a popular anesthetic, developed by my friend, Yule Bogue, of Imperial Chemical Industries.

K. F. Meyer, director of the Hooper Foundation for Medical Research, was interested in tropical medicine. He suggested that we study the chemotheraphy of amebiasis. This, we found, has about a 10% incidence in the USA, mostly as carriers. We got a dozen or so organic arsenical compounds from Lilly, and an equal number of halogenated hydroxyquinolines from Ciba, and started screening them. Hamilton Anderson handled the arsenicals, and Norman David the hydroxyquinolines.

First, Hamilton Anderson showed the unsatisfactory toxicity of emetine, the standard remedy for amebiasis. It injures heart muscle. Then, using natural amebic infestations in macaques, we found that 4-carbaminophenyl arsonic acid, called *carbarsone* for short, is only mildly effective, but safe. It also seems to have a general "tonic" effect. So we started using it clinically, after taking it ourselves, and finding that most of it is excreted within a day. Alfred Reed, a skilled clinician, directed clinical trials. Later, Hamilton Anderson, with his wife Jeanette, studied amebiasis and treated it successfully in many parts of the tropics in Africa, Latin America, and Asia. Herbert Johnstone (1903–1956) aided in much of this.

Quite as easy to show carbarsone better than stovarsol for amebiasis was it to show iodochlorhydroxyquinoline superior to iodohydroxyquinoline. Indeed, we found iodochlorhydroxyquinoline (Vioform ®) to be a useful intestinal antiseptic generally. Soon after Norman David introduced it for use in amebiasis, it was in wide use throughout the world for intestinal infections, and could be purchased by travelers over-the-counter, except in the USA. We noted no neurotoxic symptoms, as have been described, because our evidence showed it is not absorbed from the gut. A general review of our studies on the chemotherapy of amebiasis was prepared by me in 1932 (*J. Am. Med. Assoc.* 98:195–98). Norman David later became professor of pharmacology at the University of Oregon, Portland.

Our strategy in the amebiasis effort was simple: we eliminated many proposed remedies as ineffective, and concentrated on types of chemicals showing promise. We tried the same strategy in tackling the chemotherapy of leprosy, but soon abandoned the effort because we found the disease so hedged by politics and vested interests that clearly we were not welcome. We did, however, carefully study the characteristics of the organism, and used murine leprosy in test animals. George Emerson, a brilliant chemical biologist who came to us from Berkeley, devised the water-soluble chaulmoogryl-glycerophosphate for intravenous medication.

Meanwhile, Peter Knoefel studied acetals and aldehydes and added much stimulus to our efforts as he joined us each summer. Through K. F. Meyer, we brought over Myron Prinzmetal, later the distinguished cardiologist from Los Angeles, to work on "mussel poison." He persuaded us to offer a place for animal experimentation to Gordon Alles (1901–1963), a keen organic chemist from Los Angeles. Alles was trying to find a synthetic substitute for ephedrine, the price of which had gone sky-high, to use in treating asthma. Alles was supported by George Piness, the leading West Coast allergist from Los Angeles.

Alles was a most meticulous experimenter. He properly used molal solutions of the drugs he had made, thus being able to compare them in millimole doses on a strict molecular basis. He developed the amphetamines. I have told of his important work in the summary entitled *The Amphetamines* (Thomas, Springfield, Ill., 1958, 167 pp.).

Many graduate students came to work with us: Carroll Handley (1911–1958), later professor of pharmacology at Baylor Medical College in Houston; Benedict Abreu (1913–1965), later in charge of pharmacological research for Pitman-Moore in Indianapolis and professor of pharmacology at the University of Texas Medical Branch in Galveston; Nilkanth Phatek (1898–1971), a political refugee from Bombay and later professor of pharmacology at the University of Oregon Dental School; Michael Shimkin, keen administrator from Tomsk, who later became professor of medicine at Temple and professor of community medicine and oncology at the University of California at San Diego; James Morrison, later at Emory University, Atlanta; David Marsh (1919–1961), later director of research at McNeil Laboratories, Philadelphia; Jack Ferguson (1918–1959), later at the Medical College of Virginia, and E. Leong Way, later professor of pharmacology at the University of California in San Francisco, and famed for his studies on morphine derivatives.

Some of these students came from Berkeley as a result of a general course on pharmacology I offered there at the instigation of Carl L. A. Schmidt, others as a result of our cooperation with the School of Pharmacy in San Francisco. This had been reorganized by Carl Schmidt into a fine teaching and research institution, with a brilliant faculty, including the physical-chemist Troy Daniels, who later became dean; Robertson Pratt, microbiologist; John Eiler, biochemist; Warren Kumler, physical-chemist; and Louis Straight, spectrometrist. Michael Hrenoff helped develop mass spectrometry, and his brother, Arseny, was a devoted worker in our laboratory. We all worked rather closely together.

We had regular seminar sessions, which overflowed into the Crummer Room, and often for Sunday meetings in the Santa Cruz redwoods in a spot on the San Lorenzo River, which my wife and I developed for happy weekends. We had a large redwood circle with rustic benches around and a blackboard on a big tree. There, with our two sons, Chaunc and Wilson, we would entertain our friends and their families, and have vigorous scientific discussions. Arthur Guedel often came from Los Angeles, with friends, to debate metabolic effects under anesthesia. We tried out our proposed publications here, and then often reported them before the quarterly meetings of the West Coast section of the Society for Experimental Biology and Medicine. In these meetings we usually had sharp but pleasant debate with our colleagues from Stanford. Maurice Tainter, later the distinguished director of the Winthrop Laboratories, often joined us.

Maurice Tainter studied dinitrophenol as a stimulant of biological oxidation. We aided in studies on its toxicity. This suggested that we might use its respiratory-stimulating power to counteract the respiratory depression of morphine. So George Emerson easily made dinitrophenylmorphine, and it was well studied by Benedict Abreu, George Emerson, and Nilkanth Phatek. It is pain relieving without causing respiratory depression, and we had evidence that it might be less addictive than morphine. But bureaucratic red tape kept us from trying it clinically, except on ourselves.

By this time we had an arrangement with the Shell Development Company, under Clifford Williams, to test the toxicity of new organic chemicals and solvents, not only to protect the public but the workmen in the plant as well.

We had a heavy teaching load. We enjoyed it. I lectured to medical, dental, and pharmacy students jointly, but we split laboratory assignments. We offered a special course for nurses, and for collegiate students in Berkeley. We had postgraduate sessions. We made up our reference sources, and did not use texts. We tried to get our students to contribute. We were quite informal, and had the laboratory hung with pictures of the leading pharmacology contributors. Otto Guttentag, Charles Gurchot, and Salvatore Lucia added philosophical spice. Milton Silverman gave us helpful journalistic aid in writing. He got his degree from Stanford, but did the work for it (sugar synthesis under ultraviolet light) in our laboratory. He later became one of our best science writers, the author of *Magic in a Bottle* (Macmillan, New York, 1941, 332 pp.); *Alcoholic Beverages in Clinical Medicine* (Yearbook Medical Publishers, Chicago, 1966, 160 pp.); and with Philip Lee, *Pills, Profits and Politics* (University of California Press, Berkeley, 1974, 403 pp.).

My wife and I finally made the Grand Tour in 1938. We visited A. J. Clark (1885–1941) in Edinburgh, with his great collection of poisons brought together by T. R. Fraser (1841–1920). We stopped in Oxford for the meeting of the British Pharmacology Society, where I reported on dinitrophenylmorphine, and where we watched J. H. Burn and Edith Bulbring do some of their careful experimentation. We enjoyed meetings with A. V. Hill and Sir Henry Dale. In Ghent we had a marvelous visit with Corneel Heymans (1892–1968), with his fine institute, and in neat 18th Century Darmstadt, with the Mercks. We went to the Physiology Congress in Zurich, where we enjoyed a visit with Hans Fischer out on the lake, and where we met Arthur Stoll (1887–1971) contemplating one of the huge military murals of Ferdinand Hodler (1853–1918). We later became good friends with the Stolls, who had one of the greatest art collections anywhere. Stoll, a pupil of Richard Willstätter (1872–1942), the great chlorophyll chemist, worked brilliantly on digitalis glycosides and ergot alkaloids. He directed the great Sandoz drug company.

The Zurich Congress was exciting. We had an extemporaneous discussion on the status of pharmacology as a science. This became the subject of my address as retiring president of the American Association for the Advancement of Science in 1961. I try to get double duty out of ideas, if I can!

So we worked cheerfully along. Ross Hart and Elton McCawley came as graduate students. Taking up our observation that the allyl radical stimulates respiration, they made N-allylnormorphine, in an effort to get the pain-relieving properties of morphine without its respiratory depression. But it turned out to be a morphine antagonist. As "nalorphine" it was widely used to detect morphine or heroin addiction and to treat narcotic overdose, as suggested by Eddie Way, another brilliant graduate student.

In order not to use too much space in the professional journals, we started *University of California Publications in Pharmacology* in 1938. This assured us prompt publication through the University of California Press, and we could distribute as we wished. Here we published many of our toxicity studies on new solvents made by the Shell Development Company. Here Benedict Abreu and Nilkanth Phatak published their important studies on nitrofuran antiseptics. These later came to wide clinical use. We also made furan local anesthetics, but these had no particular advantage. We even tried a furan aspirin, but this came to grief: animal experiments showed its value and apparent low toxicity. But when I took it, it deposited on my bladder wall, and I had to be hospitalized to be cleaned out. We had not looked at the bladders of our animals in our routine postmortem examinations of sacrificed animals in our toxicity studies. Now we do.

We had contact with the great cyclotron radiation laboratory in Berkeley, through Joseph Hamilton (1907–1957), one of our clinical associates, who was interested in radioactive iodine for thyroid studies. This he prepared himself in the Berkeley laboratory, and somehow got exposed so that he developed leukemia. He succeeded in correlating the deposition of iodine in the thyroid with the histology of the gland. This publication of 1940 was reproduced by Lloyd Roth at the University of Chicago Symposium on *Autoradiography of Diffusible Substances* (Academic Press, New York, 1969). Another worker with us was Charles Pecher, a Belgian, who studied whole body autoradiography in mice with radioactive calcium and

strontium. He used these substances clinically in osteoblastic bone tumors. When we were blown into World War II, he enlisted and was killed within a year.

With war upon us, we turned our attention to war gases, the use of which was threatened by the Japanese. I went up and down the West Coast talking to high school students (who were sensible, and could tell their elders) about simple protection against war gases: if exposure is suspected, breathe through a wet handkerchief or rag, using urine if no water is available; get out of the area, shed outer clothing, and as soon as possible get a thorough scrubbing with soap and water. I was not popular with official stuffed shirts who issued elaborate instructions for identification of the gases and the different ways to handle each one—as if the enemy would oblige by shelling over one gas alone. David Marsh and I prepared an article for clinicians, based on our direct experiments with mustard gas on our own arms, showing that sodium hypochlorite solutions or soap and water would protect one, if applied within ten minutes of exposure.

In the midst of all this, when I was getting a little respite at the glorious Bohemian Grove on the Russian River, in the summer of 1942, I got an urgent phone call asking me to come to Texas to clear up a messy administrative situation at the University of Texas Medical Branch in Galveston. I went down, met the regents, and we liked each other, especially Lutcher Stark of Orange, who noted calluses on my hands and said I'd do. It was easy enough to get the place in order, with an open door to my office, and with Sunday afternoon receptions which Elizabeth, my always efficient wife, arranged at our home for faculty, students, and townspeople. But this all left no time for pharmacology. Actually, when we admitted two classes a year, and increased the size of each to 120, as part of the war effort, I continued to teach.

The pharmacologist at Galveston, Wilfred Dawson, had killed himself in frustration over the administrative situation, and I had to try to take over. Pharmacology had its own building, a wooden one, but quite adequate, and we soon had a seminar going, as well as classes. Both students and clinicians seemed interested in a new point of view. We used no text but asked the students to submit a couple of term papers properly documented, and graded from excellent to poor. We started publication of a quarterly *Texas Reports on Biology and Medicine,* which soon attracted contributions from all over, since we sent it without charge to the libraries of medical institutions throughout the world. The response in exchange journals made our library the best in the Southwest. It was especially gratifying to get a generous response from Russia.

As soon as the war was over, we planned and built new hospital and laboratory facilities. We promoted Galveston as a health resort, and I traveled over the South and Midwest spreading the gospel of the rational use of drugs, and the ever widening scope of pharmacology. I had helped that energetic gynecologist, William Bertner, organize the great medical center in Houston, with wise leadership from Fred Elliott, dean of the University of Texas Dental Branch, and Lee Clark, the efficient director of the M. D. Anderson Tumor Clinic and Hospital. I helped Baylor Medical School get started in Houston, getting Anderson Peoples and Carroll Handley to take over pharmacology. We gave library and laboratory equipment and books to these new developments, and even lent personnel to help get them going. Then they got the money, and soon had a huge and flourishing center. We aided in the

establishment of the University of Texas Medical School in Dallas and tried to promote one in San Antonio.

I was fortunate in persuading Charles Marc Pomerat (1905–1964) to join our staff in anatomy, which had been so well maintained by Donald Duncan. Pomerat was a brilliant cytologist and teacher, a fine artist and bon vivant. He got our students interested in etching and lithography and established as fine a tissue culture laboratory as could be found. His great contribution was to use time-lapse cinematography to record changes in tissue culture under different conditions. I worked with him on drug effects on cells in tissue culture, and reported with him on this work at a tissue culture symposium he arranged with the New York Academy of Sciences. His studies even inspired me to write a half dozen "Tissue Culture Cadences." His biobibliography appears in the June 1965, issue of *Texas Reports on Biology and Medicine,* with many of his drawings and watercolors.

Meanwhile I began serving on many national committees dealing with problems of alcohol and with various aspects of medical education. These were tiresome. Frank Fremont-Smith (1895–1973), director of the Macy Foundation, made a great success of arranging series of conference discussions. I was invited to join one on neuropharmacology, chaired by Harold Abramson. This met pleasantly in Princeton and gave me a chance to get back to that delightful place. Elizabeth and I spent several months on three occasions in Princeton, when I worked at the Institute for Advanced Study, under Robert Oppenheimer (1904–1967) whom I had known at Berkeley. I was preparing a translation and annotation of the Hearst Medical Papyrus, a drug formulary from Egypt about 1550 BC, which was a prized possession of the Anthropology Museum of the University of California, which was in San Francisco when I first went there. It had attracted my interest then, and it still does. My work resulted in the Logan Clendenning Lecture at the University of Kansas (*The Old Egyptian Medical Papyri,* University of Kansas Press, 1952, 111 pp.).

With George Emerson in charge of pharmacology, my effort therein turned to writing reviews. I prepared one on drugs acting on the central nervous system, including the hallucinogenic agents, and then a more pertinent clinically oriented one on an analysis of drugs used in allergy (*Texas Reports on Biology and Medicine* 9:322–40, 1951). Ever interested in training programs, I wrote on the training of professional pharmacologists, and also on the training of physicians for general practice. Disturbed by the McCarthy witch-hunting, I wrote on the ideals of science in relation to national security (*Texas Rep. Biol. Med.* 13:434–45, 1955), and was denied clearance to go to Ecuador to survey medical education there. But I also wrote on ideals for a community health library.

Political machinations began again in Texas. I should have been alerted when a new bunch of regents fired James Hart, a distinguished barrister, as president of the University after a year of helpful leadership. The big corporations, anxious to avoid severance taxes on natural resources, set up the Texas Research League (nonprofit, and thus tax-exempt) to advise state agencies on operating with efficiency and economy. The university was hard hit. Most of the administrators resigned, as did I. When Charles Doan, the brilliant hematologist, and dean of the Ohio State University Medical School, asked me to join his program, we packed up and left Galveston to settle in Columbus. It took a decade for the University of Texas to

recover. Now under the inspiring leadership of Truman Blocker, the University of Texas Medical Branch is flourishing, with an Oceanographic institute and an institute for the Humanities in Medicine, both of which Charles Pomerat and I had dreamed about. Galveston also has a superb seaorama, with a great aquarium, and performing seals, dolphins, and whales. We had tried to get an aquarium going years before, but it was a flop.

At Columbus my main job was to try to organize a laboratory for pharmacology. This was not easy in a predominately clinical school. Fortunately, I had the interest of Bernard Marks, and he took hold in admirable style, building a splendid group of teachers and graduate students. He worked on cardiovascular drug problems, while I went back to the stimulant action of spleen-marrow on the reticular endothelial system. I thought that stimulation of red blood cell production might aid in counteracting the fatal anemia following whole-body radiation. I used hundreds of mice, but had only slight indication that spleen-marrow fed ad lib before radiation might be helpful. The evidence was too slight to publish.

Now there were too many meetings: Macy Foundation Conferences on Central Nervous System and Behavior, National Research Council on Problems of Alcohol, The National Medical Library, Physiology Congress in Buenos Aires, History of Medicine Congress in Athens and Cos, and meetings of pharmacologists and the too big sessions of the federated societies at Atlantic City. I was up to my neck with travel. But my wife topped it off with two trips around the world.

With me home in bed, I was nominated from the floor and made president of the American Society for Pharmacology and Experimental Therapeutics. Ben Abreu told me I'd better get over to Chicago. I did not get a warm reception from the "establishment," but we soon were humming along with news letters and *Pharmacological Reviews,* and I started *The Pharmacologist.* I became involved with the American Association for the Advancement of Science, and presently was its president. My historical interests appeared in my address on retiring: "The Status of Pharmacology as a Science" (*Science,* Dec. 29, 1961).

But even with growing preclinical strength at Columbus, there were difficulties. We had a fine seminar, cooperating with Arthur Tye in pharmacy, and with Eric Ogden (1903–1973) who had built a great department of physiology. A new administration began cutting. With Bernard Marks running pharmacology well, I thought it was time to quit. We enjoyed Columbus. We helped get the symphony rolling under Evan and Jean Whalon, and the Kit-Kat Club was a stimulus to me.

Robert Featherstone had come to San Francisco from Iowa to take charge of pharmacology after Hamilton Anderson retired. John Saunders had built a big laboratory building, and pharmacology had new quarters, with much stimulus for growth. Robert Featherstone (1914–1974) was interested in mechanisms of anesthesia, promoted student research and asked me to guide it. So out we came again to San Francisco, where my brother Russell, found an apartment with a view for us near the school. I was given an office in the dining room of an old house below the school, and assured that I'd soon have fine quarters. I'm still there.

Actually I'm having a good time and enjoying it. Occasionally I'm asked to lecture in pharmacology to nurses or pharmacists, and I get to pharmacology seminars once in a while. Mostly I'm busy in my book-crowded office, trying to write

what I think is worthwhile. The ethical problems of medical practice have long interested me; now they are hot subjects of debate. I'm interested in how theories of ethics apply. There is vast confusion in ethical theory in organ transplants, for example, and human experimentation raises many questions. Even euthanasia is pharmacologically related.

Since I can do quite as I wish, I offer a no-credit course on the ethics, the logics, and the esthetics. It is fairly well attended, but not by the graduate students for whom it is designed. I think that persons holding the degree, doctor of philosophy, should know something about the subject. I also teach a no-credit course on the history and philosophy of the health professions, quite as I have done yearly for over fifty years. This course is well attended. I offer coffee and cookies as bait.

Thanks to Henry Elliott, my former colleague, and now handling both pharmacology and anesthesiology well at our Irvine campus, I was asked to write a review of reviews for *Annual Review of Pharmacology,* when Murray Luck's great series was expanded in 1960 to include pharmacology. Thanks to Henry Elliott again, I have written such a review each year since. It helps to keep me abreast of the rapidly expanding field of pharmacology and toxicology. My colleagues, Harold Hodge and Charles Hine, help with toxicology, and Eddie Way always helps, as does Vi Sutherland, with details of pharmacology.

James Dille, developing a keen pharmacology program for the University of Washington in Seattle, persuaded the West Coast pharmacologists to organize the Western Pharmacology Society. He guided it well for many years. After a decade, he turned it to me as secretary-treasurer, and I enjoyed preparing the meetings and the proceedings, until I got in trouble with a president who wanted to run things his way, so I quit and let him do so.

Meanwhile I traveled a lot. Under the auspices of our State Department (having somehow been cleared), I went to the Brussels Physiology Congress, where I put on an exhibit entitled *Some Founders of Physiology,* and then via Helsinki, to Leningrad. There I enjoyed the high morale of the devoted staff of S. V. Anichkov, and of the keen workers at the Institute for Experimental Medicine, with their high regard for Charles Darwin. In Moscow it was a joy to know P. K. Anokhin (1898–1974), director of the Sechenov Institute for Physiology, who later visited and stayed with us.

My regard for Frank Berger was always high. He had developed meprobamate as a mild tranquilizer. Thanks to him, and Charles Hoyt, we went to Japan, and had a great time in the pharmacology laboratories in Tokyo, Osaka, and Kyoto. It was a special pleasure to meet Professor Hiroshi Kumagai, and his colleague, Setsuro Ebashi, and to learn of their fine work on muscle contraction. With Frank Berger again, I had the joy of meeting Silvio Garattini at his fine Instituto Mario Negri in Milan, at a conference on anti-inflammatory drugs.

Elizabeth and I enjoyed visiting Arthur and Martha Stoll at their lovely art gallery villa at Vevey on Lake Geneva, and going to Spain for an exciting visit with Francisco Guerra, who had done so well for pharmacology in Mexico. Francisco Guerra had explored Mexican hallucinogenic drugs, and had written widely on Mayan drugs. His baronial holdings in Santillana-sur-Mar include the famed Altamira Caves. Guerra had raised a company to protect his village in the Spanish

Civil War, and after losing a leg in the fighting, had fled to Mexico, where he became professor of pharmacology at the National University.

My interest in what goes on in pharmacological and medical fields led me to put out a monthly mimeographed sheet, "Calling Attention To," for the benefit of my friends. At Galveston and Columbus this grew to over 1500 copies a month. The postage was too much on my return to California, so I restricted the effort to books, a list of which appears monthly in *Current Contents—Life Sciences.* This is one of the helpful publications of the Institute for Scientific Information in Philadelphia, started on a shoestring by my long-time friend, Eugene Garfield, and now a large and vigorous enterprise. I had worked with Garfield while trying to convert what was then the Armed Forces Medical Library into a truly national library of medicine.

My pharmacological interests may sometimes seem to be far afield. I was once president of the Sex Education Society in San Francisco back in depression days. We ran a birth-control clinic, and our effort later grew into the Planned Parenthood program. In 1940, the students in Berkeley petitioned the faculty for a sex education course. I was put in charge. I made it a non-credit affair, with emphasis on human relations. If interpersonal relations are in order, sex relations will usually be so too. It was a shock to find 2600 students showing up for the weekly illustrated lectures. World War II stopped this undertaking.

The Hastings College of the Law in San Francisco was made by Sam Snodgrass, its informal dean, into one of the best in USA, simply by asking retired deans and professors from other law schools to join his faculty. His 65 Club included some of the greatest law teachers in USA. He asked me to join, in order to teach medical jurisprudence. I knew no law, but I had had much experience as an expert witness, and I did know something about toxicological analysis. The course went well for several years, until Dean Snodgrass died and a new, more formal and pedantic dean took over. He didn't like my informal grading system of good, bad, or indifferent, since law schools grade to decimal points. So I quit. But I enjoyed the experience.

Stanley Jacob, at the University of Oregon Medical School, had found dimethylsulfoxide (DMSO) to be an excellent solvent and skin absorbable. He used it to dissolve steroids for local application in arthritis. On trying DMSO alone, as a control, he found it was effective. It tends to dissolve collagen and fibrous tissue. So he began using it in a variety of clinical conditions for which it was indicated, and ran smack into the new regulations of the Food and Drug Administration, of which he knew nothing. He was accused of violating practically all of them. I persuaded James Goddard, FDA Director, that Jacob was not criminally minded, and we arranged a big symposium on DMSO under the auspices of the New York Academy of Sciences (*Ann. NY Acad. Sci.* 141:1–671, 1967). Schering AG, under the keen direction of Gerhard Laudahn, arranged for a notable clinical conference on DMSO in Vienna (*Dimethyl-sulfoxyd: DMSO.* Salabruck, Berlin, 1966, 219 pp). In spite of countless handicaps, Stanley Jacob has persisted in the careful, patient accumulation of data, so that DMSO now has a chance again of helping people.

My Princeton classmate, Harry Hoyt, who developed the Carter-Wallace Company with Frank Berger in charge of drug research, asked me to join his board of directors. This I did, and I have learned much of the tough problems continually

faced by drug companies in trying to develop new drugs. It is nothing like the way we did it during the depression. But the drugs we introduced, spleen-marrow, divinyl ether, carbarsone, Vioform®, the amphetamines, and nalorphine, are still useful drugs, when used appropriately and properly. We never made a penny from our work, except Gordon Alles from amphetamine, but we were well content to have enjoyed the effort.

Actually, we had quite a close association at the big, open lab in San Francisco where we all worked together. We called ourselves the Blakians, in reference to James Blake (1814–1893), the brilliant London physician who by 1846 had shown clear relationships between chemical constitution and biological action using inorganic salts. He showed that their biological activities permitted their arrangement into families having similar actions, and there is the outline of the periodic table, 20 years ahead of Dmitri Mendeleev (1834–1907). Blake got into trouble and came to St. Louis in 1847, and then came to California in the Gold Rush. He was professor of midwifery and diseases of women and children at the University of California Medical School when it was organized in 1873, and became president of the California Academy of Sciences. He retired to Middletown where he returned to his earlier pharmacological studies. The Blakians made frequent pilgrimages to his grave in the Middletown cemetery. When I gave an account of his career at the Aberdeen meeting of the British Association for the Advancement of Science, I found that the old scandal, whatever it was, precluded the possibility of publishing my account in England.

When it comes to writing, scientists are often no better than their secretaries. I've been fortunate in having fine secretaries, keen, efficient, dedicated, often with us in family affairs, and always helpful in arranging laboratory parties. At Wisconsin there was Irene Blake, and at California, Marjorie Williams, both of whom died too young. At Texas there was Isobel Aiklin, now Mrs. Clemens, who visits my wife each year at Chautauqua, and Mary Jane Steding. At Columbus there was Jane Nolan, and now back in San Francisco there is Mia Lydecker, who really works for Milton Silverman, but who helps me when she can. Here also is Aline Steward, who actually is secretary for the group in environmental health, which shares the old house with me. Mrs. Steward keeps my mail in order.

My historical interest resulted in a large manuscript on the history of pharmacology. This was prepared for Pergamon Press *Encyclopedia of Pharmacology.* But I ran into editorial blocks, so now it appears from C. C. Thomas, who was my first publisher anyway. Peter Knoefel, working on Felice Fontana (1730–1804), pioneer student of the toxicity of venoms, comes over from Firenze once in a while to work with us, and to run to see what we can find on Blake. So we keep rolling along. Even at the Bohemian Grove, where each summer is "the greatest men's party on earth," I get a chance to talk at the lakeside on alcoholic beverages, and other drugs. My chief joy there, however, is lighting the Concert-at-the-Lake, throwing 250 foot beams of colored lights on the redwoods behind the orchestra in coordination with the music. This I've done for 40 years. So this is how I am: still at it for the excitement, the knowledge, and the fun of pharmacology, and related matters.