MERGERS AND GRADUATE EDUCATION

Don’t descend into the well with a rotten rope.

*Turkish proverb*

When Edgar Fahs Smith succeeded Charles Custis Harrison as provost in 1910, he sought a way for Penn to regain its lost medical leadership, at least as the Flexner report and some observers had intimated it had. He took a hint from the Flexner report, that medical education in the United States could be improved by bringing many of the private medical schools under the control of schools with academic connections.¹

**MERGER DISCUSSIONS WITH WOMEN’S MEDICAL COLLEGE AND JEFFERSON MEDICAL COLLEGE**

Smith cast his eye upon three local possibilities—the Women’s College of Medicine of Pennsylvania, Jefferson Medical College, and the Medico-Chirurgical College.² Women’s seemed interested, for the Flexner report had given it a bad rating. In 1915 Smith began discussions, but it was soon evident that Women’s did not want to join the University.³

Discussions with the other institutions were more promising. Smith was encouraged to pursue them by Henry Pritchett, president of the Carnegie Foundation, who was eager to implement the merger recommendation of the Flexner report. Pritchett wrote, none too subtly, that he had recently visited Chicago, where mergers were being explored: “and it occurred to me to wonder whether the time has not come when
the University of Pennsylvania could bring into its jurisdiction the other [independent] medical schools of Philadelphia."4

Smith agreed that medical education in Philadelphia amounted to a "confused pattern." He informed Pritchett that he was "awake to the subject" and continued to report his progress and setbacks to Pritchett, hoping, in his subtext, that the Carnegie Corporation or another benefactor would help finance any definite plans.5

Pritchett liked the looks of Jefferson and told Smith that he, as the Penn provost, should go "frankly after the Jefferson people" to sound out their interest. But he was elusive about suggesting that the Carnegie Corporation would help fund the merger.6

In the negotiations between Penn and Jefferson, Penn was the more enthusiastic partner, but an agreement did inch closer. Still, the document setting forth the union that the respective representatives drew up in 1916 was well short of a merger:

The identity of two institutions, with maintenance of the inherited values of the respective names, and without change in the rights, powers, and authorities vested in them by their respective charters and organic laws, is hereby recognized and preserved inviolate.7

The proposed name was the Medical School of the University of Pennsylvania and Jefferson Medical College. Jefferson's board would continue to control the college's internal affairs. A layer of administration would be added, one dean with two assistant deans, presumably one from each school. Finances would be jointly administered, but the endowments would remain separate.8

Pritchett deplored these arrangements. In a letter to William Potter, Jefferson's chief representative, he said that he could envision physicians proposing a double- or triple-headed organization, but not a businessman. He also predicted that Jefferson would die as an independent school. What died was further attempts at a merger.9

MERGER WITH MEDICO-CHIRURGICAL COLLEGE AND HOSPITAL AND THE POLYCLINIC COLLEGE AND HOSPITAL

Just as the union with Jefferson was disintegrating, Provost Smith turned his attention to the third merger possibility, the Medico-Chirurgical
College and Hospital. This institution, located on the southwest corner of Broad and Market Streets, was anxious to join the University because it had received a bad rating in the Flexner report and also because it was losing its property at 18th and Cherry Streets, which had been condemned to make way for the Benjamin Franklin Parkway. This medical college originated as a society founded by James Bryan in 1849 for "the dissemination of medical knowledge [and] the defense of the rights and the preservation of the repute and dignity of the medical profession." It began accepting students in 1881; it was the first medical school in the United States to have a three-year curriculum, which was later extended to five years.  

Smith's idea in the merger was to relocate the college to the Uni-
versity campus and turn it into a graduate school, where experts would investigate health problems full-time. On campus, he felt, they would be in the company of other scientists and working in dedicated scientific facilities, so that the enterprise would be academic rather than vocational.\textsuperscript{11} The official agreement outlining the details of this merger was signed July 31, 1916.

In 1917 the Polyclinic Graduate College and Hospital indicated it also wanted to join this merger with the University. An agreement was signed in 1918 merging the University with the Polyclinic College and Hospital, the only postgraduate medical school in the state. It had been founded by John B. Roberts, a surgeon who had reopened the Philadelphia School of Anatomy and realized that medical graduates needed practical experience. He opened the graduate college at 13th and Locust Streets in 1883; by 1890, pressured for space, he had a new building constructed on Lombard Street between 18th and 19th Streets. At first the name Polyclinic confused some people, who thought it was a public hospital because the old German name for a city hospital is Poliklinik. In a presage of computer-generated blunders, one creditor billed the hospital as “Polly McClintoc.”\textsuperscript{12}

Under its initial agreement with Medico-Chirurgical, Penn agreed to build a hospital of two hundred ward beds and fifty private beds. After the Polyclinic joined the merger, it increased the total capacity to 497 beds and located the hospital next to the existing Polyclinic Hospital. The building was completed in 1927. Three more institutions were folded into it: Diagnostic Hospital (formerly known as Charity) in 1926, Howard Hospital in 1929, and the assets of the North American Sanitorium in Ventnor, New Jersey, in 1930. The new Graduate Medical School and Hospital did not wait for the completion of the new beds to start operation, although its opening was delayed by America’s entry into World War I in 1917 and the enlistment of many of the faculty. By the fall of 1919, enough had returned for them to offer a short preliminary course to physicians returning from Europe. This historic course was the most comprehensive one in graduate medical education ever offered in the United States.\textsuperscript{13}

**THE RICHARDS-MILLER REPORT**

Trends in medical education had already begun to make the graduate school obsolescent, however. Rapid medical advances and the rise of
specialties and subspecialties affected the medical undergraduate. This development was recognized by A. N. Richards and T. Grier Miller, a gastroenterologist, who were appointed by Penn President Thomas S. Gates to survey medical affairs at the University and recommend directions for the future. They submitted their confidential report in March 1931. In it, they stated that most medical observers feel "that the chief medical research activities of universities should be centered in the schools and hospitals for undergraduate teaching"—just the opposite of Smith’s and Pepper’s intentions.

FATE OF THE GRADUATE SCHOOL OF MEDICINE OF THE UNIVERSITY OF PENNSYLVANIA

Financially Richards and Miller saw little hope of foundation or other outside grants for Graduate Hospital; in fact, they added, the sorry state of its finances seemed like "evidence of bad educational and administrative judgment" on Penn’s part. Furthermore, undergraduate medical education, they pointed out, was so demanding clinically that students "do not feel they are part of an organization which accepts as a major responsibility the enlargement of medical knowledge by modern experimental methods. . . . At present we have not the means to give to the young physician who has the intellect to become a leader the years of unhampered study and inspired guidance needed in preparation for his career." They recommended, among other things, that the University concentrate its assets in the undergraduate medical school. 14

The Graduate School of Medicine received a fresh breath of life after World War II, when hundreds of medical officers were discharged from the Armed Services. Older ones wanted refresher courses before they returned to practice. Younger ones, who often had entered the service after their internship, wanted to obtain board certification in a specialty. There were too few residency positions in hospitals around the country to accommodate them. The two-year course offered by the Graduate School of Medicine, combined with the G.I. Bill of Rights, offered a solution; specialty boards cooperated by allowing the graduate courses to count toward fulfilling board requirements. Further easing the customary financial plight was the emergence of the National Institutes of Health as a large resource for grants for both clinical research and basic science.
The years between 1946 and 1953 constituted the school's most glorious era. Prosperity even eased, temporarily, the tensions between the graduate and undergraduate faculties. Julius Comroe and Seymour Kety were two among many superb clinical and basic-science teachers who transferred their academic positions from the undergraduate school to the Graduate School of Medicine. Comroe also organized the first correlated course in basic science in the United States, one of the best courses ever offered anywhere. Comroe organized a clinical pharmacology correlation course, which combined ophthalmology, neurology, basic science, and advanced clinical instruction.

But in the early 1950s, the backlog of war veterans requiring residency positions dropped, and specialty boards withdrew approval of the Graduate School's courses. National Institutes of Health grants began to be given for basic science in the undergraduate medical schools, where research facilities boomed. And advanced clinical training was done in residency programs in hospitals connected to undergraduate medical schools. Time seemed to have passed the Graduate School of Medicine by. It won a reprieve when foreign students, especially from Central and South America, took its seats. They would help spread modern medical techniques abroad. The program was only partly successful, however, because of language difficulties between teachers and students and, it was short-lived.

In 1955 Comroe and Henry Bockus suggested changes to meet the crisis of falling enrollment. They recommended constructing facilities for clinical offices and teaching on the grounds of Philadelphia General Hospital. If clinicians conducted their practice close to where they taught, they reasoned, an effective teaching program could be established. It would be a refresher course of five months of basic sciences and five months of advanced clinical work; it would fill the needs of residency training programs in community and municipal hospitals distanced from large medical centers.

To John McKay Mitchell, dean of the medical school, the proposal sounded like the start of a second medical school at Penn. It had other important opponents as well, including Norman Topping, vice president for medical affairs. The discussions became quite heated. One morning Comroe gave his secretary a check for $2,000 and told her to obtain two $1,000 bills at the bank. At a meeting that afternoon, Topping made a statement against the plan. Comroe stood up, exclaiming, "What you have just said is a damn lie!" He then pulled out the two bills and
threw them on the table, saying, "Topping, if you can prove what you said isn't a lie, the two thousand is yours!" Topping quietly and sheepishly sat down and said no more. The plan, nevertheless, was not approved; the medical administrators preferred not to strain the school’s limited resources by founding a new teaching institution.\(^{17}\)

Comroe was disheartened and felt that Penn held no future for him. In 1957 he attended a professional meeting in San Francisco, which he found so beautiful that he decided to accept an offer if one came. Shortly thereafter, he was named head of a new Institute for Cardiovascular Diseases at the University of California Medical School. He remained there until he died in 1984.\(^{18}\)

In 1964 the faculty of the Graduate School was officially merged with that of the undergraduate medical school. That relationship remains; in 1979, the hospital was sold off, and currently has no formal ties to Penn.

NOTES


2. Papers of Edgar Fahs Smith (hereafter EFSP) in the Archives of the University of Pennsylvania, which include correspondence with Abraham Flexner and Henry Pritchett; letter of Henry Pritchett to Edgar Fahs Smith, April 2, 1915; letter of Edgar Fahs Smith to Henry Pritchett, April 6, 1915; July 25, 1915 mentioning possibilities for mergers.

3. EFSP, correspondence with Women’s Medical College; letter from E. F. Smith to Henry Pritchett April 6, 1915; letter from E. F. Smith to Henry Pritchett July 23, 1915; These papers are also collected and bound in a volume, “An Account of the Union of Medical Schools in Philadelphia,” September 15, 1916, Edgar Fahs Smith.

4. EFSP, correspondence regarding merger with Jefferson Medical College; letters from Henry Pritchett to E. F. Smith, August 13, 1915; December 30, 1915.

5. EFSP, letter to Henry Pritchett, April 6, 1915.


7. EFSP, Report to the Trustees of the University of Pennsylvania and the Jefferson Medical College of Philadelphia [on the merger of the two institutions]; Document of Merger, there is no date on the printed report. E. F. Smith, “An Account of the Union of Medical Schools in Philadelphia,” indicates this document was circulated to those concerned in late May or early June 1916.

8. Ibid., p. 2.


10. F. P. Henry, *Founders Week Memorial Volume* (Philadelphia: City of Philadel-


12. “Petition of the Medico-Chirurgical College of Philadelphia. The Medico-Chirurgical Hospital of the City of Philadelphia and the Trustees of the University of Pennsylvania for leave to merge and the court decree effecting the merger, Common Pleas No. 5 for the County of Philadelphia, No. 2147, June 16, 1916; Petition of the Philadelphia Polyclinic Hospital and College for Graduates in Medicine and the Trustees of the University of Pennsylvania for leave to merge and the court decree effecting the merger, 2075, December Term, 1917.


14. A. N. Richards and T. G. Miller, *Survey of Medical Affairs of the University of Pennsylvania Prepared for President T. S. Gates and Submitted to him on March 5, 1931*. Annotated on the title page “This is one of three copies, T.G.M.”

15. Memo for the Record to Mr. Blanshard, October 8, 1957, from D.T.S. Background on the Graduate School of Medicine—School of Medicine Unification Program, p. 2.


ESTABLISHING TWENTIETH-CENTURY PRACTICE OF SCIENCE

The beginning of wisdom is to call things by their right name.

Chinese proverb

David Riesman was the William Osler that the University of Pennsylvania trained. Osler's motto was "litterae, scientia, praxis," and surely Riesman was his spiritual descendant.

Riesman, born in Germany, was raised in Ohio. As a young adult, he considered a business career but decided that he did not have the personality for the marketplace. He turned to medicine, enrolling at the University of Michigan medical school, then transferring to Penn. After graduating, he served as an intern at Philadelphia General Hospital, then became an assistant instructor in pathology. He started at once publishing numerous clinical and pathological descriptions of the interesting diseases he encountered, a practice he continued throughout his career. When Alfred Stengel was made professor of medicine after the departure of David Edsall, he appointed Riesman clinical professor in charge of Philadelphia General's medical service. Riesman, like his predecessor Osler, made no discoveries in medical science but gained renown as a superb clinician and teacher thoroughly identified with Philadelphia General. Medical students stated repeatedly that Riesman had no peer as a teacher, and he is credited with developing the next generation of brilliant clinicians, including John Barnwell, David A. Cooper, and Thomas Fitzhugh.

Among Riesman's other official titles was professor of the history of medicine. He wrote Medicine in the Renaissance and numerous articles
on topics that interested him, including extinct diseases, a physician in the Vatican, and doctors in Dublin. He was an encourager of science generally, ranging as far as astronomy and physics; he convinced soap manufacturer Samuel Fels to build a planetarium in Philadelphia.

**EDWARD B. KRUMBHAAR**

Edward B. Krumbhaar served as chairman of pathology from 1934 to 1948, during which time the department distinguished itself with its analyses of diseases, especially cancer. His own most important contribution to medical science was a chance discovery about cancer, although he and others did not realize it at the time. Krumbhaar started in research medicine at Penn under Richard Pearce. His early papers,
published between 1912 and 1917, describe the pathology of white blood cells. In the Army during World War I, he was sent to France and assigned the task of conducting autopsies on victims of mustard gas. Their deaths followed a stormy clinical course, characterized by a low white blood cell count, gastrointestinal hemorrhage, and bronchopneumonia. On further investigation of these symptoms, Krumbhaar found that, in addition to causing eye, skin, and pulmonary lesions, the gas produces a profound systemic intoxication that manifests itself some hours after the initial exposure. In 1919, Krumbhaar and his wife reported that death due to sulfur mustard is characterized by leucopenia, and in cases that come to autopsy, by aplasia of bone marrow, dissolution of lymphoid tissue and ulceration of the gastrointestinal tract.⁴

The dissolution of the lymphoid tissue that he had attributed to sulfur mustard gas turned out to be a clue to the development of a chemotherapeutic agent for treating leukemias and lymphomas. But this step had to await World War II, when the United States Army renewed its interest in chemical warfare, this time in nitrogen mustards. Army scientists observed that these mustards created toxic effects on tissues other than the lymphatic system; in addition, proliferating cells were selectively vulnerable to their toxic action.

Alfred Gilman, Louis Goodman, and T. F. Dougherty figured that the mustards could be used to treat neoplasms of lymphoid tissue. When the nitrogen mustard was administered, it rapidly dissolved the transplanted lymphomas, although the dose required was close to toxic and the tumor invariably recurred. But encouraged, the three made a clinical trial of nitrogen mustard on patients in the terminal stages of various cancers. The most favorable results occurred in Hodgkin’s disease, in which there were remissions similar to those following X-ray therapy.⁵

Krumbhaar pursued the pathology of blood cells and the reticuloendothelial system throughout his active scientific life. He introduced the term “reticulocyte,” the concept of “leukemoid blood pictures,” and the “hemolytopoietic system.” He also made contributions in other fields. He edited the American Journal of Medical Sciences for years. In medical history, he edited Clio’s Short History of Medicine and translated Castiglioni’s History of Medicine into English. He helped reorganize and catalogue the historical collections of the College of
Physicians of Philadelphia and helped found the Association of the History of Medicine and the International Association of Medical Museums.

JAY FRANK SCHAMBERG

Jay Frank Schamberg, who received his medical degree from Penn in 1892, was an ardent student of dermatology. While he waited for his practice to grow, he wrote a compendium of skin diseases. To learn more about the cutaneous lesions associated with infectious diseases, he gained an appointment to the Philadelphia Hospital for Infectious Diseases. His work there led to his color-illustrated text *Acute Contagious Diseases* in 1905. At that hospital, he also studied five thousand cases of smallpox. Appalled by the ravages of a preventable disease a century after Edward Jenner discovered vaccination, he became a proponent of mandatory vaccination.

Schamberg was tall and dignified and known for his dress; he wore pince-nez glasses attached to a black ribbon around his neck, a white-laced vest, a dark suit, and spats. He was courteous, kind, unemotional, and coldly logical. At international professional meetings he impressed his colleagues because he delivered and discussed papers in French or German as well as English. He chaired dermatology at Temple University and the Jefferson Medical College prior to Graduate Hospital. He railed against socialized medicine, which he felt could be prevented if medical care were improved.

Schamberg has the distinction of having his name attached to two diseases. In 1899, early in his practice, he became intrigued by a spotty series of lesions in the pretibial skin of a fifteen-year-old boy. The dermatitis started as red dots that slowly enlarged; similar eruptions appeared subsequently on the wrists. In time these flat, asymptomatic spots became brownish-red or brownish-yellow and finally disappeared. Schamberg, who had done postgraduate studies in Europe at Duhring's urging, knew that he had not seen lesions of this nature in clinics there. Nor had Duhring or his colleagues seen them. To be certain that he was describing a condition not previously observed, Schamberg followed the patient for two years before he published his initial case report in the *British Journal of Dermatology*. The lesion was progressive pigmented purpuric dermatitis, still known as Schamberg's disease.
There was to be yet another Schamberg's disease, one that died out as the home environment became cleaner. Schamberg first noticed it in 1901, when he reported on an epidemic of a disease resembling chickenpox and accompanied by intense itching. But he could not determine its etiology until 1909.

In that year the disease broke out again, frightening Philadelphia citizens much as Legionnaires' disease alarmed them in the 1970s. The epidemic started on the steam yacht of P.A.B. Widener, when many of the crew developed severe and generalized urticarial and vesicular eruptions. It spread to other ships anchored in the harbor and to homes near the wharfs, then to homes throughout the city. Most of the cases occurred among the poor, and groups of patients contracted the disease at the same time, ruling out person-to-person contagion. It also disappeared immediately after the patients were hospitalized.

Schamberg recognized the condition as the one he had seen in 1901. When the epidemic spread to fashionable Center City hotels, city health officials called upon the United States Public Health Service to investigate. Joseph Goldberger, who later would discover the cause of pellagra, was sent. He joined his background in parasitology to Schamberg's knowledge of skin lesions, and together they discovered that the cause of the rash was an ascarine mite that infested straw mattresses.

In 1912 or so, P.A.B. Widener developed psoriasis and became a patient of Schamberg. This association led to Widener's giving financial support to Schamberg to organize a research group. In 1914 Schamberg opened the Dermatological Research Laboratories with John Kolmer, a bacteriologist and serologist, and George Raiziss, a chemist. They occupied meager space in two basement rooms of Philadelphia Polyclinic College for Graduates in Medicine (eventually Graduate Hospital).

At first they focused on psoriasis. Figuring that they could broaden their investigations without unduly increasing their expenses, they entered the newly established field of chemotherapy. They synthesized compounds designed to destroy the germs of various diseases and tested their effectiveness on animals. Making no progress with mercury compounds, they tried arsenic compounds. World War I forced another project upon them. When the British blockaded German ships from American harbors, the researchers realized that the supply of Salvarsan, a valuable remedy for syphilis made by a German pharmaceutical firm, might be cut off. After some months of experimenting in the spring of
1915, Raiziss succeeded in synthesizing Salvarsan. He and his colleagues revealed the details of the synthesis at the May meeting of the American Dermatological Association; the association and the American pharmaceutical industry expressed their awe at the small, independent laboratory.  

Throughout the fall of 1915, Schamberg received an increasing number of requests from physicians and hospitals for Salvarsan, which they could not otherwise obtain. But Schamberg feared that selling it in the United States would infringe on the German patents. He met with the American distributor of the German drug, who tried to persuade him that ample supplies could skirt the blockade. Schamberg doubted that, and he also felt morally obliged to see that America had adequate quantities of the arsenical. To clear the situation, he suggested that the German licensee obtain a court order restraining distribution of the drug. The licensee refused, knowing that no court would enjoin Dermatological Research Laboratories from furnishing a lifesaving drug when the original supplier could not or would not furnish it. He finally agreed not to interfere if the laboratory went ahead and distributed its product, as long as it stopped when the German supplies arrived.

Schamberg’s laboratory marketed its drug as Arsenobenzol and sold it at $2.50 a tube, two dollars less than Salvarsan cost. In June 1916 the German submarine Deutschland broke the blockade and brought Salvarsan to the United States, and Schamberg ceased production. But the shipment was soon exhausted, and Schamberg resumed making his product. In November 1917, when the United States entered the war, Congress passed the Trading with the Enemy Act, authorizing the Federal Trade Commission to license American citizens to operate foreign patents. The Dermatological Research Laboratories was granted license number one to produce and market Arsenobenzol. The demand was so great that the laboratory subcontracted two other laboratories to make it.

The sale of Arsenobenzol, even at its cut-rate price, brought profits sufficient to make the laboratory self-sustaining, even to allow a move to a larger facility, despite the death of Widener and the loss of his support. Schamberg was careful about how the profits were handled; he established a special fund for salaries and laboratory expenses. But when the war ended, Schamberg faced a difficult problem. His laboratory had been created for research rather than for financial gain, and critics harped that he had commercialized his work. To escape what he
called “innuendoes of this character,” he established another institute for dermatological research from the more than $500,000 of profits from Arsenobenzol. He told a newspaper reporter:

Republics are notoriously ungrateful, and the fact that we sold the government Salvarsan at one-half the price we could have legitimately charged them and, moreover, at a time when they could have got it nowhere else, is either soon forgot or else never known by the general public. In our own hearts we are satisfied that we have carried out in the best interests of our country and of the people’s health. We have gained nothing personally from the rewards of our work. The war has ended between nations, but the war against disease must go on; and it is for this purpose that we have dedicated our financial rewards.\(^\text{11}\)

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Newspaper advertisement announcing that the Submarine Deutschland had broken the British blockade and brought a new supply of Salvarsan and other drugs to America from Germany. (Schamberg Papers. College of Physicians of Philadelphia.)
He added:

We are living up to the immemorial traditions of medicine that make it incumbent upon medical men to give their inventions and discoveries freely to the world.\(^\text{12}\)

But the criticisms did not stop until Schamberg, on the advice of his counsel, sold Dermatological Research Laboratories. The German licensee offered $50,000 more than any other bidder, but Schamberg turned him down because of his previous behavior and his affiliation with Germany. Schamberg accepted a bid from Abbott Laboratories, which paid $150,000 plus $31,000 for the stock of Arsenobenzol. Schamberg used the money to organize the Institute for Cutaneous Medicine for the exclusive purpose of research.

GEORGE RAIZISS

George Raiziss was born in Odessa, Russia, earned his doctorate from Albert Ludwig University in Germany, and came to the United States in 1910.\(^\text{13}\) He served as a fellow at the Rockefeller Institute and worked for private firms before coming to Philadelphia in 1913. He was in physiological chemistry at Polyclinic Hospital when he started collaborating with Schamberg. In 1918 he was appointed professor of chemotherapy at Graduate Hospital, the first to hold this title in the world.

When Dermatological Research Laboratories was sold to Abbott Laboratories, Raiziss stayed on as its director. He also maintained his academic appointment. In 1923, he prepared Metaphen, a potent mercurial antiseptic for nose and throat infections and abrasions, used too to sterilize surgical fields and instruments. Shortly thereafter, he synthesized Bismarsen and Aldarsone, low-toxic agents against neurosyphilis and trichomonas vaginitis.

When sulfa drugs were shown to be effective against streptococci and staphylococci, Raiziss tried to synthesize and improve them. He synthesized Sulfapyrazine and Sulfathiazoline. Later he synthesized Diasone; Diasone and Dapsone are the only sulfoxones licensed in the United States for treating leprosy. Raiziss also experimented with oil suspensions of various drugs and developed the penicillin-in-oil preparation used in experimental syphilis.\(^\text{14}\)
ALFRED NEWTON RICHARDS

Alfred Newton Richards directed the medical school's policies for almost half a century and helped mobilize American science during World War II. But his most significant contribution was discovering how the kidney makes urine. His work settled an old controversy: Was urine formed by filtration and resorption of the glomerular filtrate, or through secretion by the tubules?

Richards was headed toward this question before he quite knew it. In 1903–1904 he was teaching experimental pharmacology at the College of Physicians and Surgeons in New York. In conducting work on the hepatic detoxification of drugs, he decided that an improved and more reliable perfusion system could provide answers to many circulatory and hepatic problems.

Called to Penn as head of pharmacology during the Edsall episode, he constructed, as his first project, a perfusion system. With Cecil K. Drinker, who had just graduated from Penn's medical school, Richards
perfused the brain of a cat for nearly two hours with no detectable damage.

When Drinker left to study physiology at Johns Hopkins, Oscar Plant joined the laboratory and suggested to Richards that the system be used to maintain a constant flow of blood through the kidney and thereby gain evidence on the mechanism of the diuretic action of xanthenes.¹⁶

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Accomplishing the goal was more difficult than expected. Richards worked long before the discovery of heparin, and the only anticoagulant approximating a physiologically inert one was hirudin—leech-head extract—which was expensive, not entirely nontoxic, and practically impossible to obtain during World War I. Richards, however, received some from an anonymous friend and carried out a small series of experiments using his new perfusion system. He showed that the formation of urine increased after caffeine was injected into a rabbit's kidney that had been perfused with a constant volume of blood, despite a marked fall in blood pressure. This result supported the secretory theory.

Richards's work was interrupted by World War I, during which he joined Henry H. Dale in England to study the mechanism of wound shock. He and Dale published an article on the action of histamine, a classic in medical literature. After the war, Richards, drawing on his histamine study, felt that a rise in glomerular filtration would occur with a rise in renal arterial pressure. He raised perfusion pressure by partially obstructing the renal vein, stimulating the splanchnic nerves, and adding minimally effective doses of adrenaline in the perfusing blood. Diuresis resulted in every case, which Richards regarded as strong support for the filtration-resorption theory.

A visitor to Richards's laboratory suggested that he gather data with an oncometer, which Richards used after injecting a kidney with adrenaline. The blood pressure rose, diuresis occurred, and blood volume in the kidney increased.

A major step was taken after the arrival of Joseph Wearn, who came to Penn after an internship at Peter Bent Brigham Hospital and army service. Wearn helped prepare the animal experiments in pharmacology for the medical students. Richards taught him how to prepare a living frog so that its glomerular circulation could be observed. Richards had also visited Robert Chambers at Cornell and had seen Chambers inject red blood cells with a minute glass pipette. Wearn suggested that they puncture Bowman's capsule with a Chambers pipette and obtain some glomerular fluid. The fluid could be analyzed for protein, sugar, chloride, urea, dyes, and other substances; and the results could be compared with those of similar analyses of the blood and urine.

Richards enthusiastically approved the idea. He assigned Wearn to a quiet laboratory in the basement of the Medical Laboratories Building, and they proceeded to gather equipment, much of which they had to
build themselves. The test showed that a protein-free filtrate is separated from the blood stream as it passes through the glomerular capillaries. Sodium and glucose, both normal constituents of blood plasma, were found in the glomerular fluid but not in urine in the bladder, proving beyond doubt that the renal tubule reabsorbed these substances. Richards reported this work at the 1921 annual meeting of the American Physiological Society and shared the limelight with Frederick J. Banting and Charles H. Best’s report of the first isolation of insulin (insulin was actually first successfully isolated the following January by James B. Collip in the Department of Biochemistry at the University of Toronto). Critics, noting that the work was done on amphibia, questioned whether the mechanism was similar in higher mammals. Richards felt that it was, but his intuition was confirmed only some twenty years later when scientists demonstrated essentially the same mechanism in rats, guinea pigs, and opossums.

Richards’s discovery not only laid the groundwork for understanding renal function in general but also was fundamental to the development of new diuretics and systems of dialysis for patients who have no renal function. Scientific method was an ancillary beneficiary. Richards noticed that the human eye can distinguish small color differences in fluids contained in thin glass tubes. These color differences could be expressed quantitatively by comparing them with a series of standards contained in similar tubes. Painstakingly modifying the analytical procedures of the time, Richards and his colleagues made quantitative measurements of eleven separate urinary components in fluid, then made similar measurements of foreign substances. The microtechniques they developed introduced a quantitative dimension to their studies and pioneered the development of microbiocchemistry.

**SIMON S. LEOPOLD AND CHARLES S. LEOPOLD**

In 1925 the Pepper ward was opened in the Gibson Wing of the hospital. The ward was especially designed for metabolic studies and the care of patients with renal disease. It contained an advanced diet kitchen and a unusual room in which the the temperature, humidity, and particulate matter in the air could be controlled. It was probably the first climate-controlled room in a hospital.

The “air-conditioned” room was made by Simon Leopold and his brother Charles, who was a graduate of Penn’s Towne School of Engi-
neering. Simon Leopold wanted to evaluate the effect of inhaled substances and atmospheric conditions on bronchial asthma and other respiratory diseases. In his studies Leopold found changes in barometric pressure, temperature, and humidity had no effect on the clinical symptoms of his patients. He discovered, however, that house dust contains one or more groups of specific, antigenic substances capable of producing immediate onset of asthma.  

EDMUND B. PIPER

Edmund B. Piper succeeded Hirst as professor of obstetrics. He graduated from Princeton University and entered business before going to medical school, graduating from Penn in 1911. During World War I he treated severe machine-gun and shrapnel wounds in France, gaining vast experience in managing septicemia (and, incidentally, diligently fighting the army on how military surgery should be practiced).

On returning to Philadelphia, Piper studied the use of Mercurochrome in treating urological infections, especially blood poisoning after childbirth. His experiments showed him that Mercurochrome injected intravenously sterilized the bloodstream of rabbits with experimental septicemia, and he became the chief local consultant on severe bloodstream infections. When he treated patients with puerperal sepsis by injecting Mercurochrome intravenously, he had some apparent successes but also many failures. Small doses of the compound caused marked renal damage, so that effective levels of it could not be maintained for periods long enough to sterilize the bloodstream.

Piper had better luck with instruments. He developed the aftercoming head forceps used in delivering babies with breech presentations and modified these for use as axis-traction forceps. He also invented the adjustable leg holders for obstetrical tables, modifications of which are still used today.

It was his extracurricular hobby of sports cars, however, that brought him to public attention. He increased the driving range of his Packard convertible by fitting it with an oversize gas tank; he also cut a hole in the floor and carried a funnel and tube so that he could relieve himself. He liked to race trains from city to city. In 1928, to regain the center of attention of his family which had been seized by his daughter, who was getting married, he raced from Philadelphia to Los Angeles and
Edmund Piper, Professor of Obstetrics, and his automobile in which he raced a train across the United States and arrived ahead of it in Los Angeles. (Mrs. Donaldson Cresswell, Edmund Piper's daughter.)

beat the train, and his story and picture ran in newspapers all over the United States.\textsuperscript{27}

NOTES


12. Ibid.


23. S. S. Leopold and C. S. Leopold, “Bronchial Asthma and Allied Allergic Disorders. Preliminary report of a study under controlled conditions of environment, temperature, and humidity,” *Journal of the American Medical Association* 84(1925):731–34; D. W. Presser, Penn Engineers (writeup of the work of Charles Leopold. Charles S. Leopold was a pioneer and expert in heating, ventilating, and air conditioning. Among the installations he engineered were the air conditioning of the Pentagon, the United States Senate, the House of Representatives Office Building, the New York Stock Exchange, Convention Hall, Philadelphia, Madison Square Garden, Gimbel Brothers Stores, New York and Philadelphia, Saks Fifth Ave., and the special exhaust system for the Atomic Energy Commission, Los Alamos, N. M.) *New York Herald Tribune*, November 26, 1960.


27. Personal conversation with T. Grier Miller at The Philadelphia Medical Club Meeting.
13

SCIENCE AND PRACTICE: THE NEXT PHASE

Not only is there a certain art in knowing a thing, but also a certain art in teaching it.

Cicero

CARL F. SCHMIDT

Carl F. Schmidt helped A. N. Richards observe the glomerular blood flow of the frog kidney but was forced to stop when the bright arc lights that the research required gave him eye strain. In search of activity, he visited the Office of the China Medical Board in New York City in 1921. The Chinese wanted specialists to investigate the pharmacological activity of and therapeutic possibilities in the many drugs in the Chinese pharmacopeia. The Chinese were also seeking fellows trained in pharmacology, chemistry, and physiology to teach Western methods to their own doctors and medical students. Intrigued, Schmidt signed up.¹

He arrived in Peking just after the Peking Union Medical School was organized. Charles Read was head of pharmacology there. He welcomed Schmidt because he had little training in pharmacology and needed help with the teaching. He steered Schmidt toward some native drugs—a volatile oil, a diuretic, and a nerve tonic among them—that seemed as though they should have active properties. But Schmidt came up with only negative results, as he did for a number of other drugs. He was discouraged, thinking that none of the Chinese drugs had any activity.²

At this time K. K. Chen returned to China, supported by a Boxer fellowship. Schmidt met him, and they discussed their collaboration.
Shortly thereafter, Chen visited his family in central China. While at his home, he told them that he intended to apply modern techniques to explain the chemistry and pharmacology of the ancient native drugs. He also told them about Schmidt’s frustrating results. An uncle pointed him to ma huang. Chen obtained some and took it to Schmidt.⁢

Meanwhile, Chen and Schmidt tested other drugs unsuccessfully. One day, after a class experiment, Chen suggested that they test the ma huang on the dog used by the students, which was in sufficiently good condition for a trial. He rushed home for the sample, and on his return, the two placed some of the oily powder in a beaker of hot water. After letting it sit for a few minutes, they drew some of the yellow supernatant fluid into a syringe and injected it into the dog’s vein.⁴ The dog’s blood pressure rose at once—the first promising result from any drug they had tested. They were so surprised that they wondered whether the syringe had been contaminated with epinephrine. But no epineph-
rine had been used that day; besides, that drug is short-acting, and the
dog's blood pressure stayed high for five minutes.  

Chen tried to extract the active principle from the crude sample of
ma huang. A few days later, he made a white powder which, when
injected into the dog, produced the same rise in blood pressure. He
learned in the scientific literature that, in 1884, Nagai had discovered
a similar substance, determined its structure, and named it ephedrine,
after the plant from which he extracted it (*Ephedra vulgaris helviticus*).
Others had shown that it causes the pupils to dilate and the blood
pressure to rise from vasoconstriction and, in fact, Japanese doctors
used it for eye diseases. But there was no complete investigation of its
effects.  

When Schmidt returned to the United States, he brought 500 grams
of ephedrine with him. He gave it to T. Grier Miller, a gastroenterologist,
who tested it in the hospital’s medical clinic. Miller and his associates
found that it was useful for treating nasal congestion, asthma, serum
sickness, hives, and low blood pressure.  

**ISAAC STARR**

Isaac Starr might well be the most distinguished clinical scientist Rich­
ards trained. Starr graduated from Penn’s medical school and interned
at Massachusetts General Hospital. He returned to Penn and joined
Richards’s group investigating the mechanisms by which the kidney
formed urine. But he wanted to study other physiological problems. He
told Richards, who was supportive—and unusual in encouraging his
protégés to pursue their own ideas.  

Starr decided to focus on the heart. At the time, the heart was often
conceived of as a dynamo whose pumping action could be explained by
the small currents produced by its conduction system. Starr, however,
saw it as a pump and directed his approach accordingly.  

About this time, Richards arranged to have members of the phar­
macology department work on the medical wards so that the residents
could learn about the pharmacological action of the drugs they admin­
istered to patients. Starr and Joseph Heymans assisted Richards, and
in 1928 they were both appointed assistant professors of clinical phar­
macology, probably the first use of this academic title. Starr liked the
work, and the interaction was successful. One result was a course in
clinical pharmacology for medical students, headed by Starr and Richards. Starr evidently had some personal magnetism. In 1933 he received an endowed chair, which funded everything except salaries for research assistants; but he soon learned that both ward residents and fellows in pharmacology and physiology were glad to work with him for no pay.11

In his first clinical studies, Starr measured cardiac output by a procedure using ethyl iodide; it was laborious and required needle sticks. Since Starr did not like to be stuck with needles himself, he refrained from sticking subjects and patients unless absolutely necessary. He also realized that invasive procedures altered the measurements because of the patient’s anxiety and discomfort.12

Starr had these problems in mind when he participated in a program on cardiac-output methods given by the American Physiological Society.
in the early 1930s. Another participant was Yandell Henderson, who reminisced about experiments “on the mass movement of the circulation” some thirty years earlier. Henderson had noticed that, when he stood on a spring scale, the pointer tip moved in time with his heartbeat. To study the phenomenon, he rigged a suspended bed to pick up the resonance frequency and a recorder that amplified it some one hundred times. He simplified the instrument, which he took on the Douglas-Haldane expedition up Pikes Peak in 1913 to measure heart output at high altitudes. Henderson’s ballistocardiograph was ingenious but too heavy, and the amplification distorted the record of the heart’s action.

Starr was stimulated. Back at Penn, he was helped by Detlev Bronk, head of the Eldridge Reeves Johnson Foundation for Medical Physics, who made available his machine shop and its head machinist, A. R. Rawson. Starr’s first instrument resembled Henderson’s in design but was lighter and used an optical recording system. It had such a low natural frequency that patients had to hold their breath when the measurements were taken. It was a technique that trained subjects could do much better than many patients. Starr modified the design. He opposed the motion of the bed by a stiff spring so that the frequency would be considerably higher than the heart rate. The problem of respiratory interference was solved, and patients were not required to hold their breath.

Starr used the instrument to measure cardiac output of normal subjects and of patients, some suffering from cardiac diseases. After several years, he realized that it measured not output but cardiac force, which was even more important. He then applied Newton’s laws in postmortem studies to analyze his ballistocardiograph, correlating the device’s tracings with output of blood from the heart. He attached large syringes into a cadaver’s aorta and forced blood into the circulation by striking the syringe plungers with a mallet suspended as a pendulum from the ceiling. This arrangement enabled him to control both the volume of blood ejected and the force of the ejection. The results, made in collaboration with Orville Horwitz and Truman G. Schnabel Jr., were made over a period of ten years and were the first accurate physical measurements of cardiac output.

Combining these data with those obtained from studies on normal subjects and patients, Starr began to understand in detail what the wiggles of the ballistocardiogram tracings really meant: the instanta-
neous changes of force produced by the cardiac muscle. When the ventricles of the heart contracted during the systole cycle, the rate at which blood ejected into the pulmonary artery and aorta changed—slower at first, rising, then falling at the end of the contraction. Since the ballistocardiogram is a continuous measurement (the upstroke of the wiggly curve), the rate of change of ejected blood can be estimated at each instance of systole.

Thus the ballistocardiogram measures noninvasively the heart’s ability to accelerate blood, an element of cardiac function not assessed by any clinical test (the history, physical, EKG, blood pressure, X rays, or even such special studies as cardiac catheterization and visualization of the coronary arteries). Starr realized that patients, even those with heart disease, who accelerated blood rapidly, had large, functional cardiac reserves and the best prognosis. His machine can also detect when the heart chambers do not contract simultaneously.18

HENRY CUTHBERT BAZETT

Henry Cuthbert Bazett succeeded Edward Reichert as chairman of physiology; Reichert had held the position for thirty-one years, and Bazett served for twenty-nine years. Under Bazett, and in part because of him, the department was one of the most distinguished in the world.19

Bazett was born in England and served in the Royal Army Medical Corps during World War I. He was fearless. He insisted on serving as the first subject in any experiments involving human beings. During one experiment, a catheter placed in the right side of his heart became detached and slipped into his circulation; it had to be removed surgically. He was a subject so often that a colleague quipped that he should write a book called The Physiology of H. Cuthbert Bazett. During World War II, the Canadian Air Force Command issued an order preventing him from flying G-test missions with the most daring of its pilots.20

Although Bazett worked on many scientific problems throughout his career, his primary interest was the mechanism by which the body controls its temperature. He identified the venae comites as significant and figured out the arrangement of receptors, blood flow, and thermal gradients. He went on to describe how the body, in cold temperatures,
prevents peripheral heat loss and warms the venous blood shunted from its surface, so that the temperature of the peripheral venous blood is kept in equilibrium with that of the central venous circulation. In warm environments or during exercise, he postulated, the temperature of the venous blood deep in the body rises, increasing the blood temperature as a whole. Thermal regulators in the pons respond by producing peripheral vasodilatation and sweating; local control of peripheral capillary flow and sweating is regulated by gradients near receptors in the skin. 21

This concept of temperature regulation in humans has proved to be essentially correct. Even if it had been proven otherwise, Bazett would not have been disturbed. He boldly stated his hypotheses, openly

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H. Cuthbert Bazett, Professor of Physiology, serving as an experimental guinea pig. (Lysle Peterson.)
discussed differences of opinion with his colleagues, and took those differences as stimulation to further work.

In addition, he always encouraged science at both fundamental and applied levels. The Johnson Foundation for Medical Physics stems, in part, from his realization that methods were needed to study body function in humans. At the time of his death (he died suddenly at sea while traveling to an international physiology congress), he had just been elected president of the American Physiological Society. At professional meetings he was seen more often discussing research problems with younger scientists and former students than hobnobbing with the scientifically and politically elite.²²

He was not known as an excellent teacher of medical undergraduates, because his lectures tended to be too advanced for the students, and he customarily presented too many details before he established his main idea. Even so, he recognized and backed brightness. In one class, he asked Herndon B. Lehr, then a first-year medical student, to discuss current theories of congestive heart failure. Lehr, who had studied engineering at Georgia Tech, said that he disdained the physiological theories; he proceeded to put forth a logical, mechanical approach. Bazett was impressed with the forthrightness and ingenuity of Lehr's answer. Before long, he invited the student to work as a physiology assistant. Lehr eventually became chief of plastic surgery at the Hospital of the University of Pennsylvania.²³

BALDWIN LUCKÉ

Balduin Lucké, a pathologist interested in physiology, succeeded E. B. Krumbhaar as head of pathology in 1948. Lucké was a Hessian who came to the United States as a youth. He received his medical degree from the Medico-Chirurgical College of Philadelphia and served a residency at Philadelphia General Hospital. He joined the Penn staff in 1914.²⁴

He made his first important scientific contribution during World War I. He was serving in the medical corps at Camp Zachary Taylor when the influenza pandemic of 1918 broke out. Among its victims were thousands of soldiers. Lucké examined histological and bacteriological specimens from hundreds of autopsies and concluded that death was due to such secondary invaders as pneumococci, staphylococci, and streptococci, rather than to *H. influenzae*, as was widely thought.
On his return to Penn, Lucké studied the changes in cell permeability produced by injury and the changes in electrolyte concentration. In the early 1930s, he began studying tumors of frogs. His sudden shift of interest occurred by chance. A. N. Richards was using frogs in his experiments and one day noticed a sizeable nodule on the renal cortex of a leopard frog. After satisfying himself that it was not a hematoma or a cyst, he asked Lucké to have a look. Lucké found through microscopic examination that it was a carcinoma. He examined its biological properties and found that it could be transferred by freeze-dried desiccated homogenates of the tumor. The tumor was also transferable from one frog to another by extracts free of living cell. In addition, the tumors did not metastasize at low temperatures but did so when the temperature was raised. Lucké's observations suggested a new approach to cancer research. The "Lucké carcinoma" (after decades, still one of the few "name" tumors) was the first carcinoma induced by a virus. Lucké and
Hans Schlumberger went on to investigate tumors found in other cold-blooded animals.  

During World War II, Lucké served as deputy director of the Army Institute of Pathology, where he made further discoveries. He investigated epidemic hepatitis in the pathological specimens from many service hospitals. After describing the pathological changes seen in “acute catarrhal jaundice” and “idiopathic acute yellow atrophy,” he concluded that these were not different diseases, as had been thought, but extreme forms of the same condition. He also described the renal changes associated with the “crush syndrome” and named it the “lower nephron nephrosis.” He received the Legion of Merit for his brilliant work. In return, he so valued his military associations that, according to his wishes, he was given a military funeral.

EUGENE M. LANDIS

Eugene M. Landis was still a medical student when he made an essential discovery about the physiology of blood circulation. Three hundred years before his work, William Harvey discovered that blood is pumped from the left side of the heart into the arteries and returns to the right side through the veins. His discovery led him to reason that a network of vessels invisible to the eye must connect the smallest visible arterioles and venules. Antony van Leeuwenhoek and Marcello Malphigi studied the anatomy of this capillary network.

This question remained: was fluid excreted from the vascular bed or passed back and forth by diffusion? Scientists could not understand the diffusion of gases or the transudation of fluids between tissues and the intravascular space until they knew something about blood pressure within the capillaries. In 1733 Stephen Hales made the first measurement of capillary blood pressure, but it was inadequate. Danish scientists tried to measure it in 1925, but technical difficulties stopped them.

Landis was working in the physiology laboratories when Professor Merkel Jacobs pointed out that micromanipulators and micro-injection methods newly developed by Robert Chambers at Cornell might help overcome the difficulties the Danes faced. Landis used the mesentery of a frog for his first experiments. He observed that injection of dye
Eugene M. Landis, physiologist, who while a medical student at the University of Pennsylvania was the first to measure accurately the capillary blood pressure. Subsequently he served as Professor of Physiology at the University of Virginia and Harvard Medical Schools. (Historical Collections of the College of Physicians of Philadelphia.)

solutions was variable and realized that, for meaningful results, the capillary blood pressure had to be measured over the entire period of the injection. He proceeded to hold a micropipette in the same position in the lumen for enough time to adjust the pressure within the pipette until it exactly balanced the capillary blood pressure, with no net flow of liquid in either direction. Landis was then able to determine how fluid moves by filtration and absorption through the capillary wall. 29

Landis received his medical degree in 1926, the same year that his classic paper on his research was published in the American Journal of Physiology. He continued at Penn until 1939. During that time, he continued his work on capillaries by studying peripheral circulation with John Gibbon and Hugh Montgomery. Their work led to the development of the suction boot for treating ischemic limbs.

Landis left Penn to head the Department of Medicine at the University of Virginia medical school and then became the George Higginsson Professor of Physiology at the Harvard University Medical School. He helped organize and direct several scientific societies and was given
the first Distinguished Graduate Award from Penn's medical school, when the honor was established in 1984.

R. TAIT McKENZIE

R. Tait McKenzie was the first person in America to hold the title of professor of physical education. He also was a pioneer in sports medicine and physical rehabilitation and a remarkable sculptor. McKenzie was a Canadian who loved his Scottish ancestry so much that, when he died, his heart was buried in Scotland, according to his wishes. He early had an inkling that one could mix professions; his first schooling came from a blacksmith who had become a teacher. While in medical school at McGill University, he was an assistant in the gymnasium. From the outset he wanted to be a great athlete, but his body seemed too frail. With persistent work, however, he became a gymnast champion and football player.

He was appointed medical director of physical training at McGill, a post created just for him. He took the bold step of requiring medical examinations for students entering Canadian colleges. In 1896 he extended his work to teaching and dissecting in the medical school's anatomy department. About 1900 he became interested in modeling human faces in clay.

Through the efforts of J. William White, who had heard him lecture, McKenzie came to Penn in 1904. He instituted compulsory medical examinations for matriculating Penn students. The physical exams turned up many cases of hallux valgus and Morton's toe, foot deformities that restricted the physical activities of those who had them. He was also concerned about the deformities left by infantile paralysis and scoliosis and developed programs to strengthen individuals who had had these diseases. He also wrote extensively on preventing tuberculosis through diet, exercise, and proper living conditions. His motto was "An eager mind in a lithe body" (mens fervida in corpore lacertoso).

In 1915 McKenzie volunteered for the Canadian army fighting in Europe. He was assigned to Aldershot Hospital and applied for the course it gave in physical education. One of the texts was his book Exercise in Education and Medicine. One day McKenzie was amused when his young instructor asked him if the McKenzie who wrote the book was any relation of his.
R. Tait McKenzie, Professor of Physical Education and Physical Medicine and Rehabilitation. (Historical Collections of the College of Physicians of Philadelphia.)
In time McKenzie helped establish reconstruction depots for wounded and disabled soldiers, convalescent camps which helped restore their patients to useful lives. He headed the depot at Heaton Park Camp in Manchester and wrote *Reclaiming the Maimed* and a handbook of physical therapy from his experiences.\(^{34}\)

As a sculptor, McKenzie constantly observed the bodies of athletes performing such activities as running, jumping, and pole vaulting. Their forms led him to idealize the perfect athlete’s body in such bronze statues as “The Sprinter” and “The Modern Discus Thrower.” The war, in a sense, was the antithesis of both sides of his life’s work: It destroyed the bodies of the athletes he had tried so hard to build (as a professor) and to depict (as an artist). Even so he idealized what he felt was the spirit of the unsung heroes of the battlefield in such statues as “Over the Top” (the Canadian national war memorial), “The Home Coming” (Cambridge, England), “The Victor” (Woodbury, N. J.), and “Captain Guy Drummond,” created for the soldier’s mother.\(^{35}\)

McKenzie’s art had other themes as well. “The Youthful Franklin” (at Penn), “The Call” (a Scottish war memorial in Edinburgh), and a statue of General James Wolf (in Greenwich Park, near London) depict not merely heroes but moments of first resolve, when victory, though distant, is already felt as palpable, like the first spring-like day after a harsh winter.\(^{36}\)

McKenzie graced the medical world with his work. For Penn he executed panels of Nathaniel Chapman and Samuel Jackson and medallions of Crawford Long (the alumnus who first used anesthesia), Francis Kenlock Huger, Class of 1797 (who made an unsuccessful attempt to rescue General Lafayette from Olmutz prison), among others. He made medallions for organizations to bestow as awards, including one of Joseph Leidy for the American Society of Anatomists. He also made the Mary Ellis Bell prize medal, which Penn’s medical school awards for student research each spring. He intended to push this subject further. Just prior to his death, he remarked to a friend that he hoped for another commission for a statue honoring medical research; he intended to portray a youthful, enthusiastic investigator with the inscription *Nondum, O mors* (“Not yet, O death”).\(^{37}\)

McKenzie was a charming gentleman with a sense of humor that could be grim but never caustic or demeaning. Yet he always quarreled with the medical profession’s choice of the caduceus as its symbol. He pointed out that the two-snaked caduceus is the staff of Hermes, or
Mercury, the god of commerce, bankers, usurers, and cattle thieves. The true symbol, he insisted, was a single snake coiled around a wooden club, the staff of Aesculapius, the god of medicine.38

PHYSICAL MEDICINE AND REHABILITATION

When the Agnew Wing opened in 1897, it contained a “room for the development of muscle power” equipped with apparatus for mechanical massage, gymnastics, applying super-heated air as well as mechanical massage and passive and Swedish movements.39 These facilities were under the direction of Anna S. Kite. In 1911 a Physical Laboratory was established in addition to the orthopedic gymnasium. The new facility contained baths, equipment for administering dry heat, and appliances for hydrotherapeutic measures. At this time R. Tait McKenzie was appointed professor of physical therapy and Josef B. Nylin, a Swedish physician, was appointed chief of the laboratory. McKenzie gradually phased out his work in physical medicine in the mid 1920s and retired in 1930.40 Josef Nylin continued as chief of the clinic of physical medicine and rehabilitation until his death in 1945.41 In 1947 George Morris Piersol was made the first professor of physical medicine and rehabilitation at the University Hospital. William J. Erdman succeeded Piersol as chairman of the department in 1952.42

MERKEL JACOBS

Merkel Jacobs came from an academic family; one of his ancestors founded Gettysburg College.43 The family were adventurous outdoors as well, and Jacobs took treks to the remote wilderness. During one expedition in 1907, when Jacobs was still a graduate student, Edward Heacock, a fellow student in the party, drowned after his canoe overturned in a rushing mountain stream. On another trip that year, a rock fell on Jacobs’s leg, fracturing his femur. Herbert Ives, a medical student with the expedition, set the fracture; but it took seven and a half days for Ives and the others (including Jacobs’s father and two brothers) to carry Jacobs to a railroad; he finished the trip strapped to the cowcatcher of a locomotive.44
Jacobs earned his Ph.D. from Penn in 1908, studied biology in Berlin, then returned to Penn as an instructor in zoology. In 1923 he was appointed professor of general physiology. He also devoted much scientific effort to the Marine Biological Laboratories at Woods Hole, Massachusetts. He rose through the ranks there to the post of director and then trustee.

At Penn Jacobs helped to teach medical undergraduates, although his main responsibility was the education of graduate students and medical professors, 1921. Front row: Neilason, Abbott, Piersol, Marshall, Pepper, Deaver, Lark, Fussel, Meeker, Griffith, Heisler. Second row: Riesman, McFarland, Pancoast, Burr, Gill, Taylor, Richards, Wood, Egbert, Addison, Sweet. Third row: Stangel, Thomas, Spiller, Hartsell, Grayson, Sailer, Frazier, Stevens. (David Y. Cooper, photograph saved from trash by H. M. Vars.)
students from other departments. He developed a course in advanced
general physiology with David R. Goddard, Lewis V. Heilbrunn, and
Rudolph O. A. Hoeber; by many accounts, it was acclaimed as one of
the best in the discipline offered anywhere. One of his legacies is the
generations of students whom he trained who went on to productive
academic careers at Penn and elsewhere.

In 1927 Jacobs was asked to deliver a Harvey Lecture on the subject
of the erythrocyte membrane. He had not published any work on that
membrane, and in the lecture he cited only one of his papers, a study
of the permeability of cells to ammonia gas. In this lecture he displayed
his ability to analyze mathematically the physical properties of the
diffusion process. He later published a paper called "Diffusion Pro­
cesses," which was a more detailed presentation of his analysis. A
seminal piece for its time, the article was reprinted in 1967 not from
historical curiosity but for basic information on processes of cellular
diffusion processes; it is still up-to-date, enjoying a remarkable shelf
life for a scientific paper.45

NOTES

2. Ibid.
3. Ibid.
4. Ibid.
5. Ibid.
of Ephedrine, The Active Principle of the Chinese Drug Ma Huang," Journal of
7. T. G. Miller, "Ephedrine—Its Use in the Treatment of Vascular Hypotension
Consideration of the Clinical Value of Epinephrine." American Journal of Medical
the Alkaloid of Ma Huang. Effects of Local Application on asal Mucous Membranes,"
8. Taped interview with Isaac Starr, by David Y. Cooper (March 1983).
9. Ibid.
10. Ibid.
11. Ibid.
12. Ibid.
13. Ibid.
14. Ibid.
15. Ibid.
16. Ibid.
17. Ibid.
22. Personal recollections of David Y. Cooper.
23. Conversations with Dr. H. B. Lehr.
32. Ibid., p. 131.

37. Krumbhaar, “Memoir of Tait McKenzie.”


39. Program for the Opening of the Agnew Wing at the Hospital of the University of Pennsylvania (Philadelphia: Lippincott, 1897).


Alfred Stengel, who became professor of medicine when Edsall resigned in 1911, had a profound, though largely overlooked, effect on academic medicine. He was a builder, like the Peppers, who were his in-laws (he married a cousin of William Pepper, III). He developed a strong clinical department with specialty sections and encouraged research. Medical observers have criticized Stengel for not installing a full-time medical staff in his department, but he made other contributions. He consolidated the hospital services, unified and increased the outpatient traffic, improved the service at Philadelphia General Hospital, brought fourth-year students onto the wards as clinical clerks, and increased the outpatient work of third-year students; and during his term he increased his medical staff from two to eight.¹

Perhaps most important, Stengel seized the opportunities in the advancing specialization within internal medicine, although the first step was halting enough. In 1919 the Hospital of the University of Pennsylvania established a “cardiac clinic” as part of the medical outpatient service.² For nine years it struggled on as the only specialty in medicine. Stengel realized that new sciences and specialties could be fostered by proper housing. He introduced his idea for a new out-
patient clinic at a dinner honoring Fred H. Klaer’s tenth anniversary as chief of the medical outpatient department in the early 1920s. Stengel outlined his plans for a salaried staff, elaborately equipped research laboratories, X-ray facilities, a comprehensive social-service department, and an efficient clerical force.³

Stengel’s dream materialized as the Martin Maloney Clinic, completed in 1929 and named for a donor who made a gift of $350,000.⁴ At the time the Maloney Clinic was unique. It was not a new hospital or new hospital unit with a single purpose, but a supplementary section of the medical clinic, having multiple functions all connected with the evolving requirements of modern medicine. It housed a medical outpatient department with special sections for cardiovascular disease (headed by Charles C. Wolferth), gastrointestinal disease (headed by T. Grier Miller), allergy (headed by Richard Kern), chest conditions, diabetes, thyroid problems (headed by Edward Rose), and blood diseases (headed by Thomas FitzHugh). It also contained the William Pepper Laboratory of Clinical Medicine, the Eldridge R. Johnson Foundation of Medical Physics, the Department of Physical Therapy, a
morgue and autopsy department, a pharmacy, a hospital library, a floor for animal research, twenty-three private rooms, and offices for certain members of the medical staff.\textsuperscript{5}

The first three floors of the nine-story building were devoted to the care of ambulatory patients. Organizationally the department was separated into a division for general medical care, which taught medicine to third-year students, and a division for subspecialties, which focused on clinical research, although it offered clinical experience to fourth-year students.\textsuperscript{6}

Cardiology, the first of HUP’s medical subspecialties, began, primitively enough, when Stengel purchased an early model of an Einthoven electrocardiograph just after World War I. At first Edward Krumbhaar, who was in research medicine at the time, used the instrument. When he transferred to pathology not long afterwards, the device was turned over to Charles Wolferth.\textsuperscript{7}

\begin{center}
\textbf{CHARLES C. WOLFERTH}
\end{center}

Wolferth was born at Wolferth Station (named for his grandfather) near Clarksboro, New Jersey. His father was a farmer who poked into agricultural research, so his son had early exposure to the importance of new ideas. While at Penn’s medical school, he played varsity football but attempted to drop the sport during his fourth year.\textsuperscript{8} J. William White, an ardent football fan, asked him why. Wolferth told him that he had slighted his studies for football up to that year but now preferred to concentrate on obtaining a good internship. “Where do you want to intern?” White asked. “Here,” Wolferth answered. White told him to play football and promised him the internship. Wolferth served two years as an intern and another year in clinical pathology, then became the hospital’s first medical resident, in 1915–16.\textsuperscript{9}

Wolferth was a penetrating and logical thinker, a quality which helped him master the experimental approach to clinical science. He also had a vast knowledge of cardiology and of medicine generally. After being mustered out of the Army following World War I, he worked with England’s famous heart specialist, Sir Thomas Lewis. When he returned to Penn, Stengel assigned him the task of organizing and directing a heart station at the hospital. Wolferth organized the new
Charles C. Wolferth (left) and Francis C. Wood at a medical seminar. (Scope.)

Clinic on a pattern he learned from Lewis. Shortly after it was started, Edward B. Robinette endowed the clinic.\(^{10}\)

Personally Wolferth tended to work alone. He attended few national meetings but read scientific journals avidly. He also had a dry sense of humor with which he twitted the peculiarities of his patients, his colleagues, and himself. He was heard to say, "I like my patients to have a lot of bad habits—their prognosis is better." When someone once flattered him, he observed, "It's amazing how an otherwise intelligent, critical person will believe absolutely anything about himself, no matter how fantastic, provided it's complimentary."\(^{11}\)

Although the staff concentrated on clinical practice, Wolferth encouraged the junior staff to do original work by suggesting stimulating problems that they could examine in the laboratory or the heart clinic. The Robinette Foundation was interested in correlating the heart sounds heard through the stethoscope with the electrocardiograph tracing and
the mechanism of cardiac arrhythmias. Wolferth himself, along with Francis C. Wood, a young associate, made two pertinent and important discoveries.\textsuperscript{12}

One concerned precordial electrocardiogram leads, which improved the ability to diagnose acute myocardial infarction. It also involved the current theories of the cause of angina pectoris. In the early 1930s two theories tried to explain the pain of angina pectoris. One was that it was produced by myocardial ischemia due to disease of the coronary arteries. The other was that anginal pain was caused by distension of the first part of the diseased aorta.

In 1931 one of Wolferth's patients had a spontaneous attack of anginal pain while sitting in the electrocardiographic chair. The attack occurred shortly after a tracing had been taken. A second electrocardiogram recorded during the attack showed changes not present in the first. The change in readings indicated to Wolferth that angina is due to myocardial ischemia. He suggested to Wood that they study electrocardiograms on dogs before, during, and after brief coronary obstruction.\textsuperscript{13}

Wood tried clamping the anterior descending and right coronary arteries in turn, using conventional Einthoven limb leads, but found no definite changes in the EKG readings. Pressed for time one day, he clamped all three coronary arteries at once—the anterior descending, the right, and the circumflex. Dramatic changes occurred in leads two and three. Wood later produced the change by clamping the posterior descending artery alone.\textsuperscript{14}

What puzzled Wood was that the skin appeared bluish, indicating lack of blood, after either the anterior descending artery or the posterior descending artery was clamped, but the EKG changed only when the latter was occluded. This observation prompted him to put an electrode on the anterior wall of the heart, clamp the anterior vessel, and take the EKG. He found a definite change in that tracing but not in the limb leads.\textsuperscript{15}

Since some coronary occlusions in patients do not show up on the EKG, Wolferth suggested that Wood put an electrode on the chest over a patient's heart. That afternoon, an ideal patient entered the office; she had an acute coronary occlusion that produced no diagnostic changes on the EKG. Wood set up the machine as planned. The new lead showed a dramatic change in the S-T segment. It worked simply because it was closer to the damaged region of the heart and could
readily detect the disturbed electrical changes. Wolferth and Wood's introduction of the precordial lead significantly extended the diagnostic capabilities of the electrocardiogram. The work also was one of many experiments establishing that heart ischemia caused the pain of angina pectoris.\textsuperscript{16}

Wolferth and Wood also collaborated to explain the W.P.W. syndrome. Wolff, Parkinson, and White suggested that the syndrome was due to a functional bundle branch block. Wolferth was skeptical because heart block should have produced different EKG results.\textsuperscript{17} He remembered an article by A. F. Stanley Kent, a British physician, who described a structure bridging the atrioventricular groove on the right side of the heart.\textsuperscript{18} After some research, Wolferth and Wood published an article that reconciled both the electrocardiographic and the clinical findings of patients with W.P.W. syndrome: the excitatory process was conducted through Kent's bundle as well as through the bundle of His. The present interest in studies of conduction defects originated with this pioneering work.\textsuperscript{19}

T. GRIER MILLER

The accomplishments of the gastrointestinal clinic, organized by T. Grier Miller in 1926, include the work of Joseph Stokes and John R. Neefee, who showed that there are two types of viral hepatitis; the studies of Katherine O'Shea Elsom on the effects of vitamin deficiency on the gastrointestinal tract; and a clinic for patients with psychiatric disorders related to intestinal function, the precursor of the hospital's Department of Psychiatry. Miller himself joined with William Osler Abbott to develop the first reliable method of introducing a tube into the jejunum and ileum.\textsuperscript{20}

Miller earned his undergraduate degree from the University of North Carolina and entered the textile business. But a philosophy professor, Horace Williams, had encouraged him to be an independent thinker, and Miller found himself out of step with other textile executives. He decided to try medical school for a year and chose Penn for his experiment. The term convinced him that only medicine would "satisfy his curiosities and ambitions." He expected to become a surgeon, and in fact had been helping a surgeon in his hometown of Statesville, North Carolina, during his summer vacations; but Stengel offered him the first
medical fellowship granted at the University; it paid $400 a year. Stengel's associate in private practice died at the end of the year, and Miller was given his position; thus he had a private practice while participating in the hospital’s clinical activities.21

Prior to 1934, gastroenterologists had no reliable technique for passing a tube beyond the duodenum in humans to sample intestinal contents or relieve obstructions. One method, dating from 1919, used an Einhorn's tube; but it was time-consuming, and on those occasions when it was successfully passed into the jejunum and ileum, adequate samples did not always pass through the tube’s small lumen.22

A chance conversation with Abbott changed clinical procedure. Abbott was the son of Alexander C. Abbott, erstwhile professor of bacteriology and director of the School of Hygiene and Public Health at Penn. His mother was Georgiana Osler, a niece of Sir William Osler, but the younger Abbott made every effort not to trade on his name; in
fact, he was called Pete. He specialized in pharmacology. One of his major papers was entitled “Problems of a Professional Guinea Pig.”

He had been studying the absorption of electrolytes and foods from the gastrointestinal tract of dogs. In his experiments he used two balloons attached by a cord in order to isolate segments of the bowel at representative levels of the jejunum and ileum. Miller happened to ask how the work was getting along. Abbott complained that he could not control the area of the intestinal tract he intended to isolate because the inflated balloons were pulled down the intestines by the peristaltic waves. Miller saw at once the solution to his own problem. He proposed to Abbott that they hook a balloon to a gastrointestinal tube and have the intestinal peristalsis move the tube to any area of the jejunum or ileum.

The idea seemed reasonable to Abbott. He did not believe in conducting experiments on animals when he could do them in humans, so
he built a double-lumen tube with a balloon on the end and immediately tried it in patients. It worked, but to introduce it into clinical use, Abbott and Miller had difficulty finding a manufacturer to make the small tubes. They approached some fifty manufacturers of medical rubber products before they found one to produce their apparatus. The device is still used today for experimental studies as well as for managing intestinal obstructions and for postoperative care of patients who have had serious bowel surgery.  

THE GEORGE S. COX INSTITUTE

The George S. Cox Institute was another unit developed through Stengel’s efforts. It is a clinical research division of the Department of Medicine and was founded to “find a cure for diabetes mellitus,” as a plaque on the eighth floor of the Maloney Clinic states. Institute researchers have produced interesting diabetes work, but one of the most significant studies done there was in another realm: the synthesis of 10-norprogesterone and Maximilian Ehrenstein’s discovery that this new steroid exerted its activity even when administered orally—a key step in developing oral contraceptives.

The Cox Institute was opened in 1932 and has had only three directors: Cyril Norman Hugh Long, Francis D. W. Lukens, and Albert Winegrad. Long served for only four years, but in that period made the scientific contributions that determined the remainder of his career.

He was an Englishman who began his research before he became an M.D. He was in organic chemistry when he joined A. V. Hill, a physiology professor at the University of Manchester. Hill was working on the chemical changes involved in muscle contraction, studying the breakdown of glycogen and the formation of lactic acid. He needed a chemist to develop methods for measuring blood levels of these substances in animals and humans during exercise. Long at first was not interested because he had little experience in biology. Furthermore, biochemistry was held in low esteem by pure chemists because it involved extracts of cells, blood, and other body fluids that could not be analyzed with the precise methods of pure chemistry. But Long joined Hill and shortly realized that he enjoyed unraveling the secrets contained in the “biological mess.” He published papers with Hill and
others on lactic acid formation in exercise and its relation to oxygen consumption.

Hill recommended Long for a position in muscle chemistry at McGill University in Montreal. Long went there and earned his medical degree in 1928 while continuing his research, which he extended to include conditions of anesthesia and diabetes. He was recruited as the Cox Institute's first director and quickly saw the advantages for himself: complete freedom to investigate his own ideas, contact with clinical medicine without direct responsibility for patient care, and association
with such innovative scientists as Alfred Newton Richards and Detlev Bronk. The first colleague to join him was Lukens, who was working with Miller in gastroenterology and who would, in a few years, succeed Long as the institute’s director. 29

When Long and Lukens began their work in the Cox Institute, all symptoms of diabetes mellitus were assumed to stem from an underutilization of sugar caused by a lack of insulin. A few years earlier, Bernardo Houssay had discovered that removing the pituitary gland from diabetic dogs ameliorated diabetic symptoms remarkably. Although Long realized that pancreatic dysfunction was the major reason diabetic patients could not utilize sugar, he also knew that removing the cortical portion of the adrenal gland lowered blood sugar and that the adrenal gland atrophied after the pituitary gland was removed.

Long and Lukens started to investigate the role of the adrenal cortex in regulating sugar levels in diabetes. They removed the adrenal gland and pancreas from cats and found that the animals lived eleven days longer than the usual diabetic cat and had lower blood-sugar levels than the controls with only the pancreas removed. The scientists pointed out that the diabetes was ameliorated by the absence of adrenocortical function, not by the lack of medullary or “nervous” function of the adrenal gland, as had been thought. And they observed that body sugar was lowered after the adrenalectomy because other sources of sugar, mainly protein, were reduced.

The adrenalectomy, of course, did not cure diabetes, but Long and Lukens showed that the pituitary and other ductless glands helped produce the clinical picture of diabetes. Long generalized his thesis before the American College of Physicians in 1936, and it remains sound advice today: “The clinical condition that follows hypo- or hyperfunction of an endocrine organ is not merely due to the loss or plethora of that particular internal secretion but is a result of the disturbance of the normal equilibrium of the body.” 30

By 1936, Long had filled the Cox Institute with other collaborators and guests, including the prominent Houssay, whose “office” consisted of a desk at the end of the corridor. Long’s reputation, too, had spread, and he was lured to Yale University, where he later rose to be dean of the medical school. He continued his work on the relationship of the pituitary gland to disease, focusing on the relationship of that gland to the hypothalamus. One of his collaborators was John Brobeck, who was
recruited to Penn to succeed Bazett as chairman of physiology after Bazett died in 1951. 31

REORGANIZATION OF THE UNIVERSITY AND MEDICAL SCHOOL

While the clinical work was advancing, the medical school underwent a reexamination as thorough as the original path for medical education set by John Morgan in his Discourse. It was precipitated by a change in the top administration of the University. Penn had always been headed by a "provost"; but in the 1920s the trustees created the position of president to govern the University when they tried to lure General Leonard Wood to Pennsylvania. Under this plan the provost would serve as the chief educational officer. General Leonard Wood, however, delayed assuming his duties. After two years of correspondence, the trustees became impatient and Wood resigned (1922). This dilemma was solved by electing Josiah Penniman to serve as president as well as provost. In 1926 the title of president was abolished. Four years later the trustees reestablished the office of president and elected Thomas S. Gates to fill this office.

In 1926 three vice provosts, one responsible for faculty personnel and relations, one in charge of student government, and one in charge of public relations, were created to aid Dr. Penniman in governing the university. In 1928 these duties of the three vice provosts were redifined when vice provosts in charge of undergraduate departments, administration and—a new jurisdiction—of medical departments were created. Because of the enormous responsibilities of the new position, it remained empty for three years. Finally in 1931 Alfred Stengel accepted the position. By that time, the title had been changed to vice president in charge of medical affairs (later health affairs), and he was responsible for the Schools of Dental Medicine, Medicine, Veterinary Medicine, and School of Nursing, the Graduate School of Medicine, the Hospital of the University of Pennsylvania, and the Graduate Hospital. Stenge1 retained his chairmanship of medicine. 32

THE RICHARDS-MILLER REPORT

Before Stengel was appointed, Gates commissioned a confidential assessment of the medical school, figuring that such advice would b
useful to whoever was chosen as the new vice president for medical affairs. Gates chose Richards and Miller, a basic scientist and a clinician involved in research, for the difficult but important assignment.33 Richards and Miller talked to trustees, departmental chairmen, deans, managers and superintendents of the hospitals, directors, and, going outside, leaders in American medical education and science. They concluded:

Our school embodies one major inconsistency. Our preclinical departments with one exception have become centers of experimental research, and a genuine attempt has been made to give instruction to the student in the spirit of investigation in order that he may cultivate the power of independent thought upon which his future development must rest. In the clinical subjects we think that the instruction is so largely directed at his practical training that the investigative foundation of clinical medicine suffers from relative neglect. . . . Our students in the clinical years do not feel that they are part of an organization which accepts as a major responsibility the enlargement of medical knowledge by modern experimental methods.34

The report was never released to the public. Clearly written and as candid and critical as it could be, considering that the authors were passing judgment on their colleagues, it gives a picture of the strengths and weaknesses of a great and proud and sometimes tradition-bound medical school.35 Richards and Miller felt that the administrative organization of the school was left too much in the hands of its executive committee, which, they suggested, guided the school laxly and with more regard for the problems of its particular members than for the part that individual activities played in the accomplishments and direction of the school as a whole. They suggested that the hospital replace its nurse supervisors with a male director and that that director and the anticipated vice president for medical affairs reorient the executive committee. They did not give a role to the dean of the medical school. From 1765 the medical faculty had grown in decentralized fashion into departments, and the dean traditionally served as a sort of executive secretary rather than a leader; that model was to be maintained.36

The authors were generally enthusiastic about the basic-science departments, which had staffs distinctly larger than is “required for teaching necessities, leaving for each member of the preclinical faculty an impressive fraction of his time for investigative work.” They had high
praise for anatomy, especially Eliot R. Clark’s research on the anatomy of living cells, in which he employed original techniques designed by him and his wife. As a teacher Clark de-emphasized the memorization of body parts and their interrelationships, favoring instead fine dissections, accurate observation, and penetrating interpretations. It was a freedom that students did not fully use, Richards and Miller said, but added that Clark underestimated the “wholesomeness” both of some rigid discipline and of the difficult comprehensive examination, distinctive parts of earlier teaching.37

Richards and Miller called physiological chemistry one of the best-organized departments, but considered biochemistry too theoretical; it could be made more clinically oriented by choosing chemists more familiar with clinical problems, they advised. They also praised the original research in physiology as well as its laboratory course for first-year students, but felt that the average student was not as interested in it “[as] its intrinsic interest would seem to warrant.” They wanted the faculty in both departments to make special efforts to excite students about the field.38

The department of bacteriology received the most severe criticism: it had not been reorganized, the faculty were generally unproductive, and students gave the courses neither interest nor respect. Richards and Miller stopped just short of recommending that bacteriology be dropped from the medical curriculum. The severe rebuke was successful. Following their advice, the department was moved to the Medical Laboratories Building and newly equipped for research. Stuart Mudd was appointed chairman and undertook the overdue reforms.39

Richards was able to criticize his own department of pharmacology. Its laboratory courses were so rigid and the didactic teaching so excessive that students had little time to think independently, he and Miller stated. They recommended a sort of independent study, in which students would take a subject, design and arrange their own experiments, and carry them through to decisive outcomes.40

As for the clinical departments, the physicians noted that Penn had a long-standing reputation for the teaching given to the “intending practitioner of medicine.” Even though the clinical faculty often enjoyed nationwide reputations, the authors continued admonishingly, they had not made a fundamental advance in medical science for nearly 30 years.41

Richards and Miller had other suggestions. The school should build
a new and expanded medical library. It should remember that the Hospital of the University of Pennsylvania "was not primarily established to add to the resources of the city for caring for the sick" but for "instruction and study." It should make the chairman of medicine a full-time post with a salaried staff. It should radically revamp neurology by taking advantage of a recent $200,000 gift for neurological research, plus a proposed merger of the private Orthopaedic Hospital and the Institute for the Study of Neurological Diseases. And it should assemble a faculty of first-rate scientists, clinicians, and teachers at the newly affiliated Children's Hospital of Philadelphia. There was yet more.

Some of Richards and Miller's recommendations have been implemented, some have come to pass, some persist as problems. At the time they were handed up, only a few, chiefly high-placed members of the faculty were privileged to see what had been written; and many of them criticized Richards and Miller for overemphasizing research. It was hardly a criticism that it would have behooved Penn to heed.

NOTES

1. "The Medical Story from Stengel to Wood," University of Pennsylvania Medical Bulletin (January 1956); papers of Charles C. Wolferth (hereafter WP), College of Physicians of Philadelphia; Papers of Alfred Stengel (hereafter SP) Archives of the University of Pennsylvania.
2. WP.
3. WP; SP.
4. WP; SP.
5. WP; SP.
7. WP; SP.
12. Ibid., p. 156.
15. Conversation with Wood.
18. Conversation with Wood.
21. Ibid.
27. Conversation with Francis C. Wood; conversation with Albert Winegrad.
29. Ibid.
35. Corner, p. 292.
36. RMR, pp. b–c.
37. RMR, pp. 1–3.
38. RMR, p. 4.
39. RMR, p. 7.
40. RMR, p. 13.
42. RMR, pp. 10–11.
43. RMR, p. 17.
44. RMR, p. 18.
47. RMR, pp. 80–81.
15
MEDICAL PHYSICS

Imagination is more important than knowledge.

Alfred Einstein

The Eldridge Reeves Johnson Foundation for Medical Physics was the first department in the United States devoted to applying the laws of physics to biological and medical problems. As Stengel announced at the dedication ceremonies, it was charged with studying light and optics relating to sunlight, radium emanation, mercury and quartz-lamp rays, infrared rays, and X-rays; heat in diseases and treatment; sound and instrumental methods for improving hearing (it would also investigate the reproduction and physical effects of sounds); physical measurements in the human body, including heart action, blood flow, stomach and intestine movements, and air distribution; photographic and cinemographic study of body processes and conditions; and electricity in the diagnosis and treatment of disease.¹

The foundation started with a $600,000 endowment from Eldridge R. Johnson, founder of the Victor Talking Machine Company and Stengel's patient; he gave another $200,000 to add a floor to the projected Maloney Clinic. The foundation opened in 1929 with Detlev W. Bronk as its director.²

DETLEV W. BRONK

Bronk taught physics at Penn for a year after graduating from Swarthmore College, then departed for the University of Michigan, where he began studying the physics of living organisms. To broaden his background, he earned a degree in physiology. He studied infrared spectroscopy in physics and the regulation of respiration in physiology.
Henry Cuthbert Bazett, who wanted assistance with his studies on temperature regulation by the central nervous system, brought Bronk back to the Philadelphia area. Bronk took a position in Bazett’s laboratory, directing the research of graduate students and also teaching at Swarthmore. 3

After a few years, Bronk, feeling he was not making sufficient scientific progress, took a fellowship under E. D. Adrian at Cambridge University in England. Adrian was working on nerve conduction. Bronk developed a technique for destroying most of the fibers of a nerve bundle while leaving a sufficient number intact to measure motor activity. He also developed an electrode consisting of a small needle with an insulated wire connected to an amplifier. The needle’s sharp tip measured the electrical events in a small number of motor fibers without requiring the fibers to be cut. The instrument later became the electromyograph. 4 Bronk then went to London to study heat generation during muscle activity with A. V. Hill. Bronk’s biophysical studies started him in the
design and construction of electric instruments to make accurate physical measurements of biological systems—just the background he needed for the new foundation, which he returned to Penn to head.\textsuperscript{5}

He assembled a group of associates, most of whom moved elsewhere after finishing a project or two and a few of whom followed him during his later peregrinations. One of their most important projects at Penn provided the basis for our present understanding of the regulation of blood pressure. Bronk and others investigated receptors for detecting changes in blood pressure, the central control centers, the properties of the efferent neuronal systems controlling heart rate, and the diameter of blood vessels. They also investigated the mediation of synaptic transmission. They discovered the important property of trans-synaptic excitation and the prolonged effect of previous activity. In 1937 Penn created a neurological institute to connect the biophysicists and neurological researchers.\textsuperscript{6}

Bronk was frequently courted by other research institutions but turned them down until he accepted a post as professor of physiology at Cornell University's medical school in 1940; he took many of his most creative researchers with him. It was revealed later that funding for the Johnson Foundation was in jeopardy and Bronk did not appreciate the unsettledness. But they returned to Penn a year later. Cornell, they felt, was not hospitable to biophysics as an independent discipline and intellectual enterprise. He felt that he and his staff were looked on as mere technical specialists who were supposed to build instruments for the medical faculty, teach them how to use the devices, and repair them when they broke down.\textsuperscript{7}

Meanwhile, Penn had resolved the budgetary problems that drove Bronk away. Alfred Newton Richards was not only in charge of medical research at Penn, but he directed the national effort in medical research through the Federal Office of Scientific Research and Development, created by Vannevar Bush. Richards obtained funds to study high-altitude physiology and the nocturnal visual acuity of pilots, and he knew that Bronk had been an aviator in World War I. So the Johnson Foundation, now that most of its major people had returned, collaborated with the Departments of Medicine, Pharmacology, and Physiology to study, among other things, the oxygenation of blood at high altitudes; some of the hemoglobin saturation curves used today resulted from their work.\textsuperscript{8}

Ever restless, Bronk left Penn for good in 1948, when he accepted
the presidency of Johns Hopkins University. Later he headed the Rock-
efeller Institute, which he renamed Rockefeller University.9

RAGNAR GRANIT AND HALDAN KEFFER
HARTLINE

Ragnar Granit, a Finn who had received his M.D. degree from Helsinki
University, worked with Adrian in England and was Bronk’s first ap-
pointment to the Johnson Foundation.10 He left in 1931, shortly after
Haldan Keffer Hartline arrived. Both of them were pioneers in visual
physiology and they quoted each other’s work freely, but they never
worked together. Nonetheless, they are linked forever as sharing the
Nobel Prize in Medicine or Physiology. They were the first individuals
associated with Penn to win a Nobel Prize, but they were not at the
University when they won it.

At Penn Granit investigated the retinal action potential of the eyes
of vertebrates, discovered some sixty-five years earlier. He found that
the complex time course of the retina’s response to light comprised
three components. He advanced the theory that the visual responses
are molded by an interplay of excitation and inhibition, and his repre-
sentation of the interplay of the factors forms the basis of the inter-
pretation of the electroretinogram. To explain the relationship between
receptor excitation and the generation of nervous activity, he originated
the concept of the generator potential, a mechanism that converted the
logarithmic signal of the stimulus to a linear output in the neuron.11

Scientists at the time also could not explain the change in the retina’s
sensitivity in adapting to light or to darkness. The prevailing view
attributed the changes to the bleaching and regeneration of the visual
pigment (visual purple or rhodopsin). Using microelectrodes Granit
concluded that neural factors determine the changes. Time proved him
correct; the retina adapts to light by using the less light-sensitive cones
as detectors, while in darkness its cones are activated.12

Later Granit used his microelectrodes to analyze the mechanism
underlying color vision. His work provided the first direct evidence that
specific cones are sensitive to the three regions of the spectrum repres-
enting the three primary colors on which color vision is based.13

Hartline began research on the phototropic reactions of land isopods
while still an undergraduate at Lafayette College.14 He received his
M.D. from Johns Hopkins. He reportedly graduated last in his class
and was given his degree only by promising never to practice medicine. He had an impish sense of humor and a mistrust of the medical and scientific “establishment.” When his professor in gynecology asked what a woman with a grapefruit-sized mass in her abdomen was suffering from, Hartline answered, “I suppose she swallowed a grapefruit.”\textsuperscript{15}

Equally independent in his approach to science, Hartline planned his own experiments and built unique equipment, which he used along with antique instruments scrounged from any source. They were connected by tangles of wire and cables covered with black tape and strung throughout his disheveled laboratory. He draped sheets of tin foil and black cloth over optical parts of the equipment to prevent leaks of light. One collaborator described the scene as “a slightly disorganized but extremely fertile chaos.”\textsuperscript{16}

At Hopkins Hartline recorded the action potentials of the retinas of living animals and showed that it was feasible to study electrical events in the eye and relate them to the visual processes in humans. At the Johnson Foundation he and Clarence Graham, a physiology graduate from Temple University, developed a method to dissect out and record the output from a single optic nerve fiber of the horseshoe crab. At Woods Hole in the summer of 1931, they made the historic dissection, the earliest record of single-unit activity in the visual system. It enabled them to show that neural impulses in the optic nerve are related to the logarithm of the intensity of the quality of light to which the visual cell is exposed. Their work also demonstrated that the impulses transmitted by the optic nerve are essentially identical and that the intensity of the light incident on the photoreceptor is coded in terms of the frequency of discharge, rather than the shape or amplitude of the signal.

Hartline also showed that the activity of individual fibers differs markedly—some discharge steadily in response to a constant light stimulus, others are activated only by the onset and cessation of illumination, still others discharge when the light is off—but that the response of the whole nerve results from the combined activity of the fibers. He also found a high sensitivity to moving light patterns. He postulated that the processing of visual information begins in the retina with the specialized activity of the ganglia there.

Hartline mapped the retina in detail and determined that a retinal ganglion can receive excitatory and inhibitory influences over many convergent pathways from many photoreceptors. The optic nerve arising from the ganglion is simply the common pathway that carries the impulses, which result from the interaction of impulses from many recep-
tors. As he put it, "Individual nerve cells act independently. It is the integrated action of all units of the visual system that gives rise to vision."17

PHILIP W. DAVIES AND FRANK BRINK JR.

Until the early 1940s, medical scientists and clinicians could not easily measure oxygen tension in animal tissues.18 Oxygen content of blood and plasma could be measured fairly accurately, but tension could merely be estimated by injecting a small bubble of gas and allowing it to equilibrate with the gases in the surrounding tissues, then withdrawing it and analyzing its gas content—a slow, technically difficult technique that permitted only intermittent measurements. The obstacle hindered studies of metabolic and blood gas.

Work that originated in the Johnson Foundation formed the basis of the polarograph used today to measure oxygen tension in biological systems. Bronk involved a graduate student, Frank Brink Jr., in polarographic methods. Brink had learned as an undergraduate at the Pennsylvania State University that oxygen could be measured electrolytically by a dropping mercury electrode. He also was aware that the same process occurred at platinum surfaces. He proposed constructing a respirometer in which a nerve is placed in a closed space containing a known amount of an oxygenated solution and measuring the oxygen consumed with a platinum wire sealed in a glass container.19

At this point Bronk packed and left for Cornell. Brink accompanied him and, with Philip W. Davies, a foundation fellow, built such a respirometer. In their first experiments they were unable to record any current because they allowed too much time to elapse after closing the chamber.

They returned to Penn with Bronk and refined their oxygen electrodes. Davies, who later left Penn for Johns Hopkins, where he remained, concentrated on studies of the brains of cats. Brink, who followed Bronk to Hopkins and then to the Rockefeller Institute, focused on peripheral nerves. They covered the electrodes with a collodion membrane to reduce the problem of "electrode aging," which had made long-term measurements in blood particularly difficult. Brink invented a recessed electrode, which eliminated the effects of change in the oxygen diffusion coefficient of the medium and allowed the electrode to be moved from place to place so that wider areas could be evaluated.20
Others quickly began using the oxygen electrode. Britton Chance used it to measure oxygen consumption of tissue slices and mitochondria. Hugh Montgomery, chief of the Peripheral Vascular Clinic, was the first to use it clinically to measure the oxygen tension in ischemic limbs. He also used it to explore the extent of gangrenous tissue in patients requiring amputation and to assess the effects of physical procedures and drugs on peripheral oxygen tension. John Sayen and Orville Horwitz used it in their pioneer studies on dog hearts to measure changes in oxygen tension in regions around experimental coronary infarcts. Elsewhere, too, the oxygen electrode was increasingly used until polarographic techniques almost totally replaced their rivals.\textsuperscript{21}

\textbf{JOHN C. LILLY}

John C. Lilly developed two of the first electronic devices that continuously measured physiological parameters in human subjects.\textsuperscript{22} He grew up in Minnesota and was led to medicine after his eighteen-year-old brother, whose liver had been lacerated in a riding accident, died on the operating table. On the advice of Will Mayo of the Mayo Clinic, Lilly attended Dartmouth's two-year medical program, then transferred to Penn, where he received his M.D. in 1941.

As a medical student and also a member of the Johnson Foundation, Lilly developed a manometer to measure blood pressure and arterial pulse curves electronically. In the 1930s physiologists had made manometers with metallic diaphragms or membranes, but the diaphragms were inconvenient; they had to be fixed rigidly with respect to the recording device. Lilly used the diaphragm as the movable plate of an electrical capacitance electrode. As the diaphragm moved, variations in capacitance were measured by a radio-frequency circuit, amplified, and displayed on an oscilloscope or a strip-chart recorder, essentially the principle of the radio microphone.\textsuperscript{23}

Lilly's device was useful in aviation research during World War II, as was a meter he made to measure the percent of nitrogen in respired gases. Lilly used a vacuum system to pull gases through a tube. A high electrical voltage applied to a hollow electrode caused the flowing gas to emit light in the manner of a neon sign so that it could be measured photoelectrically. The device gave continuous and accurate recordings and was used to study nitrogen concentrations in the gas delivery.
systems of pilots and others who breathe oxygen at high altitude. Later Julius Comroe and Ward Fowler used the meter to measure changes in dead space during the respiratory cycle. They also used it to compare the degree of respiratory mixing in normal subjects to that in subjects with respiratory diseases.²⁴

After World War II, Lilly turned to neurological research. In the late 1940s he developed a 25-channel television-like display device to measure brain activity. He left Penn in 1953 for the National Institutes of Health. He became interested in the physiology and life habits of dolphins, studies of which gained him international attention.

GLENN MILLIKAN

Glenn Millikan invented an oximeter with which he measured the amount of oxidized and reduced myoglobin in muscle without removing the muscles from the animal.²⁵ This in vivo technique enabled him to calculate the metabolic activity of muscles and estimate their oxygen supply under physiological conditions. His thinking pioneered the development of difference spectroscopy, a type of spectral analysis that could be applied to turbid solutions.

His oximeter cleverly uses the spectral properties of oxidized and reduced hemoglobin, the properties of red and green gelatin filters, and the response characteristics of Weston photocells to tungsten light. The subject’s ear lobe is fitted comfortably in a trough between a small tungsten light source and a colorimeter fitted with two small photocells. One photocell reflects the amount of tissue and blood in the optical path, the other reflects the degree of oxygenation of blood.²⁶

Although Millikan felt that the instrument would be widely applied clinically, its most important uses have been in physiology and biochemistry. Even before he came to Penn, he met Britton Chance and showed him an early version of his idea. Chance realized that the approach could be used to measure oxidation reduction in respiratory pigments of mitochondria, which he was studying then. But the concentration of pigments in mitochondria are so small that Chance had to improve the optics and sensitivity of the instrument. He substituted a grating or prism monochrometer for the filters, which enabled him to obtain many wave lengths of monochromatic light. He ultimately developed the dual-wavelength spectrophotometer, later modified into a
split-beam device, so that scientists could scan wide ranges of the spectrum rather than being restricted to reaction rates at one wavelength.

Coincidentally Millikan, Chance, Davies and Brink, and Lilly all published papers on their respective inventions in the same issue of *Review of Scientific Instruments*—surely one of the most significant issues of that journal. Millikan, whose father was the physicist Robert A. Millikan, was an inveterate designer. He liked to hike and camp in the wilderness but also enjoyed the comforts of home, so he made a shower bath that folded into the trunk of his car so that he could bathe during expeditions. His career was cut short when he was killed in a mountain-climbing accident.\(^\text{27}\)

**RAYMOND E. ZIRKLE**

Raymond Zirkle was one of the early scientists who investigated what parts of the cell X-ray irradiation damaged. While at the Johnson Foundation he developed methods that allowed him to study these processes and found that radiosensitivity was altered by changes in pH within the cell.\(^\text{28}\)

**LESLIE A. CHAMBERS**

The use of ultrasound to disrupt cells, make emulsions, and cleanse surfaces is an important technique in use in science, dentistry, and industry today. Leslie A. Chambers and his collaborators did much in the mid-1930s while he was a member of the Johnson Foundation to explore the use of this method for disrupting the cell walls of bacteria and viruses and forming emulsions.\(^\text{29}\)

**THOMAS F. ANDERSON**

Thomas F. Anderson, one of the early electron microscopists in America, provided an important experimental base for much of the information required to discover the double helical structure of DNA. Anderson was born in Manotowoc, Wisconsin.\(^\text{30}\) His father organized and built a power and light company, which consisted of a dam and an electric
generator; he also organized a company that sold electrical appliances to subscribers and repaired the instruments. Thus the son grew up in a technical world, and he enhanced his knowledge of science at the California Institute of Technology and later by studies in Europe. Anderson was studying at the University of Wisconsin when he was offered a fellowship by the National Science Foundation to explore the biological and medical uses of an electron microscope, the nation’s first, at the RCA facility in Camden. He was skeptical initially because so little had been written about the microscope, but his doubts were quickly dispelled after he arrived and worked with it.

Since the endeavor was new, Anderson worked under the guidance of a committee headed by Penn bacteriologist Stuart Mudd. Mudd and David Lackman had already published excellent pictures taken with the new machine that showed bacterial chains of streptococci held together by their cell walls. Within weeks Anderson and Harry Morton took electron micrographs of Corynebacterium diphtheriae grown in potassium tellurite and showed that tellurite crystals had developed inside the bacteria.

Anderson pushed on. With Wendel Stanley he obtained the first electron micrographs of several plant viruses, directly confirming the dimensions that had been estimated from suspensions containing $10^{10}$ viral particles per milliliter. These studies helped persuade a doubting scientific community that DNA and RNA were large polymers. He and Salvatore Luria examined phage through the electron microscope. Virologists had thought that there was only one type of phage, but the micrographs showed several different morphologies, indicating many phage families.

When Anderson’s fellowship expired, Bronk brought him to the Johnson Foundation. Anderson and L. A. Chambers worked with the first commercial model of the RCA electron microscope, applying themselves at first to the structure of Rickettsia. But Anderson soon returned to phage, which was rapidly becoming an exciting subject.

As more phages were discovered, it was obvious that each phage carried an increasingly elaborate set of instructions to the host bacterium for assembling the daughter particles. With various collaborators, Anderson showed that 37 percent of T2 phage was DNA, then that the DNA of the phage was contained mostly in the head of the virus and released by osmotic shock. This discovery was made in two steps. First,
Anderson discovered that T4 phage would not adsorb to the host bacterium unless it was activated by an aromatic amino acid; the amino acid frees the phage’s long tail fibers so that the connectors on their tips can attach to the surface of the host.

Second, he devised an experiment to test osmotic pressure. When the pressure is lowered rapidly, water passes into the phage faster than sodium chloride passes out; the increased pressure ruptures the viral membrane. When the pressure is lowered slowly, sodium chloride escapes as rapidly as the water enters, and the cells do not rupture. The high viscosity of the suspension solution in which the phage particles are ruptured suggested to Anderson that DNA is released into the solution. He confirmed his supposition when he saw that the solution contained DNA; by contrast, the heads sedimented by centrifugation contain only protein. Since the phage “ghosts” were not infectious, it was evident that infection requires DNA.\(^{35}\)

Anderson also answered the question of whether the phages attach to the bacterium by their heads or tails. Electron micrographs of air-dried specimens were inconclusive, seeming to show both ways. Anderson developed methods to eliminate surface tension when the sections were being prepared. Through improved micrographs he demonstrated that phage attach by their tails.\(^{36}\)

The work of Anderson and others did not totally dispel the skepticism of some scientists that DNA is a string of genetic material directing an organism’s development or that it is a two-dimensional structure which transfers three-dimensional information. In 1952 Hershey and Chase improved on the experiments of Anderson and his colleagues by using double-labeling radioisotope techniques. They finally convinced the skeptics that DNA is the material that transfers genetic information. Two years later, James Watson and Francis Crick further clarified the genetic mechanism when they resolved the double helical structure of DNA.

Anderson was on the threshold of discovering the role of DNA in phage genetics, but he stated later that he was not prepared to advance any further than he had at the time. He stayed at Penn until 1958. By then his old RCA microscope was outdated, but the Johnson Foundation could not afford to buy him a modern one. The Institute of Cancer Research at the Fox Chase Cancer Center in Philadelphia lured him away with a new, more powerful instrument.\(^{37}\)
NOTES


6. Brink, pp. 8–18.


8. Brink, pp. 30–33.


13. Ibid., pp. 134–42.


16. Experience visiting and working in the Johnson Foundation.


18. Letter to David Y. Cooper from Frank Brink, Jr., describing work on the oxygen electrode and some of his experiences in the Johnson Foundation.


20. Letter from Frank Brink to David Y. Cooper, February 17, 1984; Letter from Philip Davies to David Y. Cooper, June 15, 1984.


27. Personal conversation with Thomas Redman.


