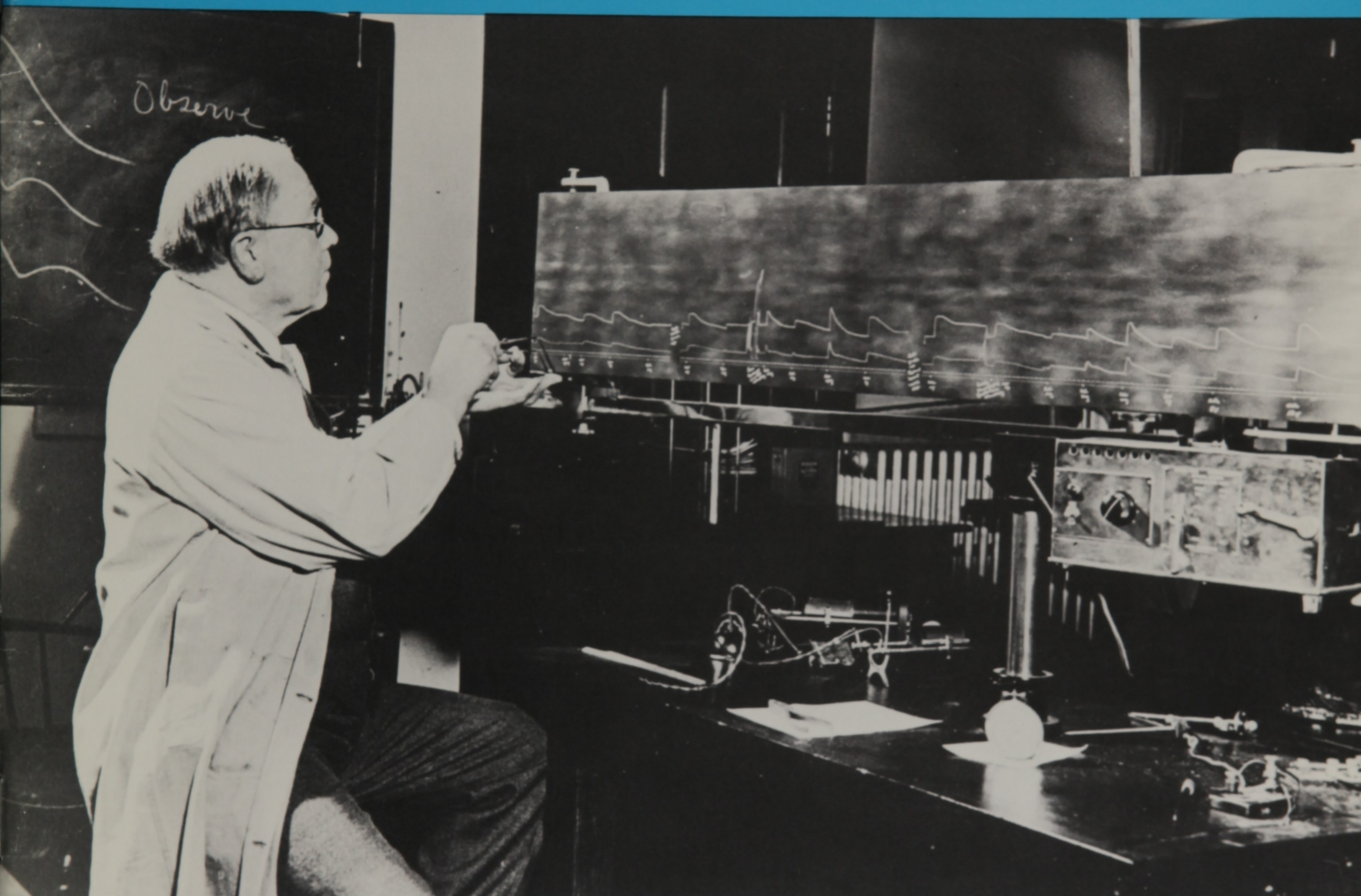
A CENTURY OF AMERICAN PHYSIOLOGY



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This booklet is based on an exhibit entitled "A Century of American Physiology" at the National Library of Medicine, February-April, 1987. The exhibit commemorates the centennial of the American Physiological Society, founded in 1887. The exhibit and booklet were prepared by John Parascandola, Chief, History of Medicine Division, National Library of Medicine; Toby A. Appel, Centennial Historian, American Physiological Society; and Daniel L. Gilbert, Laboratory of Biophysics, National Institute of Neurological and Communicative Disorders and Stroke. Art work for the exhibit and brochure was done by Daniel Carangi, National Library of Medicine. Appreciation is expressed to Ralph H. Kellogg, Melvin J. Fregly, Louise H. Marshall, and John S. Cook for assistance with this project. The Division of Medical Sciences, National Museum of American History, Smithsonian Institution was kind enough to loan several objects for use in the exhibit.

Cover photograph: Walter Cannon in his laboratory at Harvard University, 1940. (All photographs used in this booklet are from the collections of the National Library of Medicine or the American Physiological Society unless otherwise indicated.)

A CENTURY OF AMERICAN PHYSIOLOGY

Based on an Exhibit Commemorating the Centennial
of the American Physiological Society
at the National Library of Medicine
February-April, 1987

National Library of Medicine Bethesda, Maryland 1987

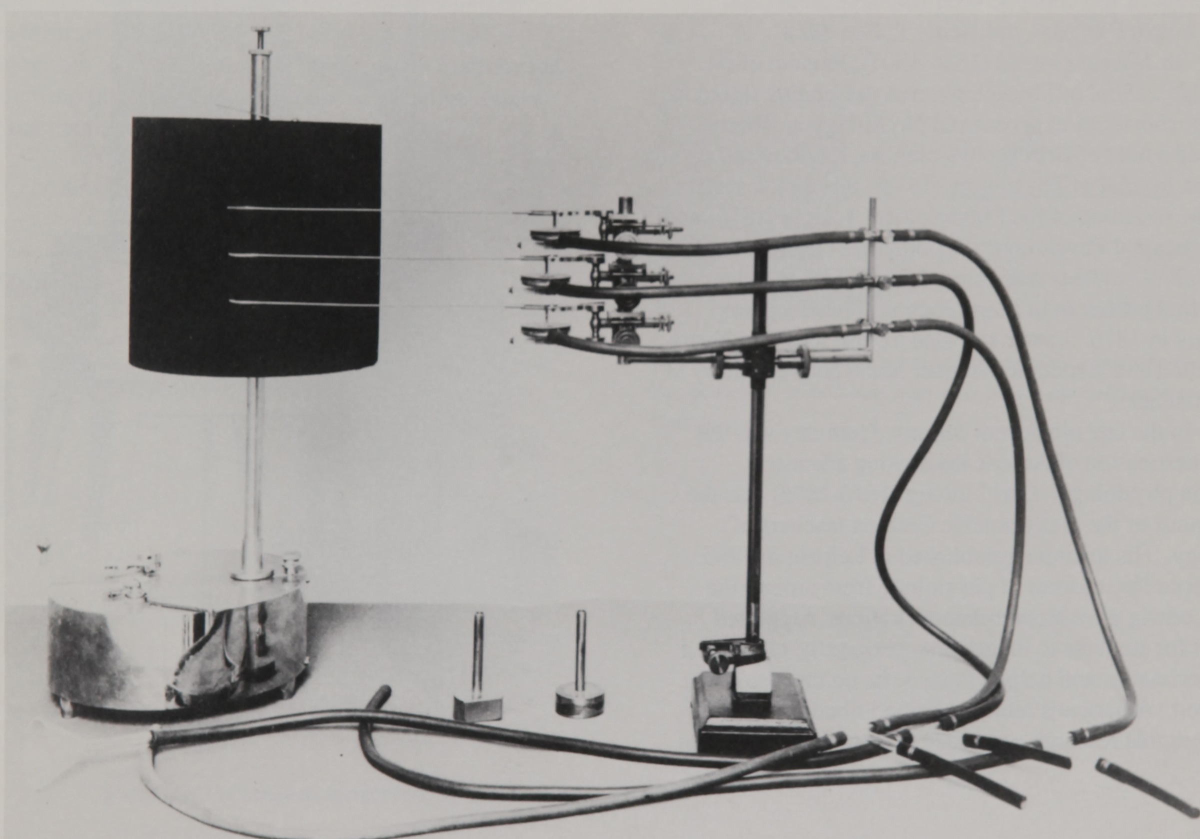
Single copies of this booklet may be obtained without charge by writing:

Chief, History of Medicine Division
National Library of Medicine
Bethesda, Maryland 20894

Introduction

This booklet on "A Century of American Physiology" is based on a 1987 exhibit at the National Library of Medicine commemorating the Centennial of the American Physiological Society, founded in 1887. Physiology has played a crucial role in the development of modern medicine. The booklet highlights those important contributions of Americans to physiology which are featured in the exhibit, covering the period from the beginings of the science in this country up to about the middle of the twentieth century. Of necessity it is representative rather than comprehensive in its coverage as space does not permit inclusion of all of the significant developments in American physiology.

The exhibit consists of two introductory cases on the European roots of American physiology and the emergence of American physiology in the late nineteenth century. Seven cases in the main lobby of the library highlight through books, journal articles, and photographs a few of the many significant contributions in each of seven areas of physiology: general and comparative physiology; nutrition, digestion, and renal physiology; nervous and muscular physiology; endocrine and reproductive physiology; blood and cardiovascular physiology; respiratory, exercise, and environmental physiology; and regulatory physiology. A special feature of the exhibit is a videotape of a film from the Library's historical film collection of the 13th International Physiological Congress held in Boston in August, 1929. This was the first international congress of physiologists to be held in America and was attended by many eminent foreign scientists including I. P. Pavlov.



Kymograph and tambours. This apparatus was arranged for formal photography by physiologist George Baumann of Jefferson Medical College about 1906.

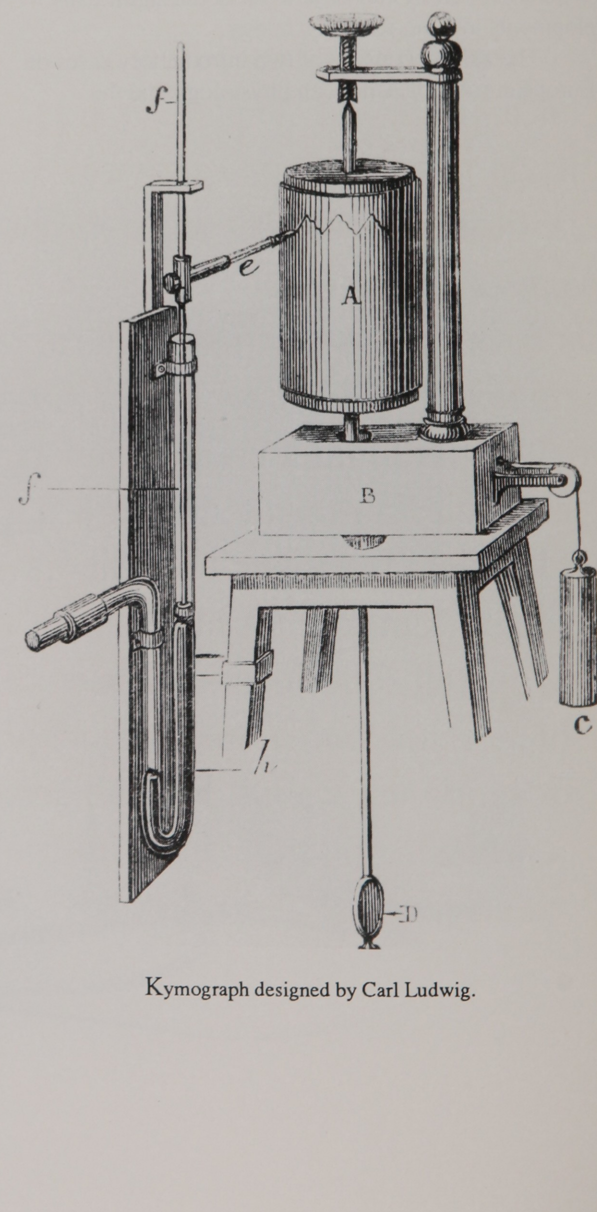
European Roots of American Physiology

The experimental physiology which began to flourish in the United States in the late nineteenth century was an import from European laboratories. Of the men who founded the American Physiological Society in 1887, a good portion of them had studied abroad, especially in German laboratories. There they learned new instruments and techniques, especially methods for graphic recording of physiological phenomena, and were inculcated with the ideal of pure research.

Modern physiology first appeared in France where a succession of great researchers and teachers perfected techniques of animal experimentation. The beginnings of physiology as a discipline are often associated with the work of Francois Magendie (1783-1855) in the early nineteenth century. The greatest representative of the French school was Magendie's pupil Claude Bernard (1813-1878). Many Americans attended his lectures and demonstrations including S. Weir Mitchell, John Call Dalton, Austin Flint, Jr., and Henry P. Bowditch.

Sir Michael Foster (1836-1907), founder of the Cambridge School of Physiology, was the leading figure in the establishment of experimental physiology in Britain. He trained a host of British physiologists, founded and edited the Journal of Physiology (1878), and took a major role in the founding of the Physiological Society (1876) and the International Physiological Congresses (1889). One of Foster's chief students was Henry Newell Martin, who became first professor of physiology at Johns Hopkins University in 1876. Foster was also a close friend of Henry P. Bowditch and visited his summer home and laboratory in the Adirondacks.

In the late nineteenth century, Germany was the favorite destination of Americans seeking advanced training in physiology. Carl Ludwig (1816-1895) was the most famous of the many notable German teachers of physiology. His institute, established in Leipzig in 1865, was a mecca for students of physiology from around the world. Ludwig gave lecture-demonstrations, suggested problems for students to investigate, personally supervised their experiments, and helped them write up the results for publication. Americans returned home imbued with the ideal of original research and eager to foster it in American



Kymograph designed by Carl Ludwig.

universities. Among Ludwig's numerous American pupils were John J. Abel, Henry P. Bowditch, G. Stanley Hall, Henry Newell Martin, Frederic S. Lee, Warren P. Lombard, Franklin P. Mall, Charles Sedgwick Minot, E. T. Reichert, Henry Sewall, and William Henry Welch.

The kymograph, first described by Ludwig in 1846, became the prototypical physiological instrument and long remained the symbol of the science. It represented graphically physiological phenomena that had until then been too fleeting and inaccessible to measure. The French physiologist Etienne Jules Marey (1830-1904) was especially responsible for popularizing "the Graphic Method" in physiology. The new registration techniques enabled physiologists to obtain preservable and quantifiable records of a variety of internal physiological events. Marey's books described instruments, gave directions for their use, and illustrated the forms of records that could be obtained. Marey himself invented tambours (pneumatic devices for transmitting pressure changes to a stylus), a sphygmograph (for measuring the pulse), and a cardiograph (for recording pressure changes in the atria and ventricles during the cardiac cycle).

Henry Pickering Bowditch, a pioneer in American physiology, traveled to Europe to study with Claude Bernard in France and Carl Ludwig in Germany.

Henry Newell Martin, first professor of physiology at Johns Hopkins University.

Emergence Of American Physiology

Physiology was considered by many to be the foundation of scientific medicine. The discipline played a crucial role in the reform of medical education in America in the late nineteenth and early twentieth centuries. In the pre-Civil War period in the United States, physiology remained a subject of study largely outside of the laboratory. Some work in experimental physiology was done by physicians who were basically clinicians, such as William Beaumont, whose classic work on digestion is discussed elsewhere in this booklet. In the post-Civil War period, however, Americans who studied abroad brought the European tradition of experimental physiology to the United States.

John Call Dalton (1825-1889), who became professor of physiology at the College of Physicians and Surgeons of Columbia University, was perhaps America's first full-time "professional" physiologist. A student of Claude Bernard, he extended European researches on the action of the gastric juice and bile, and was a prolific writer of textbooks of physiology. His Human Physiology (1859), a text for medical students, went through seven editions by 1882.

Silas Weir Mitchell (1829-1914) was probably the most talented physiologist of the period before the formation of university laboratories. After receiving his M.D. in 1850, he studied in Paris and attended Claude Bernard's course in physiology. He conducted experiments on the physiological effects of snake venom, the knee jerk and other subjects in his private Philadelphia laboratory in time spared from medical practice. One of America's most prominent physicians and an ardent promoter of medical reform, Mitchell was said to have initiated the formation of the American Physiological Society. He served as second president of the Society in 1889 and 1890.

Henry Pickering Bowditch (1840-1911), after graduating from Harvard Medical School in 1868, spent a year in France and two years at Carl Ludwig's institute in Germany, before being invited to teach physiology at Harvard Medical School in 1871. At Harvard Bowditch established the first university laboratory for the training of advanced students. A number of medical students and medical graduates at Harvard worked with him in his laboratory including Walter B. Cannon, his successor at Harvard. Greatly admired as a teacher, a researcher, and a spokesman for "scientific medicine," Bowditch received many honors including that of election as first president of the American Physiological Society.

Henry Newell Martin (1848-1896) came to America from England in 1876 to become the first professor of physiology in the newly founded Johns Hopkins University. His laboratory there produced the first Ph.D.'s in physiology in America. His doctoral students included William T. Sedgwick (later professor of biology at the Massachusetts Institute of Technology), Henry Sewall (later professor of physiology at the University of Michigan), and William Henry Howell (his successor at Johns Hopkins), who were among the charter members of the American Physiological Society.

Physiology laboratory for medical students, University of michigan, about 1900. The professor, Warren P. Lombard, is the bearded man standing in the rear center. (Courtesy of Horace Davenport.)

The founding of the American Physiological Society in 1887 marked a turning point in the professionalization of American physiology. The organizational meeting of the Society was held on December 30, 1887 at the College of Physicians and Surgeons of Columbia University. The constitution defined physiology broadly but limited membership to those who had published original research. There were twenty-eight charter members.

William T. Porter (1862-1949), trained like many of his generation in Germany, contributed to the professionalization of American physiology through founding the American Journal of Physiology in 1898 (see below). Porter was one of the earliest and strongest advocates of the introduction of laboratory teaching in the medical school. He organized one of the first such courses at Harvard Medical School in the 1890s. His founding of the Harvard Apparatus Company in 1900 to provide low-cost laboratory equipment enabled medical schools and colleges throughout the country to institute laboratory courses in physiology. Laboratory instruction --learning by hands on experience -- became a regular feature of courses of physiology not only for medical students, but for students of veterinary medicine, dentistry, nursing, biology, home economics and physical education.

An American Text-book of Physiology (1896) was the first American compendium of the state of physiological knowledge derived from the new experimental methods. Edited by William Henry Howell (1860-1945), the two-volume work had as contributors the leading physiologists in America, all of them early members of the American Physiological Society.

Another major step in the professionalization of American physiology was the founding of the American Journal of Physiology in 1898. Previously American physiologists had to rely on foreign physiological journals or on American medical journals covering the entire range of medical research. The American Journal of Physiology was founded, edited and financed by William T. Porter under contract to the American Physiological Society. Porter gave full ownership of the journal to the Society in 1914.

William T. Porter.

General and Comparative Physiology

The term general physiology can be traced to Claude Bernard, who used it to refer to the study of life processes common to a wide range of organisms. Frequently such mechanisms can be studied more conveniently in one or another particular organism and the findings applied in a general way to many or all organisms. Related to general physiology are biophysics and cellular physiology. Comparative physiologists study the evolution of organ systems and physiological processes and their variation in the animal kingdom. They are concerned with how various organisms have solved the same problem in either the same or sometimes quite different ways. Though primarily nonmedical in orientation, general and comparative physiology in America have contributed significantly to knowledge of human function.

Jacques Loeb.

General physiology in America owes much to Jacques Loeb (1859-1924) who promoted its study and founded in 1918 the Journal of General Physiology. His own research dealt with such subjects as the effects of ions on the development of invertebrate eggs, artificial parthenogenesis, and the physicochemical properties of colloids. A German immigrant, Loeb taught physiology at Bryn Mawr, Berkeley and Chicago before joining the staff of the Rockefeller Institute for Medical Research. Among the many books that he authored was Studies in General Physiology (1905).

E. Newton Harvey (1887-1959), professor of physiology at Princeton University, was known for his pioneering studies on bioluminescence in the animal kingdom summarized in The Living Light (1940). He investigated the chemical nature of the luciferin-luciferase system by which the light in such organisms as fireflies is generated. This form of light is associated with very little heat formation and thus has been called cold light.

Lewis Victor Heilbrunn (1892-1959) of the University of Pennsylvania is known for his work on the key role of calcium in the regulation of cellular functions. His An Outline of General Physiology, which appeared in three editions from 1937 to 1952, became the standard text and reference work in general physiology used in universities throughout the country. The aim of general physiology, he wrote, was "to discover, in so far as possible, the nature and mechanism of living matter."

Kenneth S. Cole (1900-1984) and Howard Curtis (1906-1972), experimenting with the giant nerve axon of the squid, made fundamental contributions to our knowledge of electrical events during nerve conduction. In 1939 they showed that during a nerve action potential, the membrane barrier to ions breaks down and the membrane potential becomes reversed. Cole's invention of the voltage clamp, allowing measurement of currents due to ions crossing the membrane as a function of time and voltage, was employed by the British physiologists A. L. Hodgkin and A. F. Huxley to elucidate the mechanism of ion transfer during nerve conduction, for which they were awarded the Nobel Prize in 1963. In 1954, Cole became Chief of the Laboratory of Biophysics at NIH.

Comparative physiology in America owes its major impetus to C. Ladd Prosser (b. 1907). Physiologists have learned about the functions of an organ by observing the effect of various environmental conditions on the functioning of that particular organ. Prosser has taken the view that one can also learn about the functions of an organ by observing how this organ functions in different species. Prosser's Comparative Animal Physiology, which he edited in 1950, became the standard work in the field and stimulated numerous other researches.

Nutrition, Digestion and Renal Physiology

The earliest American contributions to physiology centered on the study of digestion. An 1803 dissertation for the M.D. degree at the University of Pennsylvania titled An Experimental Inquiry into the Principles of Nutrition and the Digestive Process, by Maryland physician John Richardson Young (1782-1804), was one of the earliest American publications in physiology. Young carried out a series of experiments in frogs on the action of gastric juice.

The first publication to bring American physiology to the attention of European scientists was William Beaumont's Experiments and Observations on the Gastric Juice and the Physiology of Digestion (1833), which reported his important conclusions about gastric motility and the nature and action of the gastric juice. Beaumont (1785-1853) carried out these studies on a French Canadian voyageur named Alexis St. Martin, who had suffered a gunshot wound resulting in a gastric fistula. Some of the experiments were made in vivo, in the interior of St. Martin's stomach, and the rest with the patient's isolated gastric juice. The book is dedicated to Army Surgeon Joseph Lovell, who began the collection of books that was eventually to become the National Library of Medicine.

In 1896, only a few months after the existence of X-rays became known, Walter B. Cannon (1871-1945), then a student at Harvard Medical School, began a series of investigations on the motion of the gastrointestinal system studied by means of X-rays. To bring out the shape of the stomach and intestines, he used bismuth salts which are opaque to X-rays. Cannon's research first published in 1898 and described in his first book, The Mechanical Factors of Digestion (1911), led to a method for diagnosing malignancies of the gastrointestinal tract.

Anton J. Carlson (1875-1956), professor of physiology at the University of Chicago, studied the relation between contractions of the empty stomach and the sensation of hunger, and established the role of the vagus

Anton J. Carlson.

Graham Lusk.

Homer W. Smith.

nerve in controlling the hunger mechanism. Carlson recorded stomach movements by means of a balloon inserted through a gastric fistula. His research is summarized in The Control of Hunger in Health and Disease (1916). Carlson's department at Chicago became a prolific center for the training of physiologists in America.

Russell Chittenden (1856-1943) of the Sheffield Scientific School, Yale, was the founder of the first laboratory of physiological chemistry (biochemistry) in the United States. His most noted contribution to biochemistry was his study of the protein requirement in man. From nutrition experiments made upon himself, his students, and a group of volunteers from the Hospital Corps of the Army, he concluded in Physiological Economy in Nutrition (1904) that good health could be maintained by consuming less than half of what was previously assumed to be the necessary protein intake. Biochemistry, originally part of physiology, separated to become an independent science. In 1906 Chittenden became the first president of the newly formed American Society of Biological Chemists.

Graham Lusk (1866-1932), who became professor of physiology at Cornell Medical College in 1909, devoted his career to the study of metabolic processes using the large calorimeter installed at the Russell Sage Institute of Pathology. His textbook, Elements of the Science of Nutrition, first published in 1906, synthesized and popularized the results of calorimeter research. The 4th and last edition (1928) has become a classic.

Modern renal physiology begins with Carl Ludwig and Arthur Cushny (1866-1926), a Scottish pharmacologist who spent twelve years at the University of Michigan. Their theory of kidney function posited that a filtrate containing all the water-soluble constituents of the blood was separated out in the glomeruli of the kidney and that portions of this filtrate were reabsorbed in the uriniferous tubules. This fundamental theory was confirmed experimentally by Alfred Newton Richards (1876-1966) and his coworkers at the University of Pennsylvania. In a 1924 paper, Richards and Joseph T. Wearn (1893-1984) were able for the first time to collect and analyze the fluid from a single glomerulus and demonstrate that substances were indeed reabsorbed from the uriniferous tubules.

Homer W. Smith (1895-1962), of New York University, was one of the great renal physiologists of the century. He studied the kidney in the broadest manner possible, relating the form and function of the organ to its evolutionary history. He and A. N. Richards independently discovered that inulin, a metabolically inert carbohydrate, could be used as a tracer to enable measurement for the first time of the glomerular filtration rate. His Lectures on the Kidney (1937), later enlarged and republished, was the first comprehensive work on renal physiology since that of Cushny twenty years before.

Nervous and Muscular Physiology

Over the past century, three major concepts have contributed to the advance of American neurophysiology. The first was the replacement of the use of muscular contraction as indirect evidence of nervous system activity by direct measurements of processes within the nerve cell, with the aid of such devices as the cathode-ray oscillograph and the microelectrode. The second, derived from biophysical research on the neuronal membrane, was the the elucidation of the electrochemical nature of the nerve impulse (see the section on general and comparative physiology). And third, the initial preoccupation with the peripheral nervous system gave way to studies of evoked physiological events in the brain itself which were possible to localize with the aid of the Horseley-Clarke stereotaxic apparatus.

Alexander Forbes (1882-1965) of Harvard and Alan Gregg (1890-1957), then a medical student, compared by means of a string galvanometer nerve impulses arising in the central nervous system with those elicited artificially by stimulation of an isolated peripheral nerve. They showed that however evoked nerve impulses were always of the same nature. Their 1915 paper giving a coherent interpretation of reflex activities is now considered a landmark in neurophysiology.

Wallace O. Fenn (1893-1971), professor of physiology at the University of Rochester, made significant contributions to many areas of physiology including electrolyte physiology, respiration, and space physiology. The work by which he first became known in animal physiology was his pioneer study of heat production in muscle which he began while working in A. V. Hill's laboratory in England in 1922-23. Fenn showed that if a muscle is shortened, it produces more heat than in an isometric contraction and that the extra heat produced is proportional to the external work done by the muscle. A. V. Hill named this phenomenon the "Fenn Effect."

In 1921 Joseph Erlanger (1874-1965) and Herbert S. Gasser (1888-1963) of Washington University, St. Louis, began a series of pathbreaking researches on conduction in peripheral nerves. By amplifying currents by means of thermionic valves and recording action potentials on a cathode ray oscillograph, they were able to distinguish in a mixed nerve the different functions of single nerve fibers. Their results were synthesized in Electrical Signs of Nervous Activity (1937). Erlanger and Gasser shared the Nobel Prize for physiology and medicine in 1944.

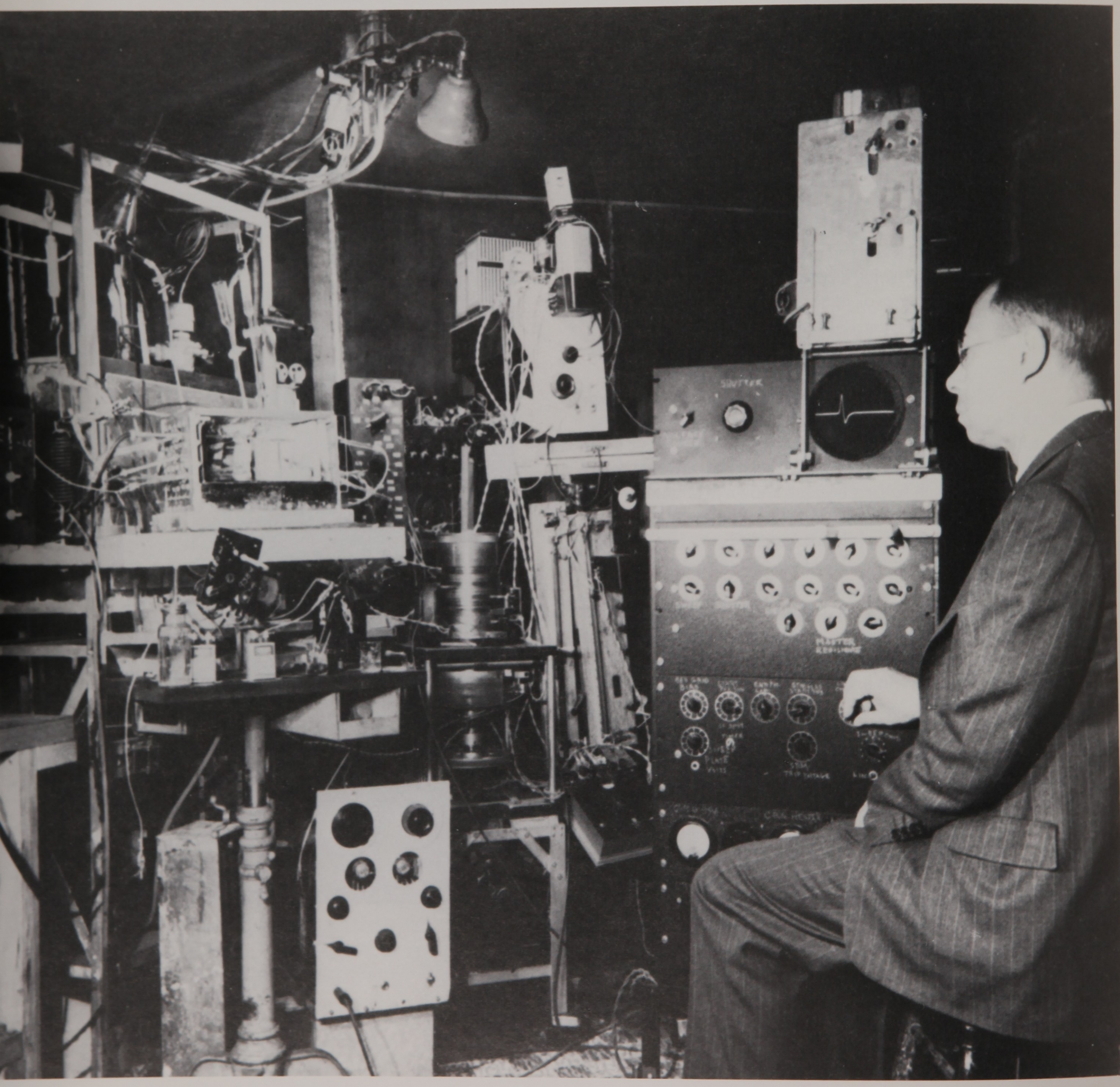
The work of Haldan K. Hartline (1903-1984) on visual mechanisms, extending the researches of British physiologist E. D. Adrian on electrical discharges from the optic nerve, won him a Nobel Prize in 1967, which he shared with Ragnar Granit of Sweden and George Wald of Harvard University. In a classic 1938 paper, Hartline described impulses, amplified and recorded by means of an oscillograph, in a single optic fiber nerve.

Hallowell Davis (b. 1896) pioneered in the study of the physiology of hearing. In 1930 he set up a laboratory at Harvard with a cathode ray oscilloscope, amplifiers, sound-generating equipment and a sound treated animal

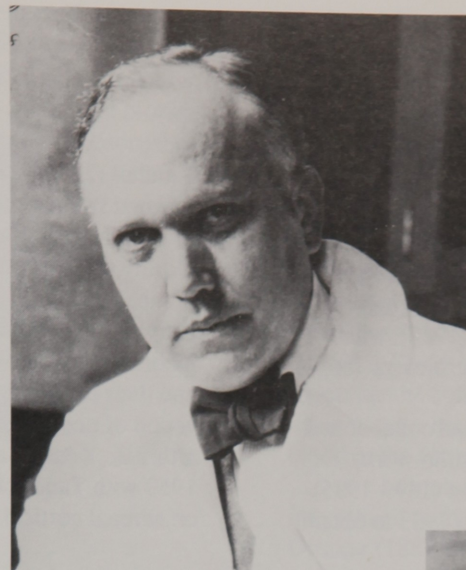
Wallace O. Fenn.

room and began experiments to test competing theories of audition. His collaboration with Harvard psychologist S. Smith Stevens, a student of Edwin G. Boring, resulted in a book, Hearing: Its Psychology and Physiology (1938), which has become a classic in both psychoacoustics and auditory physiology. Davis went on to a long research career at the Central Institute for the Deaf in St. Louis.

Research on the brain itself was made possible by the stereotaxic apparatus which was especially used in the 1930s for investigating the function of the hypothalamus. Horace W. Magoun (b. 1907), one of the pioneers in the use of this instrument, is known for his studies of the reticular formation in the brain. He was one of the founders of the Brain Research Institute at UCLA in 1959.



Joseph Erlanger and the cathode ray oscillograph, 1940. (Courtesy of Washington University School of Medicine Archives.)



Herbert Mclean Evans.

John J. Abel.

Endocrine and Reproductive Physiology

The beginnings of the study of the endocrine glands date back to middle of the nineteenth century, but the term "hormone" was not introduced until 1905. The British physiologist Ernest Starling coined the term (from the Greek hormao, I excite) to describe the internal secretions of the endocrine glands.

The first hormone to be isolated in a chemically pure form was epinephrine, or adrenaline. Three years after George Oliver and Edward Sharpey-Schafer in England had discovered that extract of the adrenal glands causes a rise in blood pressure, the active principle was isolated in the form of its monobenzoyl derivative in the laboratory of John J. Abel (1857-1938) at Johns Hopkins University. In their 1897 paper on the subject, Abel and coworker Albert Crawford (1869-1921) named the active principle epinephrine. In 1901, Jokichi Takamine (1854-1922) and Thomas Bell Aldrich (1861-1938) independently isolated pure epinephrine, or adrenaline, free of the benzoyl group.

The discovery of insulin is a major contribution of North America to physiological research. Four Canadians at the University of Toronto, Frederic Banting (1891-1941), Charles Best (1899-1978), J. B. Collip (1892-1965), and J. J. R. Macleod (1876-1935), played a role in the work, for which Banting and Macleod received the Nobel Prize in 1923. The first report on the subject was given at a meeting of the American Physiological Society on December 28, 1922, with the abstract being published in the American Journal of Physiology.

Herbert Mclean Evans (1882-1971) and Joseph A. Long made important contributions to hormone research. In 1921, they showed that continued injections of anterior pituitary extract produced an acceleration in the growth rate of laboratory animals, evidence that the pituitary gland secretes a growth hormone. Their 1922 publication, The Oestrous Cycle in the Rat and its Associated Phenomena, has become a classic of endocrinology. Much of the early research on sex hormones was summarized in an important book by Edgar Allen (1892-1943), Sex and Internal Secretions: A Survey of Recent Research (1932), which served as the "bible" of reproductive endocrinology for some two decades.

Canadian James B. Collip, who had collaborated with Banting, Best and Macleod on the insulin work, teamed up with American Evelyn Anderson (1899-1985) and Scot David Landsborough Thomson in 1933 to obtain an extract from the anterior pituitary which contained a hormone that acted on the adrenal cortex. This substance, which stimulates the adrenal cortex to secrete several steroid hormones, was later called ACTH (adrenocorticotropic hormone). In 1934, Edward C. Kendall (1886-1972) and his associates at the Mayo Clinic isolated from adrenal extract a small amount of active crystalline material that was soon found to be a mixture of closely related compounds. Over the next decade, a large number of chemical compounds of varying physiological activity were isolated from the adrenal cortex in various laboratories. In 1949, Kendall, Philip Hench (1896-1965) and their coworkers demonstrated the anti-inflammatory action of one of these hormones, cortisone, in rheumatoid arthritis. Kendall and Hench shared the Nobel Prize in 1950 with Tadeus Reichstein of Switzerland for their work on adrenal cortical hormones.

James B. Collip.

Edward C. Kendall.

Carl Wiggers.

Blood and Cardiovascular Physiology

The heart and the blood have been subjects of intense interest in physiology since antiquity. William Harvey's experimentation on the circulation of the blood in the seventeenth century remains one of the classics of physiological research. The twentieth century has witnessed dramatic advances in our understanding of cardiovascular physiology and in the application of this knowledge to the diagnosis and treatment of disease.

Henry Newell Martin at Johns Hopkins University devised a method in 1881 for perfusion of the isolated mammalian heart. Garrison and Morton's medical bibliography cites this development as "one of the greatest single contributions ever to come from an American physiological laboratory." It paved the way for much later research on the heart.

William Henry Howell began investigating the coagulation of blood while working as a graduate student under Martin in the 1880s. The physiology and morphology of blood continued to occupy his interest throughout his career. In a 1911 paper, Howell demonstrated that a substance which inhibits coagulation (antithrombin) is a constituent of normal mammalian blood. The specific anti-coagulant substance heparin was also discovered in Howell's laboratory at Johns Hopkins by Jay Mclean in 1916.

It was not until 1926 that the direct measurement of the blood pressure within the capillaries was achieved by Eugene M. Landis (1901-1987), then a medical student at the University of Pennsylvania. Landis' method involved the injection of micropipettes into the capillary.

Carl Wiggers (1883-1963) made several notable discoveries in cardiovascular physiology through his application of instrumentation to the study of the circulation. His pioneering studies of hemodynamics and his early efforts at resuscitation were especially significant. Wiggers' textbook on the circulation, which first appeared in 1915, represented an important contribution to the literature of circulatory physiology and pathology. Shown in the exhibit is his autobiographic Reminiscences and Adventures in Circulation Research (1958).

The physicochemical equilibrium of the blood was studied by Lawrence Joseph Henderson (1878-1942) and his colleagues, including Arlie Bock and David Bruce Dill, at Harvard University. The results of the investigations of Henderson's group were summarized in his classic book, Blood: A Study in General Physiology (1928). Henderson found that he could simultaneously express the interrelations between a large number of variables in the blood in the form of a nomogram.

Lymph and the lymphatic system are closely interrelated to the blood and the vascular system. Cecil Drinker (1887-1956) and his colleagues at Harvard contributed significantly to the study of the physiology of the lymphatic system. Drinker's 1933 book, Lymphatics, Lymph and Tissue Fluid, in collaboration with Madeleine Field, summarized much of the knowledge on the subject up to that time.

André Cournand (b. 1895) and Dickinson W. Richards, Jr. (1895-1973), working at Bellevue Hospital in New York, were the first to make practical use of the technique of cardiac catheterization developed by the German physician Werner Forssmann in 1929. Cournand and Richards used the technique to study the physiology and pathology of the heart. Their studies proved, for example, that in congestive heart disease the right atrial pressure may be four or five times higher than normal. In 1956, the Nobel Prize was awarded to Cournand, Richards and Forssmann for the development of cardiac catheterization, a method which has led to improvements in cardiac diagnosis and treatment.

William H. Howell.

David Bruce Dill during the 1935 International High Altitude Expedition in the Chilean Andes.

Respiratory, Exercise, and Environmental Physiology

Respiratory physiology in America has been closely related to exercise and environmental physiology, especially to the physiology of man at high altitudes. The modern study of physiological response to high altitudes, founded by Paul Bert in France and Angelo Mosso in Italy, gained much from the introduction of new instruments, techniques and concepts of the Oxford School of Physiology. Two Yale physiologists, Yandell Henderson (1873-1944) and Edward C. Schneider (1874-1954), joined two leaders of the Oxford School, C. Gordon Douglas and John Scott Haldane, in one of the most famous early high altitude expeditions, the Anglo-American Expedition to Pike's Peak, Colorado in 1911. From their summit observatory at 4300 meters, they carried out studies on alveolar carbon dioxide pressure, periodic breathing, blood hemoglobin concentration, and acclimatization, and tested the theory, since disproved, that the lung secretes oxygen.

Another of the century's celebrated high altitude expeditions in which Americans played a prominent role was the 1935 International High Altitude Expedition to Aucanquilcha in the Chilean Andes organized by Ancel Keys (b. 1904) and under the scientific leadership of David Bruce Dill (1891-1986). Experiments were carried out at the summit camp at 6100m as well as at lower altitudes. The expedition was especially noted for its studies of blood chemistry, of the effects of exercise on respiration and circulation, and of mental impairments at high altitude. Since 1935 Americans have organized several other major high altitude expeditions, one of the most recent being the American Medical Research Expedition to Mount Everest in 1981.

The Harvard Fatigue Laboratory, founded by Lawrence J. Henderson at the Harvard School of Business Administration in 1927, and directed by David Bruce Dill, became the leading center in America for studies of exercise and environmental physiology. Much of this research was summarized in Dill's, Life, Heat, and Altitude: Physiological Effects of Hot Climates and Great Heights (1947). The Fatigue Laboratory was in operation until 1947.

Major General Harry G. Armstrong (1899-1983), founder in 1935 of the Aeromedical Laboratory at Wright Field in Dayton, Ohio, now the Harry G. Armstrong Aerospace Medical Research Laboratory, was a pioneer in aerospace physiology. He set up the first human centrifuge to collect data on human response to acceleration and developed the oxygen system for the first military and commercial airplanes with pressurized cabins. His book, Principles and Practice of Aviation Medicine (1939), which went through three editions, became the world's most authoritative work in the new and burgeoning field of aviation medicine. Research on the human response to acceleration eventually helped make possible voyages into space. Studies of man and animals in space has become an active area of environmental physiology.

Knowledge of the physiological requirements of man in extreme climates was of pressing military concern during World War II. The Rochester Desert Unit led by Edward F. Adolph (1895-1986) of the University of Rochester School of Medicine and Dentistry conducted studies of water requirements and temperature regulation under contract with the Office of Scientific Research and Development. The results were published in Physiology of Man in the Desert in 1947.

World War II also encouraged pioneering researches in respiratory physiology. Wallace Fenn, Hermann Rahn, and Arthur B. Otis became known for their studies, carried out during and after the war, on the mechanics of breathing, and the gas exchange of oxygen and carbon dioxide in the lung. Fenn and Rahn showed how gas exchange in man at normal and high altitudes can be presented in a useful graphical form known as the O2 - CO2 diagram.

The Lung (1955) by Julius H. Comroe (1911-1984) and his associates at the University of Pennsylvania, Robert E. Forster II, Arthur B. Dubois, William A. Briscoe, and Elizabeth Carlsen, played an important role in introducing into clinical practice measures of pulmonary function developed by physiologists. Several of the tests described in the book were invented by Comroe himself. The use of such physiological data in diagnosis is now taken for granted.

Edward F. Adolph.

Regulatory Physiology

In the second half of the nineteenth century the French physiologist Claude Bernard introduced the principle of the constancy of the milieu intérieur, or internal environment. The study of the physiological mechanisms that regulate the conditions within the organism has become an important part of twentieth-century physiology.

Bernard's thesis of the constancy of the internal environment was elaborated by a number of American physiologists, including L. J. Henderson (discussed elsewhere in this booklet) and E. F. Adolph in his Physiological Regulations (1943). Probably no one advanced the idea more than Walter Cannon through the introduction of his own concept of "homeostasis" (to describe the stability of the organism) in 1926. Much of his influential research on the concept of homeostasis and on the neurological and other mechanisms of maintaining homeostasis was summarized in 1931 in The Wisdom of the Body. An important aspect of homeostasis is the regulation of body temperature, a subject that was studied by various investigators, including Eugene F. DuBois (1882-1959) and his colleagues in New York's Cornell Medical School.

James Gamble's (1883-1959) Chemical Anatomy, Physiology and Pathology of Extracellular Fluid (1942) was extremely influential in extending the general understanding of the chemical composition of body fluids and their significance. Gamble's innovation of expressing concentration of components in milliequivalents per liter (so that their relative magnitudes and interrelations could be correctly displayed) and his extensive use of graphs helped to clarify the chemical relationships involved in the regulation of physicochemical conditions in body fluids. Horace Davenport's The ABC of Acid-Base Chemistry, first published in 1947, eventually received widespread distribution and use among medical students and practitioners. It served as a guide to an understanding of physiological blood gas chemistry, an important aspect of the field of regulatory physiology.

Walter B. Cannon.

Epilogue

The exhibit has only been able to highlight some of the significant contributions of Americans to the science of physiology, and no attempt has been made to deal with the more recent (i.e., post-1950) history of the subject. Nevertheless, the accomplishments described in the exhibit and in this booklet provide ample documentation of the important role that Americans have played in the development of physiology in this century.

SUGGESTIONS FOR FURTHER READING

1. Atwater, Edward C. "Squeezing mother nature": experimental physiology in the United States before 1870. Bulletin of the History of Medicine 52: 313-335, 1978.

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3. Borell, Merriley. Extending the senses: the graphic method. Medical Heritage 2(2): 114-121, March-April, 1986.

4. Brobeck, John R., Orr E. Reynolds, and Toby A. Appel, eds. History of the American Physiological Society, 1887-1987: The First Century. Bethesda, MD: American Physiological Society, 1987.

5. Brooks, Chandler McC. The development of physiology in the last fifty years. Bulletin of the History of Medicine 33: 249-262, 1959.

6. Cranfield, Paul F. Microscopic physiology since 1908. Bulletin of the History of Medicine 33: 263-275, 1959.

7. Davenport, Horace W. Physiology, 1850-1923: The View from Michigan. Supplement to The Physiologist, 24(1), 1982.

8. The Excitement and Fascination of Science. 2 volumes. Palo Alto, CA: Annual Reviews, Inc., 1965-1978.

9. Fulton, John F. and Leonard B. Wilson, eds., Selected Readings in the History of Physiology. Springfield, IL: Charles C. Thomas, 1966.

10. Fye, W. Bruce. The Development of American Physiology: Scientific Medicine in the Nineteenth Century. Baltimore: Johns Hopkins University Press, 1987.

11. Geison, Gerald L. ed. Physiology in the American Context, 1850-1940. Bethesda, MD: American Physiological Society, 1987.

12. The Physiologist. Many historical articles and departmental histories have appeared in this bimonthly journal, published since 1957 by the American Physiological Society.

13. Rothschuh, Karl E. History of Physiology, translated and edited, with a new English bibliography by Guenter B. Risse. Huntington, NY: Robert E. Krieger, 1973. See especially pp.318-325 on "American Physiology, 1870-1930."

14. Warner, John Harley. Physiology. In: The Education of American Physicians: Historical Essays, ed. by Ronald L.Numbers. Berkeley: University of California Press, 1980, pp.48-71.