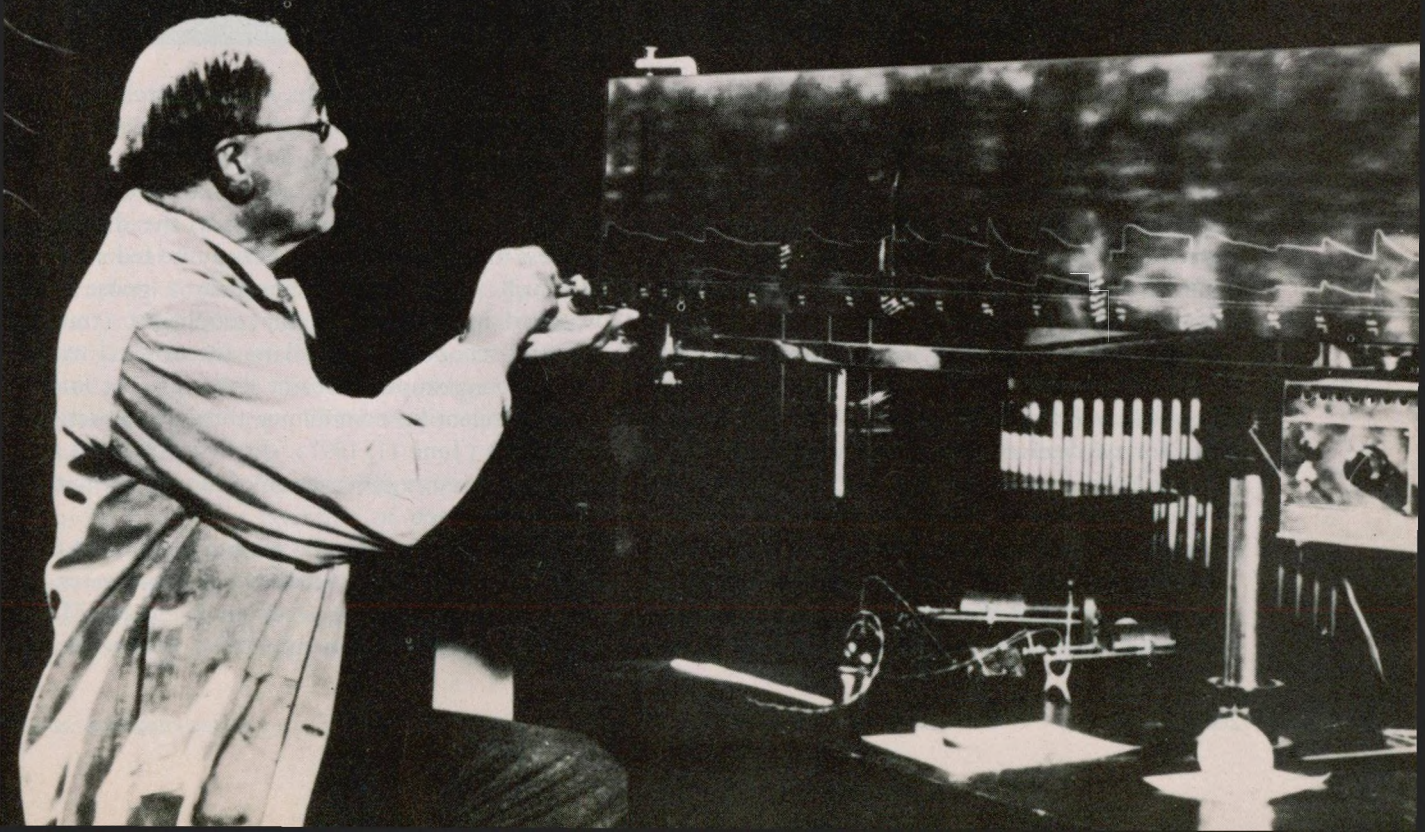
PIONEER PHYSIOLOGIST

Dr. Walter Cannon in his laboratory at Harvard University studying kymograph recordings of the processes of digestion.



A century ago two events occurred that were to mark the emergence of physiology as a major branch of medical science in the United States. One was the establishment at Harvard University of the first full-time professorship of physiology, a chair first held by Dr. Henry Pickering Bowditch. The second was the birth in Wisconsin of Dr. Bowditch's future pupil and successor, Walter Bradford Cannon who was to gain international recognition while still a medical student for his innovations in physiologic research.

START. Walter Bradford Cannon was born on October 19, 1871 in a small town on the upper Mississippi River, Prairie du Chien, where his father, Colbert Hanchett Cannon, had met and married Sarah Wilma Denio, who had come from her home in Elba, Minnesota, to teach in a public school. Walter was 10 when his mother died of pneumonia.

His father, who had little education, served as

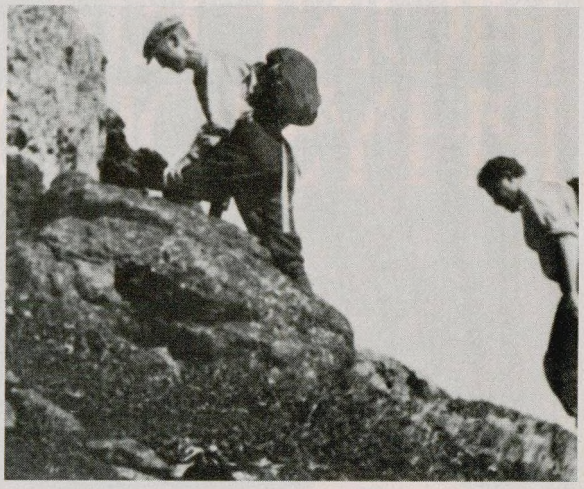
a railway traffic manager, but was more interested in agriculture and medicine. He read extensively in both subjects, and urged his son to become a doctor. He provided a library for Walter and his three younger sisters, refused to buy ready-made toys for the boy but helped him to build his own, encouraging a manual skill which later proved useful in laboratory work.

Cannon attended primary and grammar schools in Milwaukee and St. Paul, but after grammar school his father put him to work in a railroad office for two years because he thought the boy had not been attentive enough to his studies. At 17 Walter entered St. Paul high school and completed the course in three years.

During his high school years he colsely followed the controversy between the defender of Darwinism Thomas Huxley, and the bishop of Peterborough. Under the influence of Huxley's agnosticism he rebelled against his Calvinist upbringing and, to the distress of his father, withdrew from the Church.

With the encouragement of a Harvard alumnus and support from a high school teacher who helped him to secure a freshman scholarship, Cannon entered Harvard in 1892. His father helped to give him a start with a contribution of $180. Thereafter he supported himself through four years of college and four years of medical school by scholarships and outside work. He graduated *summa cum laude* in 1896 and at the end of his first year in medical school was granted a master's degree because he had completed a number of graduate courses in addition to those required for the B.A.

As an undergraduate he had been attracted to a career in neurology and psychiatry, and in medical school he closely followed the courses on dis-



eases of the nervous system, but a research project he began as a first-year medical student redirected his interest toward physiology. At the suggestion of Dr. Bowditch he pioneered in using the newly discovered x-rays to study the digestive process in animals. In his first study he fed a bolus of mush mixed with bismuth to a goose and watched its progress in the esophagus (transit time: 12 seconds). A year later the original work of the young student became known to the international scientific community through his article in *Science* (June 11, 1897), the first published account of an x-ray observation of movement in the alimentary tract.

In his fourth year he was invited to conduct the course in comparative anatomy of vertebrates at Harvard and Radcliffe; after receiving his M.D. degree in 1900 he was appointed instructor in

physiology in Harvad's medical school; he became assistant professor two years later and in 1906 succeeded Dr. Bowditch as George Higginson professor of physiology.

Before graduating from medical school he had published several additional papers on the mechanics of digestion, and in the following years he continued his observations on gastrointestinal motility.

He next undertook a study on the neuromuscular functions in the digestive process, publishing accounts of the myenteric reflex, the receptive relaxation of the stomach as an adaptive reflex mediated by the vagus nerves, and the role of the vagi in maintaining the normal functioning of the gastric neuromusculature. In an extension of the work of Pavlov, he suggested that the arousal and satisfaction of appetite produces through a vagal discharge to the stomach not only the psychic secretion of gastric juice discovered by the Russian physiologist but also a physiologically important psychic tonus of the gastric musculature. He ended his studies of the digestive tract with a demonstration in 1912 that human hunger pangs are associated with cramplike contractions of the stomach wall.

Opposite: Dr. Cannon with surgeons Fred T. Murphy and Harvey Cushing in New Hampshire. Photograph of Drs. Cannon and Murphy mountain climbing was taken by Dr. Cushing. Left, Dr. Cannon is seen as a medical officer in France in 1918. Below, in Boston in 1929 he poses with Russian physiologist Ivan Pavlov.

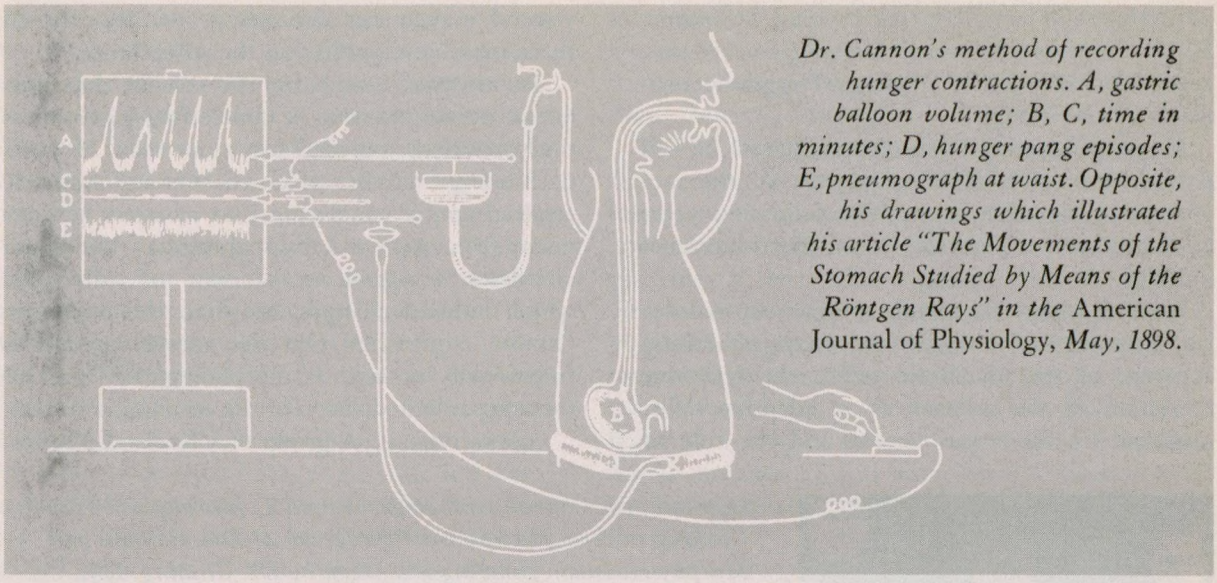
ENDOCRINES. Frequent interruptions of his observations because of cessation of visceral movements during emotional disturbance in the experimental animals led Cannon to investigate the overall functional significance of the sympathetic nervous system. He discovered that inhibition of visceral movements depends preponderantly on the sympathetic outflow in the splanchnics.

An intensive search for the role of the autonomic nervous system in controlling gastrointestinal functions, pursued for more than 20 years with a large number of coworkers and students, resulted in the conclusion that in stress (excitement, pain, asphyxia, hypoglycemia) the blood circulates a significant amount of adrenaline which induces changes useful to the organism. Cannon emphasized that the adrenal medula is functionally as well as morphologically part of the sympathetic division of the autonomic system.

CONTROVERSY. A group of Cleveland physiologists, who had found adrenaline output increased by electric stimulation, denied that physiologic stimulation during stress, pain or excitement would increase the secretion.

Cannon responded to this challenge by devising a new and more precise method of measuring adrenin, the denervated heart. Cut off from the nervous system, the heart remains so sensitive to adrenin circulating in the bloodstream that it beats faster when adrenin is increased by as little as one part in 1.4 million parts of blood; in asphyxia adrenin secretion and the heart beat were both increased.

These demonstration showed that the rapid acceleration in heart beat (70-90 extra beats per minute) in excitement entirely disappeared when the secretions of the adrenal glands and the liver were cut off, but a belated and less pronounced increase



Dr. Cannon's method of recording hunger contractions. A, gastric balloon volume; B, C, time in minutes; D, hunger pang episodes; E, pneumograph at waist. Opposite, his drawings which illustrated his article "The Movements of the Stomach Studied by Means of the Röntgen Rays" in the American Journal of Physiology, *May, 1898.*

in the heart rate (about 30 beats per minute) persisted after elimination of adrenal and hepatic discharges.

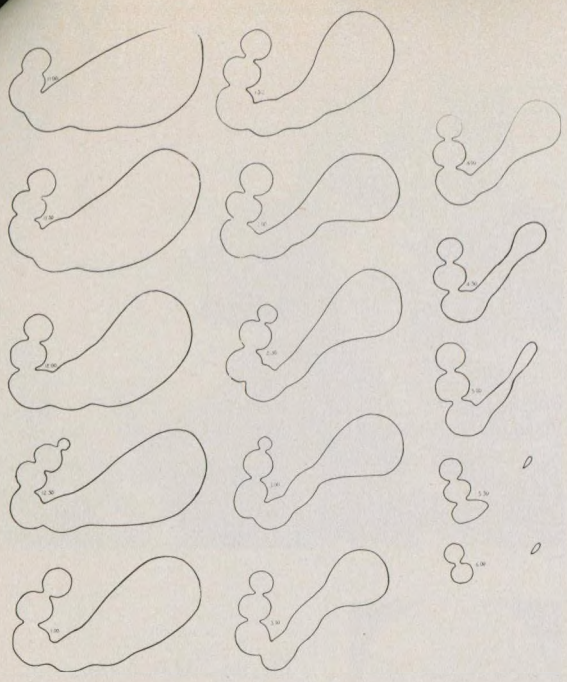
This was a puzzle and Cannon's team solved it by showing that by stimulating the sympathetic nerves of any region they could induce the faster heartbeat. Shutting off the blood flow through the region under stimulation deferred the effect on the heart rate until circulation was restored. The conclusion: the parts of the body subjected to sympathetic nerve impulses produce a substance, named sympathin by Cannon, which circulates in the bloodstream and increases the heartbeat. Cannon and his collaborator, the Mexican physiologist Arturo Rosenbleuth, summarized the work on chemical mediation in the book *Autonomic Neuro-Effector Systems.*

Research on animals without a sympathetic nervous system provided support for Cannon's concept that the sympatho-adrenal system plays a major role in keeping the body fluids in a relatively stable state when that state is jeopardized by changes in the environment or by internal changes due to muscular work. In an extension of Claude Bernard's view that normal existence of the higher animals depends on constancy of the *milieu intérieur*, Cannon described in *The Wisdom of the Body* the physiologic mechanisms involved in the preservation of an essential physio-chemical balance, for which he suggested the now generally accepted term of homeostasis.

SHOCK. The entry of the United States into World War I interrupted Cannon's laboratory work and at 46 he enlisted in the Harvard hospital unit. At his own request he investigated shock among the seriously wounded in Béthune, France, a center for these studies. For emergency treatment of badly wounded soldiers whose high respiratory rate indicated acid accumulation in the blood, he injected a sodium bicarbonate solution into the bloodstream and achieved dramatic improvement in respiratory rate, pulse, and blood pressure. Experience showed that the beneficial effects were only temporary, and the acidosis only a late, secondary phenomenon: the primary condition was inadequate oxygen supply to the tissues owing to deficient blood circulation.

After studying shock during his two years of war service and three years after the war, Dr. Cannon published the results of his studies in the book *Traumatic Shock* (1923). Two decades later he resumed his work in this field as chairman of the National Research Council's Committee on Shock and Transfusion, which defined safe methods of drying blood plasma for use of the armed forces in World War II. It also initiated research in preparing plasma albumin as a more concentrated substitute for dried plasma, especially valuable in naval ships with limited storage space.

INTERNATIONAL. The close ties Cannon formed with French, Belgian and British scientists during World War I were renewed and extended a decade later, when he lectured as exchange professor at the Sorbonne during the second half of the academic year of 1929. During that European stay he was made a *doctor honoris causa* by the universities of Paris, Liege, Strasbourg, Barcelona and Madrid. In Madrid he first met Juan Negrín, professor of physiology and acting dean of the medical school, with whom he had previously exchanged scientific papers. The two met again at an international physiological congress in 1935,



after Dr. Negrín became premier of the Spanish republic. Cannon showed his support for the government by serving for two years as national chairman of the Medical Bureau to Aid Spanish Democracy, which sent medical personnel, ambulances and hospital equipment to loyalist Spain.

On a visit to the Peking Union Medical School in 1935 he witnessed the encroachment of Japanese military power in China. Out of sympathy with the Chinese effort to resist the invaders he became affiliated with the Bureau for Medical Aid to China and the United China Relief before the United States became a military supporter of China in World War II.

Besides visiting China in 1935 Cannon attended an international physiological congress in the Soviet Union and there saw for the last time his friend Ivan Pavlov, then 86, whom he had first met in the United States in 1923 and later entertained in his home in Cambridge. On his return home Cannon, who was at that time the only person elected to membership in both the National Academy of Sciences of the United States and the Academy of Science of the U.S.S.R., accepted the presidency of the newly formed American-Soviet Medical Society which was specially effective in maintaining liaison between scientists of the two countries during World War II.

In 1939 he was elected to the foreign membership of the Royal Society. In 1942 he became foreing secretary of the National Academy of Sciences and in this post devoted himself particularly to improvement of scientific relations with Latin America.

TEACHER. As a senior medical student Cannon published an article in *The Boston Medical and Surgical Journal* on "The Case System of Teaching Medicine," which he advocated instead of the prevailing method of four hours of continuous lectures and recitations. He contended that this would stimulate interest, enable students to correlate the scientific and clinical sides of medicine, and train them to distinguish between important and unimportant symptoms, which could not be learned from textbooks that listed symptoms without indicating their relative weight or importance. Harvard adopted the case method, and several other medical schools followed suit.

During the 36 years that Cannon served as George Higginson professor of physiology, a disciple, Joseph Charles Aub, who became professor of research medicine at Harvard, declared: "His outstanding success was not due to his lectures; it was due to the clashing of intellects which he fostered; and to the discussions, as though among equals, between students and master. From my own class at the medical school, six men were stimulated sufficiently so that they finished problems worthy of publication in their first year at school, and they all became imbued with the excitement for new knowledge."

REFLECTIONS. Cannon summed up in his final book *The Way of An Investigator* (1945) his most significant experiences and his guiding principles in research (with due attention to the role of "hunches"); he evaluated the qualities essential to leadership in research, and pointed to the positive value of controversy free from personal antagonism and aimed only at scientific truth.

In this book he also recalled his activities in defense of medical research against the distorted strictures of the antivivisectionists. After a virulent antivivisectionist attack on the Rockefeller Institute in 1908, the American Medical Association organized a special defense committee in support of medical research, which Professor Cannon headed for 18 years. He emphasized that researchers in opposing restrictive legislation "act for the public to protect from ruthless interference a method of investigation which has done more for mankind, by bringing release from devastating diseases and from premature death, than any other human endeavor."

TELEOLOGY. His observations of the numerous organic adjustments that promote bodily welfare led him to adopt a teleologic view of bodily reactions, a process that he considered purposive but not conscious and therefore not implying "intelligent foresight working toward a predetermined end." He also affirmed the belief that all phenomena have a natural explanation: "As science has

become more and more exact it has explained obscure processes and mysterious influences. The explanations have in fact liberated mankind from fettering superstitions and baseless fears." He also expressed the hope that the methods of maintaining bodily stability "may have suggestive importance in showing what might be done in the social organism to assure its stability."

PERSONALITY. A year after graduation from medical school the young physiologist married Cornelia James, whom he had known at St. Paul high school and later when she attended Radcliffe. On their wedding trip the young couple paddled down the St. Croix River in Wisconsing in an Indian birchbark, continued their adventures in the United States forest reserve in Montana (now Glacier National Park), where they climbed a peak never before scaled, later named Mt. Cannon in recognition of their exploit. Canoeing and mountain climbing remained for many years the favorite diversions of the Cannons.

In the family summer home in New Hampshire the researcher found relaxation in making furniture and toys for the children (four girls and one boy). Advised to seek less strenuous recreation than canoeing and mountain climbing, he took up sculpture, entered a portrait of his youngest daughter Helen in a Boston exhibition of a physicians' art association, and won an award. He later recalled: "To my surprise and delight I received about eight inches of blue ribbon, a token which I have prized as much as any other honor that has ever come to me."

He also engaged in gardening because he found that like fishing it was favorable to the gestation of scientific thoughts. At concerts of the Boston Symphony orchestra he likewise found himself more immersed in scientific speculation than in music appreciation.

Associates and students have described him as entirely free of ostentation. For many years he rode a bycicle, then used a Model T Ford until replacement parts were no longer available, finally replacing the dilapidated car with a Model A. Foreign students were much impressed with his ready approachability in contrast with the rigid formality of European professors. In 1931, when funds were raised for a portrait to mark his 25th anniversary as George Higginson professor of physiology, he insisted on posing in a plain laboratory coat.

In the spring of 1897 Cannon had disclosed the peeling of layers of skin from his hand to Dr. Bowditch, who cautioned him that it might be related to the use of x-rays in his research. To protect himself he inclosed the fluoroscope tube with lead except for a small aperture at the top to permit passage of the rays; he worked with this apparatus until 1908.

Dr. and Mrs. Cannon at their New Hampshire summer home where they did most of their writing. Mrs. Cannon was a novelist and author of children's books. Dr. Cannon's portrait of his daughter Helen, left, won him an award at a Boston exhibition of a physician's art association.

Twenty-three years after he had ended x-ray research there appeared itching and red papular lesions on his back, chest, thighs, knees, elbows. Biopsies of the lesions showed mycosis fungoides. Radiation therapy was followed with vitamin therapy. An ulcerated lesion on the left wrist was excised in 1940 and found to be a slow growing epidermoid carcinoma. A small recurrent basal-cell carcinoma beneath the right nares was excised in April, 1944.

Throughout the 15 years since the first manifestation of mycosis fungoides Cannon remained actively at work and continued to travel. In 1945 he spent three months in research in Mexico. In September of that year he suffered dyspnea accompanied by severe weakness, and died on October 1, of intercurrent pulmonary infection.

SUMMING UP. By a Cannon pupil: "Within the four walls of his laboratory he has crossed many frontiers, broken new and tough ground, settled in and then moved on to further fields, driven always by a searching spirit."