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GEORGE RICHARDS MINOT

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A Biographical Memoir by

W. B. CASTLE

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GEORGE MINOT was born in Boston, Massachusetts, on December 2, 1885, the eldest of three sons of Dr. James Jackson and Elizabeth Frances (Whitney) Minot. His ancestors had been successful in business and professional careers in Boston. His father was a private practitioner and for many years a clinical teacher of medicine as a member of the staff of the Massachusetts General Hospital. In the second half of the nineteenth century his great uncle, Francis Minot, became the third Hersey Professor of the Theory and Practice of Physic at Harvard; and his cousin, Charles Sedgwick Minot, a distinguished anatomist, was Professor of Histology there in the early years of the twentieth century. George Minot's grandmother was the daughter of Dr. James Jackson, the second Hersey Professor and a cofounder with John Collins Warren of the Massachusetts General Hospital, which opened its doors in 1821. Thus his forebears, like those of other Boston medical families, were influential participants in the activities of the Harvard Medical School and its affiliated teaching hospital.

George was regarded by his physician-father as a delicate child who required physical protection and nourishing food. Brief vacation visits to Florida provided escape, thought desirable for him, from the rigors of Boston winters. Most of a winter spent with his parents in southern California gave

further opportunity for outdoor life and amateur studies of butterflies. This led to the publication in 1902 of his first scientific paper, an early expression of his lifelong interest in natural history. George Minot's early education was at private schools in Boston in the "Back Bay" near the home in which he grew up. As a matter of course he went on to Harvard College, from which he was graduated in the spring of 1908. After a summer in Europe, despite anxiety about his physical capacity for the busy life of a doctor, he enrolled in the Harvard Medical School armed merely with the documentation that his college courses had included physics and chemistry.

During the summers of his second and third years in medical school Minot worked in an outpatient clinic operated by the faculty at the medical school for the benefit of employees and neighborhood residents. During his third year he achieved modest renown by demonstrating to the satisfaction of the medical staff of the Massachusetts General Hospital that a patient considered to have pernicious anemia was in reality suffering from a congenital hemolytic anemia. Among his teachers at the medical school were Walter B. Cannon in physiology, Otto Folin and Lawrence J. Henderson in biochemistry, Theobald Smith in comparative pathology, Richard C. Cabot and Henry A. Christian in medicine, and Maurice B. Richardson in surgery. Christian's systematic lecture presentations of medical topics were admirably balanced by Cabot's novel "case teaching" exercises, in which students in their clinical years participated actively. This educational technique, employed earlier in the Harvard Law School, had been proposed by Cannon when he was a senior medical student at Harvard. It was during Minot's final year that he first showed a serious interest in hematology by enrolling in an elective course in clinical pathology given at the medical school by Dr. J. Homer Wright, inventor of the well-known polychrome stain for blood films.

A few months after graduation young Dr. Minot began a

coveted appointment as medical "House Pupil," as the interns at the Massachusetts General Hospital were then called. There, while working on the East Medical Service under Dr. David Edsall, the recently appointed Jackson Professor of Clinical Medicine at Harvard, he displayed increasing interest in diseases of the blood. For some reason, perhaps the familial insistence on the importance to health of good food, he began taking meticulous histories of the dietary habits of his anemic patients. He also exhibited an active interest in the laboratory findings, especially in the microscopic examination of stained films of their blood. Sixteen months later, at the end of November 1913, Minot completed his tour of duty as "Senior" and was borne in traditional fashion to the front door of the hospital in a wheelchair propelled by his "Junior." Among recent graduates of the medical services he was in good intellectual company with such future distinguished physicians as James Howard Means and Paul Dudley White. Like them he was advised by Dr. Edsall to go elsewhere for further training before returning to the Massachusetts General Hospital with the prospect of becoming a junior member of its staff.

It was soon arranged that Minot should go to Johns Hopkins and serve as Resident Physician under Dr. William S. Thayer, to whom Minot's special interest in patients with hematological problems soon became apparent. Consequently, after a few months Minot transferred his activities to the laboratory of William H. Howell, Professor of Physiology, whose principal research interest was in the coagulation of the blood. With another young physician from Boston, George Denny, Minot published in 1915 an article demonstrating that circulatory stasis during perfusion of the liver of the dog produced an increase in the antithrombin content of the blood in the hepatic vein. This insight, together with studies by others of his pupils, led three years later to Howell's successful preparation from liver of the valuable anticoagulant drug, heparin. Minot's other

work, on the prothrombin and antithrombin factors involved in the abnormal clotting of the blood of various patients, would be interpreted somewhat differently today. However, oxalated blood samples from jaundiced patients with bleeding tendencies were observed to show abnormal delay in coagulation after recalcification. This Minot and Denny correctly attributed to a diminished level of prothrombin as then defined.

When Minot returned to Boston, in January 1915, he received appointments in the Harvard Medical School and in the Massachusetts General Hospital as Assistant in Medicine with a small stipend as a Dalton Scholar. In June he married Marian Linzee Weld in the Unitarian church in Milton, Massachusetts. At the hospital, Edsall's influence had brought to Boston the new era of scientific investigation of disease already begun in Baltimore and New York. In addition to participation in the care of patients Minot, as well as James H. Means and Paul D. White, who had returned from their studies abroad, and shortly Walter W. Palmer and James L. Gamble were attempting to apply scientific methodology to bedside medicine with the help of various types of simple equipment in improvised laboratories. This atmosphere of young inquiry was highly appropriate for Minot, who had an inherent faith in causality that made him optimistic that scientific understanding would lead to a bright future for clinical medicine. He found a bench with north lighting suitable for microscopic work in a small room next to the inner sanctum of the hospital's irascible pathologist, Dr. Wright. This was the man who had discovered that blood platelets were formed by large specialized cells in the bone marrow.

At that time the study of the blood of patients with anemia, leukemia, low platelet levels, and other abnormalities depended largely on the enumeration of the corpuscles and the microscopic examination of peripheral blood films stained by the use of the aniline dyes introduced by Ehrlich. This permitted recognition under the oil immersion lens of morphological

abnormalities of the blood's three formed elements: red cells, white cells, and platelets. In hematology the only useful drug was iron, but a recent therapeutic advance was the transfusion of fresh blood. This, owing to the work of Landsteiner, Moss, and others in enabling the identification of suitable donors, had become a relatively safe, though technically demanding procedure.

In the fall of 1915 Minot began work with Dr. Roger I. Lee, Clinical Professor of Medicine at Harvard and Chief of the West Medical Service at the Massachusetts General, in an attempt to learn more about the function of blood platelets—insignificant particles, but already thought to be intimately involved in hemostasis and blood coagulation. After meticulous washing in physiological saline, a suspension of normal platelets derived from blood samples rendered incoagulable by addition of oxalate was found by Lee and Minot to be seventy-five times as efficacious as a similarly prepared suspension of hemophilic platelets in shortening the prolonged clotting time of fresh hemophilic blood plasma. This last was derived by centrifugation of fresh blood in chilled, paraffin-coated tubes. Thus encouraged, the two physicians gave a transfusion of normal blood to a hemophilic patient and found that it caused a prompt reduction of the patient's prolonged blood clotting time. The effect lasted for three days, an interval then considered to correspond to the life-span of the platelet. From these observations they concluded, understandably but erroneously, that the platelets in hemophilia were defective. This interpretation, because of the impossibility of completely freeing platelets from a subtle plasma factor, was only corrected thirty years later when work in Minot's laboratory at the Boston City Hospital showed that platelet-free, citrated, normal blood plasma could shorten the coagulation time of hemophilic blood owing to the presence of a specific globulin.

From the Massachusetts General Hospital Minot published

papers describing and classifying patients with anemia and markedly reduced numbers of blood platelets. He pointed out that a faltering bone marrow, in addition to producing too few new red cells, was often unable to sustain a normal number of circulating granular leukocytes and platelets. In clinical instances of low levels of platelets associated with normal production of red cells and leukocytes, he suggested that excessive destruction of platelets was responsible. He speculated that the great increase in platelets sometimes following splenectomy was due to enhanced production by an uninhibited bone marrow. Although today the role of the spleen as combined pool and filter in causing low platelet levels is better understood, the mechanism of the sometimes prolonged increase in numbers of platelets after surgical removal of the spleen is not. In an extensive study in 1916 of a young girl with idiopathic purpura hemorrhagica, who eventually bled to death because of her low level of blood platelets, Minot sought without success for evidence of platelet-agglutinating or -lysing properties in her serum. Even today these are detected only with great difficulty and only in some of such patients. In other work, with Dr. Wright, Minot studied the plasma factors involved in the so-called viscous metamorphosis of platelets, a step preliminary to their participation in normal blood-clot formation.

While in Baltimore in 1914 Minot had studied the effect of splenectomy in a patient with pernicious anemia, then almost invariably a fatal disease although for some months subject to apparently spontaneous remissions and discouraging unexplained relapses. The result of removal of the spleen in the patient had been temporarily favorable. Three years later in Boston Minot joined Lee and Beth Vincent, a surgical colleague, in studies of fifteen such patients skillfully subjected to splenectomy as a last resort. In some of these patients the results were beneficial for a few weeks or months, but they failed to be of a permanent value in any. However, Minot's careful ob-

servations of the peripheral blood were of great significance to his future work on the successful dietary treatment of pernicious anemia. Wright had shown Minot a method of supravital staining that the latter applied to the demonstration of reticulocytes in films of the peripheral blood of these anemic patients. That reticulocytes were newly formed red cells released by the bone marrow, rather than degenerating forms as originally supposed by Ehrlich, had first been demonstrated by Theobald Smith in 1891 in bleeding experiments with Texas cattle. Vogel and McCurdy in 1913 had proposed that anemias could be classified as being due either to increased blood destruction or blood loss with an active marrow response (increased reticulocytes) or being due to bone marrow inadequacies of various sorts (decreased reticulocytes). Now, Minot stated that in pernicious anemia "curves plotted from frequent observations [of the number of reticulated red cells] are reliable indicators of bone marrow activity and [increases] are the forerunners of increased red cell counts and clinical improvement."

When during World War I Base Hospital No. 6, organized by the Massachusetts General Hospital, sailed from New York for overseas duty, the work of the hospital staff of doctors and nurses left behind was greatly increased. Minot was directly involved with this extra burden of patient care as well as with his laboratory research and private practice. In addition, he was employed for a short time as Contract Surgeon by the army in examining recruits. He soon found much more interesting contributions to make to the war effort. At the suggestion of Dr. Alice Hamilton, then the only woman on the Harvard Medical Faculty and already an authority in industrial medicine, the army asked Minot to investigate the anemia of New Jersey ammunition workers engaged in filling shells with trinitrotoluene. He discovered the coexistence of methemoglobin and signs of a red cell-destroying process. A similar investigation concerned with manufacture of smokeless powder disclosed

little but the anesthetic effects of various degrees of exposure to the ethyl ether used as a solvent. In the fall of 1918 Minot was involved in a desperate effort to prevent the spread of influenza among the students of Harvard College, many of whom were candidates for the Student Army Training Corps. Then in another month the epidemic waned, and the Armistice was signed.

After the war Minot continued to study patients with blood diseases at the Massachusetts General Hospital, but with increasing involvement in work at the Collis P. Huntington Memorial Hospital, where he had been appointed Assistant Consulting Physician in 1917 and Consulting Physician in 1919. Meanwhile, another essay in industrial medicine disclosed interesting changes in the blood of workers in an artificial silk factory. This led to a report in 1921 that an increase in the large mononuclear cells of the blood was a clear signal of liver damage to come, if exposure to tetrachlorethane—the volatile solvent inhaled—was not discontinued. The results of an attempt with Dr. Chester M. Jones to establish as a clinical entity the sporadic cases of infectious jaundice that appeared subsequent to the epidemics of World War I was published in 1923. Here, too, immature and abnormal lymphocytes and mononuclear cells appeared in the blood and resembled those seen in cases of so-called glandular fever or infectious mononucleosis. Indeed, at the time no serological test was available to discriminate glandular fever from infectious jaundice with certainty.

From the time of his first appointment at the Huntington Hospital Minot found himself becoming evermore interested in the special purposes of this "cancer hospital." Supervised by the Cancer Commission of Harvard University, composed of six distinguished physicians with Ernest E. Tyzzer as Director, the hospital had opened in 1912 for the purpose of providing what would be called today a "clinical research facility" where,

in addition to the latest diagnostic and therapeutic modalities for the care of patients, basic research in the nature and cause of cancer and neoplastic blood disease could be conducted. Located close by the Harvard Medical School and the new Peter Bent Brigham Hospital, the Huntington Hospital was in no sense an institution merely for custodial care. Minot saw in this hospital setting a rare opportunity to extend his interest into new areas of blood disease with possible valuable repercussions on what he already knew. Moreover, in accepting the original appointment he was attracted by the delightful personality, broad clinical and research experience, and scholarly wisdom of the hospital's Consulting Physician, Dr. Francis W. Peabody. At the Huntington, Minot's clinical and research contributions were highly valued by his colleagues and by the Cancer Commission. When Peabody became Director of the new Thorndike Memorial Laboratory at the Boston City Hospital, in 1923, Minot was appointed to succeed him as Chief of the Medical Service at the Huntington.

At the cancer hospital Minot became impressed with a relationship between polycythemia vera, a disease producing too many red blood corpuscles, and myelogenous leukemia, a form of cancer of the blood in which too many abnormal white cells are formed. With his associates, Drs. Thomas E. Buckman and Raphael Isaacs, he published careful descriptions of the blood findings, clinical course, and results of x-ray treatment in myelogenous and other varieties of chronic leukemia. He concluded—as is still true today, with modern x-ray and chemotherapy—that the benefits of treatment were chiefly to extend the period of reasonably good health, rather than to prolong the life of the patient. In another classical paper, in 1924, Minot and Dr. Roy G. Spurling described the different durations of the effects of x-ray treatment on the formed elements of the blood of patients with localized cancer, including the value of the number of circulating white corpuscles as an indication of the

amount of such radiation that could safely be applied. It was shortly before this time that Dr. Minot began to urge his private patients with pernicious anemia to improve their diets.

Meanwhile, a serious change in Minot's health and personal life had taken place. In October 1921, after noting for some days feelings of fatigue, weakness, and thirst, he tested his urine and found sugar. The next day Dr. Elliott P. Joslin confirmed the fact that at the age of thirty-six Minot had developed severe diabetes, for which the treatment was currently a form of semi-starvation. In those dark days Minot's cousin and medical school classmate, Dr. Francis M. Rackemann, and his wife gave cheerful support and wise counsel to the Minot family. The discovery of insulin by Banting and Best, announced in 1922, came in the nick of time to save Minot's life. After a year of dietary restriction and weight loss, during which Minot managed to struggle each day to the hospital, Dr. Joslin was able to secure for his patient small amounts of insulin. For the rest of his life Minot ate no food at home that was not weighed or measured and recorded. When dining out, advance knowledge of the menu aided him in estimating calories and carbohydrates. His wife, a charming and intelligent woman, was indispensible in sustaining the strict balance of dietary intake and insulin injections prescribed by Dr. Joslin.

Under these circumstances, it was a distinct advantage to Minot to be able to continue his private practice as a member of the small group of physicians that he had joined at the invitation of Dr. Edwin A. Locke in September 1921, shortly before the onset of his diabetes. This arrangement provided office space at 311 Beacon Street, with shared secretarial services and a laboratory with a technician trained to perform the usual simple studies of patients' blood and urine. Included in the group was a succession of younger physicians who in this way were entering the practice of medicine in Boston. Among them was Dr. William P. Murphy, who later was asked by Minot to be his col-

laborator in an effort to treat pernicious anemia by dietary means.

This disease was first briefly reported to colleagues in London in 1849 by Dr. Thomas Addison of Guy's Hospital. In 1855 Addison published, in the same monograph with his classic account of destructive disease of the suprarenal capsules, a description of an "idiopathic anaemia." His description, however, included none of the triad of clinical features that would have identified pernicious anemia, then as now, without benefit of laboratory studies: sore tongue, jaundice, and, especially, neurological manifestations, such as tingling and numbness of fingers and toes progressing in some patients to instability of gait and paralysis. Nevertheless, Addison's contemporaries seem to have recognized similar cases, perhaps at first retrospectively because the lack of explanatory postmortem findings, such as hemorrhage, tumor, or gross disease of any organ, served to separate Addison's anemia from other varieties.

By the beginning of this century it was recognized that the peripheral blood picture was characterized by the presence of large red cells well filled with hemoglobin. This feature of the blood was well known to Minot, as was the paucity of young red cells (reticulocytes) and frequently also of white corpuscles and platelets. Thus the findings in the peripheral blood, which were suggestive of diminished production of red cells, presented a puzzling contrast to the jaundice, increased iron deposits in liver and bone marrow, and large fecal excretion of bile pigments that were regarded as characteristic of increased red cell destruction. Indeed, in 1916 Minot and Sellards had demonstrated that, in pernicious anemia, an endogenous hemolytic process presumably interfered with the similar catabolism of experimentally injected hemoglobin. In 1922 Dr. George H. Whipple had suggested that the excessive bile pigment excretion might be a result of the breakdown of hemoglobin from other than the diminished number of circulating red cells in the

anemic patient. Nevertheless, only with the modern advent of isotopic biological labels for hemoglobin during its formation has it been possible to demonstrate that the disturbed production of red cells in the bone marrow also involves excessive destruction of red cell precursors, including reticulocytes, in the marrow. Today all of these abnormalities are quickly corrected by injection of vitamin B_{12}: The jaundice and anemia promptly diminish, the sore tongue heals within days, and progression of the spinal cord lesion is arrested.

This conversion of an almost inevitably fatal disease into one that is now perhaps the easiest of all to manage, and with the fewest complications, was initiated as a result of combined insights derived from animal experimentation and careful clinical observation. The story of this therapeutic triumph begins in 1918 with the work of Dr. George H. Whipple, who was experimenting at the Hooper Foundation in San Francisco with the effect of various foods on hemoglobin production in anemic dogs. Later, as Professor of Pathology and Dean of the new University of Rochester School of Medicine and Dentistry, Whipple and his principal associate, Dr. Frieda Robscheit-Robbins, had evolved a reliable protocol for experiments with dogs whose hemoglobin concentration in the circulating blood was kept at about half the normal value by bleeding at regular and frequent intervals. By 1923 they had demonstrated that this chronic anemia provided a strong stimulus to hemoglobin regeneration by the animal's bone marrow to which, however, the marrow was unable to respond significantly unless supplements such as liver, pork muscle, or spinach were added to the basal diet. Of these, liver was the most potent. Fortunately, it was not until a decade later that it was realized that the available iron present in the dietary items tested had had the most significant influence on hemoglobin formation. This fact had been obscured by the variable assimilability of the food iron. Consequently, Whipple's early experiments left open the possibility

that liver contained something novel that might benefit other types of anemia in man. In Minot and Murphy's hands this prospect was amply confirmed in 1926. It was not until 1932 that workers in Minot's laboratory showed in patients with iron deficiency anemia, often due to chronic blood loss as in Whipple's dogs, that when soluble iron was given parenterally it was quantitatively utilized in the production of new hemoglobin. Whipple confirmed this finding with intravenous injections in his experimental dogs, and thereafter he and his associates wrote yet another new chapter in experimental hematology by introducing the use of radioactive iron to the study of anemia.

Whipple's experimental observations were the immediate stimulus for attempts in the early twenties in more than one American clinic to treat pernicious anemia by dietary means. However, physicians familiar with pernicious anemia considered the modest improvement that sometimes followed to be no greater than what occurred in the so-called "spontaneous remissions" of the disease. Minot, however, had the advantage of a prior clinical suspicion that "something in food might be of advantage to patients with pernicious anemia." Ever since he had been a house officer at the Massachusetts General Hospital it had been his custom to cross-question such patients as to the details of their dietary history. In this way he came to believe that pernicious anemia patients often had lived on unbalanced diets for many years and sometimes developed a distaste for meat shortly before the onset of their fatal illness. To him the high fat content of the diet of some of these patients was consistent with the then-current notion of a blood-destroying effect, possibly the result of intestinal putrefaction. The idea of a relationship between good food and good health was a family tradition and instinctive with him; and the then-recent evidence from the work of Gibson and Howard that diets rich in protein and in iron could restore positive nitrogen and iron

balances in pernicious anemia was at least consistent with his clinical impression of a prior nutritional defect. Finally, the quantitative dietary regulation required of him in the management of his own illness exemplified the rigorous program essential for a thorough therapeutic trial of dietary improvement in pernicious anemia.

At any rate, Minot's response to the suggestion provided by Whipple's work was to begin, during 1922, efforts to improve the diets of a few private patients with pernicious anemia. In some of these patients Minot thought that he detected clinical signs of improvement. This led to more detailed study of hospitalized patients, in which he and Dr. Murphy employed a regimen, "rich in iron and purine derivatives," containing 100–240 grams of liver, 120 grams of "muscle meat," leafy vegetables, "especially lettuce and spinach," fruit, and egg and milk. This was a large order, especially for patients with the characteristically poor appetite of the established disease, and it was by no means successfully achieved in their early efforts. Moreover, the dietary regimen was regarded skeptically by the few other physicians who knew about the work, and its application strained the patience of hard-working hospital dietitians and nurses. Yet by 1925, with the stout assistance of Dr. Murphy, the dose of lightly cooked liver was increased in some patients to an "optimal," though sometimes nauseating daily amount. The clinical improvement in these patients became regular and impressive, especially in one of them who really enjoyed eating liver and did so with enthusiasm.

Eventually, on May 4, 1926, Minot and Murphy reported their observations on forty-five patients to the Association of American Physicians, noting that the condition of all "became much better rather rapidly, soon after commencing the diet." Although admitting that these consistent improvements in health in their own series of cases "may not last longer than those of others," they felt it wise to urge pernicious anemia

patients to take a diet of the sort described. The subsequent discussion, as recorded, suggests only limited appreciation of the momentous advance clearly defined by the description of the regular and striking improvement in this large group of patients. Indeed, the fact that Minot and Murphy made no report until this number had accumulated seems remarkably conservative. Perhaps this delay was in order to make the initial presentation of the successful control of a hitherto fatal malady to the most distinguished audience in American medicine.

The close correspondence between the initiation by their patients of the special diet and the beginning of the clinical improvement a few days later was clearly apparent to Minot and Murphy. In many of the later patients a more objective criterion of the prompt antianemic efficacy of the diet was provided by the daily enumeration of the newly formed reticulocytes that appeared within a few days in the patients' blood. That the significance of an orderly augmentation of these young forms as an index of enhanced red cell production by the bone marrow was well known to Minot as early as 1916 has already been mentioned. Moreover, in 1923 Minot and Sampson had refuted the claim that germanium dioxide was a useful remedy for anemia by showing that it lacked ability to cause reticulocyte responses in experimental animals or in man. In 1927 the significance of the reticulocyte reaction as a therapeutic index in the treatment of pernicious anemia was fully discussed by Minot in a presentation concerning the hematopoietic effects of the first liver extract.

Referred to by Minot and Murphy in their initial reports in 1926 merely as a "special diet" for the treatment of pernicious anemia, by 1927, as shown by the titles of other articles, liver had been recognized by them as the essential ingredient of the diet. In that year appeared the first of a series of articles based on collaborative work with Edwin J. Cohn and his associates under the title "The Nature of the Material in Liver Effective

in Pernicious Anemia." This development had arisen from Minot's desire to provide a more convenient means of administering the active ingredient of liver in treatment and, if possible, to learn its exact nature. He discussed these objectives with Dr. Cohn, who was Professor of Physical Chemistry at the Harvard Medical School. It was agreed that Cohn would undertake chemical analysis of liver with respect to its therapeutic activity in pernicious anemia, guided by clinical responses to successive experimental fractions to be supplied by him for tests of efficacy by Minot in patients with untreated pernicious anemia. Fortunately, the promptness of the reticulocyte response made it possible to determine within ten days whether or not an experimental fraction of liver was therapeutically active. Indeed, the reticulocyte method sometimes permitted the study of a single anemic patient to yield information about the comparative activity of two or more liver preparations. This technique required daily counts of reticulocytes during successive and contiguous periods of the uniform daily administration of one after another of the fractions to be tested. Through arrangements with colleagues, patients were so studied at several of the hospitals affiliated with the Harvard Medical School. The discomforts of whole-liver feeding were soon eliminated when it was shown that the active principle was water-soluble and that the bulk of the liver proteins were inert. Thereafter the biochemical methods first employed for further liver fractionation resembled those used by others for concentrating what was then called "water-soluble vitamin B."

So began the protracted effort to identify the nature of the principle in liver that was active in pernicious anemia, an effort that engaged the attention of clinicians and scientists on both sides of the Atlantic for many years. Progress was slow because of the lack of any biological assay other than patients with untreated pernicious anemia. It accelerated only with the tardy discovery of a microbiological assay and culminated with the ap-

plication of partition and adsorption chromatography to water-soluble liver fractions. In 1948 the active principle, vitamin B_{12}, was isolated as cyanocobalamin at Merck & Co. in the United States by Karl Folkers and his associates and almost immediately thereafter by E. Lester Smith at Glaxo Laboratories in England.

Happily for the treatment of patients, Cohn and his associates as early as 1928 had reduced the daily requirement from 300 grams of liver to about 12.5 grams of a yellow powder, the so-called "fraction G," that possessed consistent activity in the treatment of pernicious anemia. In order that this experimental liver extract could be produced in quantity by a commercial process and submitted to clinical trial, a Committee on Pernicious Anemia of the Harvard Medical School was established. This committee, of which Cohn and Minot were members and Walter B. Cannon, Professor of Physiology, was chairman, undertook the responsibility of establishing the potency of successive lots of the commercial product before authorizing their release by the manufacturer to the medical profession. Through the scientific collaboration of its Research Director, Dr. G. H. A. Clowes, Eli Lilly and Company, which a few years before had successfully produced the first commercial preparation of insulin, was asked to undertake the manufacture of liver extract. Under the supervision of the committee, successive lots of this preparation were tested in Boston hospitals and supplied to fourteen medical centers in this country and one in Europe for therapeutic trials in pernicious anemia. The patent for the manufacturing process was dedicated to the public by the Lilly company.

Although Cohn, Minot, and their associates shortly produced, through further chemical fractionation, experimental extracts for intravenous trial, in which the activity of the original liver was increased more than three thousand times, the losses of activity in preparation were great. It remained for Gänsslen

of Tubingen in 1930 to achieve a crude, nearly protein-free extract for parenteral use of which the amount derived from only 5 grams of fresh liver constituted the necessary daily dose for the treatment of pernicious anemia.

By 1936 the pharmaceutical industry was marketing relatively purified or concentrated extracts of liver for intramuscular injection. However, by that time it had become apparent that, owing to variations in the efficiency of manufacture, the therapeutic activity of these preparations did not necessarily correspond to the original amount of liver from which they were derived. Thus in 1936 the United States Pharmacopeia authorized the establishment of an "Anti-anemia Preparations Advisory Board," of which Minot was a member. The Board, with the voluntary cooperation of the pharmaceutical manufacturers, evaluated the results of the clinical assay procedures it prescribed. Each manufacturer arranged for appropriate clinical tests of his product and submitted the hematological data to the Board for evaluation. The amount of material that would produce specified reticulocyte rises and rates of red-cell increase, when given in uniform daily amounts to untreated patients with pernicious anemia, was defined by the Board as a USP Unit (oral or injectable) according to the route of administration of the product. This amount was stated on the label of each manufacturer's product. In this way the benefit of Minot and Murphy's discovery became reliably available to the medical profession long before the isolation of the active principle of liver, vitamin B_{12}, in 1948.

As a result of the latter accomplishment, it was soon discovered that the successful management of a patient with pernicious anemia required less than one millionth of a gram of vitamin B_{12} a day, conveniently supplied in practice by a monthly injection of 30 to 100 micrograms of cyanocobalamin. It is now understood that the need for parenteral injection of the vitamin arises from a primary failure of a specific gastric

secretion essential for the assimilation of the small amounts of vitamin B_{12} in the normal diet. The vitamin is produced by microbial fermentation in the stomachs of ruminants whose forage contains cobalt and is absorbed and stored in the liver. The feeding of half a pound of beef liver a day was successful in treating pernicious anemia because the concentration of the vitamin in that animal organ was great enough to allow passive assimilation by patients lacking the special mechanism normally involved in the absorption of the low concentration of vitamin B_{12} in the usual diet.

In 1928, following the tragic early death of his friend and colleague, Francis Peabody, Minot, already internationally famous, was appointed Professor of Medicine at Harvard and succeeded Peabody as the second Director of the Thorndike Memorial Laboratory of the Boston City Hospital and Chief of the Fourth (Harvard) Medical Service there. The Thorndike Laboratory is better described as a metabolic ward for patients, together with upper floors for laboratories and animal quarters as well as offices for a small full-time staff. It was thus similar in its more general scientific purposes to the categorical objective of the Huntington Hospital. The Thorndike Laboratory, the first of its kind in a municipal hospital in this country, had been opened in 1923 and was a joint undertaking of the City of Boston and Harvard University that functioned brilliantly until 1973 when the hospital trustees dissolved the fifty-year affiliation. The Thorndike was part of the Harvard Medical Unit that provided medical care to hospital and clinic patients and offered research and educational opportunity for Harvard's undergraduate and postgraduate students as well as for the academic staff. In those days of limited opportunity for careful clinical investigation, this building, despite its relatively restricted bench space and equipment-laden corridors, was attractive to young physicians seriously interested in scientific research. Among Minot's younger associates in the early years

were Herrman Blumgart, W. B. Castle, Maxwell Finland, Chester S. Keefer, Robert Nye, Joseph T. Wearn, and Soma Weiss.

With the production of experimental liver fractions well under way in Cohn's laboratory and their clinical evaluation in patients proceeding in the Harvard-affiliated Boston hospitals, Minot and his young pupils turned their attention to the study of the patients with so-called hypochromic anemia. In these patients, in contrast to those with pernicious anemia, the red corpuscles in the blood are pale and deficient in hemoglobin. Although it had been known since the Middle Ages that iron was therapeutically useful in an anemia of this sort affecting young women (known as "chlorosis"), the fact had become obscured during the nineteenth century by theoretical considerations concerning iron absorption. However, in 1932 Minot and Dr. Clark W. Heath showed that the administration of iron caused reticulocyte responses and improvement of hypochromic anemia in elderly female patients subsisting on limited diets. In many of these patients with "chronic chlorosis" the normal secretion of hydrochloric acid by the stomach was also greatly reduced or absent. This suggested a possible basis for the apparent failure of these patients to assimilate food iron, because iron salts were well-known to be insoluble in neutral or alkaline solutions. Consequently, Dr. Stacy R. Mettier and Minot, using serial reticulocyte responses as an index, showed that iron salts given by mouth in an acid-buffered medium produced a greater reticulocyte response than when given to the same patient in a neutral-buffered medium. Still, the variable effects on hemoglobin production when iron was given by mouth left uncertainty about its mode of therapeutic action. However in 1932 Heath and his associates showed that soluble iron, when injected in small daily amounts into patients with hypochromic anemia, reappeared almost quantitatively incorporated in the resulting increased amounts of hemoglobin in their blood.

Minot was interested in other clinical manifestations that he suspected to be the result of faulty diet as well as in nutritional deficiency anemias. In 1928 Dr. George C. Shattuck, a member of the Department of Tropical Medicine at the Harvard Medical School, had suggested that defective diet might be a factor common to both oriental beriberi and to various forms of so-called "toxic" or "alcoholic" polyneuritis. Shattuck's clinical resident, Dr. Maurice B. Strauss, working in Minot's laboratory, had demonstrated the beneficial effect of improved nutrition in the so-called "toxic" neuritis of pregnancy. Minot recalled that his great grandfather, Dr. James Jackson, had written a classic description of alcoholic polyneuritis under the title, "On a Peculiar Disease Resulting from the Use of Ardent Spirits." Minot, Strauss, and Stanley Cobb, noting the defective diet and the digestive disturbances of patients with chronic alcoholism, together with the generally beneficial effect of better food, concluded that dietary deficiency, possibly of vitamin B_1, played an important role in the production of these patients' neurological disturbances. Two years later, in the Thorndike Ward, Strauss confirmed this supposition under controlled nutritional conditions by showing that a well-balanced diet, supplemented with components of the vitamin B complex, resulted in improvement of the neuritis of patients "allowed to continue their customary daily intake of spirituous liquor." This was certainly clinical investigation with the informed and happy consent of the patients.

As already mentioned, Minot as a young man had studied blood coagulation under Professor Howell in the Physiological Laboratory of the Johns Hopkins University School of Medicine. At the Thorndike he continued his interest in clinical disorders of platelets with the publication, in 1936, of an article describing varieties of purpura with low levels of platelets in the blood associated with lymphocytosis or occurring intermittently with menstruation. More significant was his interest in hemophilia,

regenerated through the work of some of his young colleagues. In 1936, encouraged by Minot, Drs. Arthur J. Patek, Jr., and Richard P. Stetson undertook to analyze the effect of transfusion of normal citrated blood in promptly shortening the coagulation time of the blood in hemophilia. It was recalled that substantial *in vitro* evidence for regarding this phenomenon as a response to the replacement of defective plasma rather than of defective platelets had been presented by Thomas Addis in 1911. In the course of a series of studies in which F. H. L. Taylor, the biochemist of the Thorndike, played a prominent part, Minot and his associates prepared a so-called "globulin substance" from citrated cell-free normal plasma and showed it to have the effect of the parent platelet-free plasma in shortening the coagulation time of hemophilic blood both *in vitro* and when given intravenously. Globulin fractions of normal plasma devoid of prothrombin and of fibrinogen were equally effective. The corresponding fractions of hemophilic blood had little or no activity. Much of this work was carried out with the willing and intelligent cooperation of a single hemophilic patient, Russell White, who was in residence for many years on the Thorndike Ward. Thus was discovered and initially defined the component of normal plasma known today as antihemophilic globulin or factor VIII.

The development of plasma fractionation during World War II by Cohn and his associates provided opportunity for testing the fractions' antihemophilic activity in Minot's laboratory. Cohn's fraction I was found to contain most of that activity and to be suitable for clinical use by intravenous injection in the hemophilic patient. Unfortunately, at the time the potential therapeutic value of these fractions was found to be limited in practice by the expense of commercial preparation and because some patients developed circulating antibodies against the active principle. More recently the development of cryopre-

cipitates and other concentrates of factor VIII has become of lifesaving value in the management of hemophilic bleeding.

In 1930 the Second Medical Service of the City Hospital had come under Minot's direction to complete the formation of the Harvard Medical Unit. He soon found this added responsibility to be too taxing a burden, and in 1932 he relinquished the conduct of the two clinical services to his trusted and brilliant younger colleague, Dr. Soma Weiss. Nevertheless, as the years passed Minot became ever more deeply involved in the administrative duties of the Thorndike Laboratory and in the responsibilities of a senior professor in the medical school. He was often busy on the home telephone for long periods in the evenings. However, somehow he found time for stimulation and encouragement of his pupils, often implemented by handwritten notes on scraps of paper referring to recent articles of special relevance to their research work. Or in discussion with them he would cross each of four fingers of his left hand over the adjacent digit as a reminder of individual points to be made as each was subsequently released.

In these and other ways Minot fostered the development of a healthy degree of autonomy in members of his department who were carrying out investigations in various clinical fields. He also carried on an extensive correspondence with other professors and with physicians seeking advice about patients. Blood films on glass slides often accompanied such inquiries. The characteristic care with which he composed his replies added to the burden of these "paper consultations." Alone, or with his associates, Minot contributed chapters on blood diseases to leading textbooks of medicine through several revisions. In 1936, with W. B. Castle, he published his only book, a pioneering description of the pathophysiology of the anemias reprinted from a chapter in *The Oxford Medicine.* Minot also maintained a small consultation practice that involved seeing patients

one or two afternoons a week at the office of the Beacon Street group. Some of these patients, as well as many of those on the medical wards of the City Hospital, had chronic conditions to which anxiety, fatigue, economic deprivation, and undesirable living conditions, as well as dietary abnormalities, at least contributed. He saw that correction of these defects could be beneficial and, in teaching and published articles, advocated proper attention by physicians to what he called "social medicine."

Despite the best of medical care, Minot developed in his middle fifties some of the vascular and neurological complications of diabetes. Informal conferences with close associates in his hospital office often took place while he was changing his socks and warming his feet dangerously close to an electric sun bowl near his desk. In 1942 he experienced transient numbness and tingling of his left arm and leg, and in April of 1947 he had a stroke that paralyzed his left side and resulted in a wheelchair existence for the rest of his life. His devoted and competent wife now became more than ever a source of encouragement as well as a perceptive judge of his needs and capacities.

With the physical assistance of the family chauffeur, Minot made occasional trips to the hospital or to visit friends. In 1948, he resigned from the directorship of the Thorndike Laboratory, but continued his kindly interest in the activities of its staff and in the progress of their research. As always, although he tired readily, he was ready to discuss medical matters with old friends and associates in the quiet of the book-lined study of his Brookline home. With the help of his young son he was able to renew stamp collecting, one of the hobbies of his early years. Despite an inexorable decline in health during the last weeks of his life, he carried on bravely to the limits of his ability and died quietly on February 25, 1950, at the age of sixty-five.

Honors and awards began early to come to Minot because of his great contribution to medicine and human welfare. In

1928, only sixteen years after graduation from the Harvard Medical School, he was given the honorary degree of S.D. by his alma mater. In the same year the University of Toronto awarded him the Charles Mickle Fellowship, and the Association of American Physicians, of which he was later elected president, gave him its Kober Medal. In 1937 he was elected to the National Academy of Sciences.

Three years earlier Minot had shared the Nobel Prize in Physiology or Medicine with Whipple and Murphy. This well-deserved joint award appeared at the time to recognize judiciously the experimental demonstration of a novel biological principle involved in normal blood formation and its dramatic application to a fatal human disease. In retrospect the work of these men, though, as discussed above, differently interpreted today, seems even more noteworthy. The journey to Stockholm, with lecture appearances en route in England, Holland, and Denmark, no less than the impressive ceremonies and banquets attendant upon the Nobel award, taxed the control of Minot's diabetes and his physical endurance. However, owing to his characteristic attention to detail, the advance preparations for the journey were complete and all went well, despite a great Atlantic storm on the return voyage. In addition the reassuring presence of medical expertise, if needed, was provided by Dr. Richard Stetson, a young colleague and friend, who with his wife accompanied the Minots and their two adolescent daughters.

Among foreign honors that came to Minot were honorary fellowships of the Royal College of Physicians, Edinburgh; the Royal College of Physicians, London; the Royal Society of Medicine, London; and a corresponding membership in the Royal Academy of Medicine, Belgium. He was awarded the Cameron Prize of the University of Edinburgh and the Moxon Medal of the Royal College of Physicians of London. He also received various awards in the United States. The admiration

and affection of his Harvard colleagues was expressed at a sixtieth birthday dinner in his honor held in Boston at which he was officially presented with the Distinguished Service Medal of the American Medical Association. Some of his associates conceived the idea of a *Festschrift.* A worldwide committee was formed, and eighty-four distinguished contributors to hematology wrote articles that were published together in 1949 as the *George R. Minot Symposium on Hematology.*

Minot's scientific contributions to medicine were inspired by a persistent curiosity about many things, important or even trivial, in the world about him. He was in essence a naturalist whose interests included flowers, insects, and every organic aspect of his patients as well as their emotional and social problems. His scientific work was implemented by his genius for taking infinite pains, and its relevance to clinical medicine changed the study of diseases of the blood from a largely descriptive to a dynamic subject that ever since has attracted productive basic and clinical investigation. In the area of nutritional anemias alone, the work of Minot and his pupils provided insight into matters not previously suspected to exist. Studies inspired by their work led eventually to the isolation of two new vitamins—folic acid and vitamin B_{12}—of fundamental importance to cellular proliferation and metabolism. Knowledge of the structure of folic acid (a B vitamin) permitted chemists to synthesize growth antagonists and inhibitors of the leukemic process. The discovery of cobalt in the vitamin B_{12} molecule explained its importance as a trace element in animal nutrition. Analysis of the relation of the secretory failure of the stomach in pernicious anemia to vitamin B_{12} deficiency has disclosed the specialized enteric mechanisms normally involved in the assimilation of the vitamin. The primary gastritis bids fair to be explained as an instance of a delayed cellular immune response of lymphocytes and macrophages occurring in genetically susceptible persons.

Although Minot is known to the world as the discoverer of the liver treatment of pernicious anemia and to clinical investigators for other discoveries as well, perhaps in the long run his greatest contribution to American medicine was through his personal influence over two decades as Director of the Thorndike Laboratory. During this time, guided by Minot and his small group of younger physician–scientists, there was a turnover of about a dozen young doctors a year, recruited as research fellows from all parts of the United States. Many of them had just completed training as residents on the clinical services of the Harvard Medical Unit. A few, usually more mature, came from across the Atlantic. All hoped to learn at first hand something of the scientific study of disease in patients and in the process, as often happened, to make original contributions themselves. After one, two, or three years with few exceptions they left the Thorndike in many instances to take up positions on other academic medical ladders. In 1948, at the time of Minot's resignation, more than four hundred young doctors had served in the Harvard Medical Unit, either as resident physicians on its medical services or as research fellows in the Thorndike. In 1956 almost fifty of these held professorships in medicine, pediatrics, preventive medicine, or in a preclinical department of medical schools in the United States. In addition, sixteen foreign physicians who had worked at the Thorndike occupied distinguished posts abroad. Thus was George Minot's great influence on academic medicine extended and multiplied through the men and women whose early medical careers he had moulded.

This account of George Minot owes much to the book about his life and times written by his cousin and medical classmate, Dr. Francis M. Rackemann.* Following Minot's death the minute of the Harvard Faculty of Medicine described him as:

* *The Inquisitive Physician,* Harvard University Press, Cambridge, Massachusetts, 1956, 288 pp.

"Generically . . . a Yankee of the Yankees, specifically . . . a proper Bostonian, . . . culturally an aristocrat, he was in behavior a democrat." His obituary in the *Transactions of the Association of American Physicians* for 1950 reads in part as follows: "Doctor Minot was a character in the best New England sense of that expression. His personality, like his hat, bore the impress of one who goes his accustomed way without concern that the way is different. Despite his achievements he was inherently modest and entirely democratic toward those who were sincere. He was an indefatigable correspondent and author of notes and memoranda to friends and colleagues. He loved to talk and a scheduled five-minute conference with him could easily extend to an hour of interesting conversational excursions. He had hobbies in which he took serious delight in every detail. Indoors he was an avid stamp collector. Outdoors he paid careful attention to the habits of birds and animals; and was proud of his flower garden in which he grew irises of prize-winning quality. Like many New Englanders, the sea was in his blood and as a summer sailor he was familiar with much of the rocky coast of Maine as well as with the warm waters of Buzzards Bay.

"George Minot's life was closely interwoven with his family and with his home. Family friends and foreign visitors alike found his a hospitable household. For serious discussions there was the study with its cheerful wood fire in winter and glimpses of the garden through the door in summer. The miracle of insulin saved his life, but without the understanding and constant devotion of his charming wife, Marian Weld Minot, his great work could never have been accomplished. She and their children Marian, Elizabeth, and Charles survive him."

DEGREES, APPOINTMENTS, AND HONORS

Degrees

1908	A.B., *cum laude,* Harvard University
1912	M.D., *cum laude,* Harvard University
1928	S.D., honorary, Harvard University

Hospital and University Appointments

1912–1913	Medical House Pupil, Massachusetts General Hospital
1913–1914	Assistant Resident Physician, Johns Hopkins Hospital
1914–1915	Assistant in Medicine and Research Fellow, Physiology Laboratory, Johns Hopkins Medical School
1915–1916	Assistant in Chemistry, Harvard University
1915–1918	Assistant in Medicine, Massachusetts General Hospital Assistant in Medicine, Harvard Medical School
1916–1918	Visiting Physician, St. Luke's Convalescent Home
1917–1919	Assistant Consulting Physician, Collis P. Huntington Memorial Hospital
1918–1923	Associate in Medicine, Massachusetts General Hospital
1918–1927	Assistant Professor of Medicine, Harvard Medical School
1919–1923	Physician, Collis P. Huntington Memorial Hospital
1922–1924	Consulting Physician, Massachusetts Charitable Eye and Ear Infirmary
1923–1928	Chief of Medical Service, Collis P. Huntington Memorial Hospital Physician to Special Clinic, Massachusetts General Hospital
1925–1927	Special Consultant in Diseases of the Blood, Massachusetts General Hospital
1925–1928	Associate in Medicine, Peter Bent Brigham Hospital
1927–1928	Clinical Professor of Medicine, Harvard Medical School
1927–1950	Member Board of Consultation, Massachusetts General Hospital
1928–1930	Chief, Fourth Medical Service, Boston City Hospital
1928–1948	Director, Thorndike Memorial Laboratory, Boston City Hospital Visiting Physician, Boston City Hospital
1928–1950	Professor of Medicine, Harvard Medical School Consulting Physician, Peter Bent Brigham Hospital

1929–1950	Consulting Physician, Beth Israel Hospital
1930–1932	Director, Second and Fourth Medical Services, Boston City Hospital
1943–1950	Consultant in Hematology, Palmer Memorial Hospital, N.E. Deaconess Hospital
1947	President, Senior Staff, Boston City Hospital

Member

1911	Alpha Omega Alpha
1917	American Society for Clinical Investigation
1921	Association of American Physicians Council (1931) President (1938)
1923	American Clinical and Climatological Association President (1933)
1927	American Academy of Arts and Sciences
1937	National Academy of Sciences
1946	Advisory Council of Physicians Forum

Honorary Member

1927–1928	The Harvey Society
1929	Phi Beta Kappa
1931–1939	Corresponding Member, Royal Academy of Medicine (Belgium)
1935	Kaiserlich Leopoldin—Carolinische Deutsche Akademie der Naturforscher (Halle)
1936	Society of Biological Chemists (India)
1938	Finnish Society of Internal Medicine (Helsingfors)
1939	Honorary Member, Royal Academy of Medicine (Belgium)
1945	Academy of Medicine of France

Fellow

1912	American Medical Association
1928	American College of Physicians
1935	American Philosophical Society

Honorary Fellow

1931	Royal College of Physicians, Edinburgh
1932	Royal Society of Medicine, London

1933	New York Academy of Medicine
	Institute of Medicine of Chicago
1938	Royal College of Physicians, London
	Vice President étranger, Société Française d'Hematologie
1945	Medical Association of Finland
1947	College of Physicians of Philadelphia

Awards

1928	Charles Mickle Fellowship, University of Toronto
1929	Kober Medal, Association of American Physicians
1930	Cameron Prize, University of Edinburgh (with William P. Murphy)
	Gold Medal, National Institute of Social Sciences
	Gold Medal and Award, Popular Science Monthly (with George H. Whipple)
1933	Moxon Medal, Royal College of Physicians, London
	John Scott Medal of City of Philadelphia
1934	Nobel Prize in Physiology or Medicine, jointly with William Parry Murphy and George Hoyt Whipple, for "discoveries respecting liver therapy in anaemias"
1935	Gold Medal of Humane Society of Massachusetts
1936	Scroll Award of Associated Grocery Manufacturers of America
1939	Gordon Wilson Lecturer and Medalist, American Clinical and Climatological Association
1945	Distinguished Service Medal, American Medical Association
1949	*George R. Minot Symposium on Hematology*

BIBLIOGRAPHY

KEY TO ABBREVIATIONS

Am. J. Med. Sci. = American Journal of the Medical Sciences
Am. J. Physiol. = American Journal of Physiology
Ann. Internal Med. = Annals of Internal Medicine
Arch. Internal Med. = Archives of Internal Medicine
Boston Med. Surg. J. = Boston Medical and Surgical Journal
Brit. Med. J. = British Medical Journal
Bull. Am. Assoc. Med. Social Workers = Bulletin of the American Association of Medical Social Works
Entomol. News = Entomological News
Harvard Med. Alumni Bull. = Harvard Medical Alumni Bulletin
J. Am. Med. Assoc. = Journal of the American Medical Association
J. Biol. Chem. = Journal of Biological Chemistry
J. Clin. Invest. = Journal of Clinical Investigation
J. Exp. Med. = Journal of Experimental Medicine
J. Ind. Hyg. = Journal of Industrial Hygiene
J. Med. Res. = Journal of Medical Research
Med. Clin. N. Am. = Medical Clinics of North America
New Engl. J. Med. = New England Journal of Medicine
Trans. Am. Clin. Climat. Assoc. = Transactions of the American Clinical and Climatological Association
Trans. Assoc. Am. Physicians = Transactions of the Association of American Physicians

1902

Chrysalis of *Melitaea gabbi*. Entomol. News, 13:158.

1903

The Tussock moth peril. Boston Evening Transcript, February 21.

1909

Notes on the occurrence of some butterflies rare in Massachusetts and Maine. Entomol. News, 20:437–38

1912

With Channing Frothingham, Jr. Normal temperature of rabbits. Am. J. Physiol., 30:430–35.

With Channing Frothingham, Jr. The effect of the injection of bovine bile into rabbits. J. Med. Res., 27:79–82.

1914

With L. H. Newburgh. The blood pressure in pneumonia. Arch. Internal Med., 14:48–55.

Nitrogen metabolism before and after splenectomy in a case of pernicious anaemia. Johns Hopkins Hospital Bulletin, 25:338–42.

1915

With George P. Denny. The origin of antithrombin. Am. J. Physiol., 38:233–47.

With Francis M. Rackemann. Respiratory signs and symptoms in trichinosis. Am. J. Med. Sci., 40:571–82.

The effect of chloroform on the factors of coagulation. Am. J. Physiol., 39:131–38.

1916

With George P. Denny. Prothrombin and antithrombin factors in the coagulation of blood. Arch. Internal Med., 17:101–39.

With George P. Denny. The coagulation of blood in the pleural cavity. Am. J. Physiol., 39:455–58.

The effect of temperature upon the clotting time (prothrombin time) of oxalated plasma with calcium. J. Med. Res., 33:503–6.

Methods for testing donors for transfusions of blood and consideration of factors influencing agglutination and hemolysis. Boston Med. Surg. J., 174:667–74.

With Andrew Watson Sellards. The antagonistic action of negative sera upon the Wassermann reaction. J. Med. Res., 34:131–47.

Studies on a case of idiopathic purpura hemorrhagica. Am. J. Med. Sci., 152: 48–65.

With Andrew Watson Sellards. Injection of hemoglobin in man and its relation to blood destruction, with especial reference to the anaemias. J. Med. Res., 34:469–94.

With Roger I. Lee and Beth Vincent. Splenectomy in pernicious anemia: studies on bone marrow stimulation. J. Am. Med. Assoc., 67:719–23.

With Roger I. Lee. The blood platelets in hemophilia. Arch. Internal Med., 18:474–95.

1917

With Roger I. Lee. Coagulation time of the blood in pneumonia. J. Am. Med. Assoc., 68:545–46.

With Roger I. Lee. The significance of blood platelets. Cleveland Medical Journal, 16:65–87.

Diminished blood platelets and marrow insufficiency: a classification and differential diagnosis of purpura hemorrhagica, aplastic anemia, and allied conditions. Arch. Internal Med., 19:1062–84.

Hemorrhagic conditions. Boston Med. Surg. J., 177:222–23.

With Andrew Watson Sellards. The preparation of hemoglobin for clinical investigations. J. Med. Res., 37:161–70.

With J. Homer Wright. The viscous metamorphosis of the blood platelets. J. Exp. Med., 26:395–409.

With Roger I. Lee. Treatment of pernicious anemia, especially by transfusion and splenectomy. Boston Med. Surg. J., 177:761–73.

1918

Pathologic hemorrhage: a group of cases illustrating this condition, with a note on the early diagnosis of pernicious anemia. Med. Clin. N. Am., 1:1003–24.

With Robert F. Loeb. An attempt to prevent influenza at Harvard College. Boston Med. Surg. J., 179:665–69.

1919

Four cases with enlarged spleens. Med. Clin. N. Am., 2:1349–74.

Blood examinations of trinitrotoluene workers. J. Ind. Hyg., 1: 301–18.

1920

Two cases with chronic gastrointestinal symptoms: comments on the use of transfusion in pernicious anemia. Med. Clin. N. Am., 3:1001–22.

With Alice Hamilton. Ether poisoning in the manufacture of smokeless powder. J. Ind. Hyg., 2:41–49.

Clinical discussion of the anemias. Chapter XVI in: *The Oxford Medicine,* ed. by Henry A. Christian, Vol. 2, pp. 589–679. New York, Oxford University Press, Inc.

With Roger I. Lee. Chapters for the section on diseases of the blood: ten colored plates drawn by Miss Elizabeth D. Gray under supervision; the anemias; hemorrhagic diseases and conditions; transfusion of blood. In: *The Nelson Loose Leaf Living Medicine,* Vol. 4, pp. 15–171. New York, Thomas Nelson & Sons.

1921

Two curable cases of anemia. Med. Clin. N. Am., 4:1733–50.

With Lawrence W. Smith. The blood in tetrachlorethane poisoning. Arch. Internal Med., 28:687–702.

Report on anemia of myxedema and relation of polycythemia to leukemia. Boston Med. Surg. J., 185:804. (A)

1922

Two cases of anemia simulating pernicious anemia. International Clinics, 1:39–55.

A case of acute blood loss due to pathologic hemorrhage, with a consideration of bleeding from surgical operation in such cases. Med. Clin. N. Am., 5:1231–49.

Megacaryocytes in the peripheral circulation. J. Exp. Med., 36:1–7.

Discussion of paper by Francis W. Peabody, "The physician and the laboratory." Boston Med. Surg. J., 187:327–28.

With Arlie V. Bock. Transfusion of blood. In: *Endocrinology and Metabolism,* ed. by Lewellys F. Barker, R. G. Hoskins and Herman O. Mosenthal, Vol. 3, pp. 821–43. New York, D. Appleton & Company.

1923

With Thomas E. Buckman. Erythremia (polycythemia rubra vera): the development of anemia; the relation to leukemia; consideration of the basal metabolism, blood formation and destruction and fragility of the red cells. Am. J. Med. Sci., 166:469–89.

The role of a low carbohydrate diet in the treatment of migraine and headache. Med. Clin. N. Am., 7:715–28.

With Chester M. Jones. Infectious (catarrhal) jaundice: an attempt to establish a clinical entity. Boston Med. Surg. J., 189:531–51.

With John J. Sampson. Germanium dioxide as a remedy for anemia. Boston Med. Surg. J., 189:629–32.

1924

With James H. Means. The metabolism–pulse ratio in exopthalmic goiter and in leukemia: with remarks on certain similarities in the symptomatology of these diseases. Arch. Internal Med., 33: 576–80.

With Thomas E. Buckman, Geneva A. DaLand and Margaret Weld. Blood phosphorus: its relation to cancer and anemia. Arch. Internal Med., 34:181–90.

With Thomas E. Buckman and Raphael Isaacs. Chronic myelo-

genous leukemia: age incidence, duration and benefit derived from irradiation. J. Am. Med. Assoc., 82:1489–94.

With Raphael Isaacs. Lymphatic leukemia: age incidence, duration and benefit derived from irradiation. Boston Med. Surg. J., 191:1–9.

With Roy G. Spurling. The effect on the blood of irradiation, especially short wavelength Roentgen-ray therapy. Am. J. Med. Sci., 168:215–41.

With Edwin A. Locke. Hematuria as a symptom of systemic disease. J. Am. Med. Assoc., 83:1311–15.

1925

With Raphael Isaacs and Thomas E. Buckman. Progress in the knowledge of blood conditions. Boston Med. Surg. J., 192: 10–19.

A case of generalized enlargement of lymph nodes and hypertrophy of spleen, associated with chronic focal infection; the importance of habit in the regulation of the bowls; remarks concerning the fatal diseases of the lymphoid tissue. Med. Clin. N. Am., 8: 1411–30.

With Thomas E. Buckman. The blood platelets in the leukemias. Am. J. Med. Sci., 169:477–85.

With Raphael Isaacs. Transfusion of lymphocytes: their rapid disappearance from the peripheral circulation of man. J. Am. Med. Assoc., 84:1713–15.

With Raphael Isaacs and Benjamin Brock. The resistance of immature erythrocytes to heat. J. Clin. Invest., 1:425–33.

The physician, student and medical social worker. Boston Med. Surg. J., 193:1090–92.

1926

With Raphael Isaacs. Lymphoblastoma (malignant lymphoma): age and sex incidence, duration of disease, and the effect of Roentgen-ray and radium irradiation and surgery. J. Am. Med. Assoc., 86:1185–89, 1265–70.

With William P. Murphy. Observations on patients with pernicious anemia partaking of a special diet. A. Clinical aspects. Trans. Assoc. Am. Physicians, 41:72–75.

Lymphoblastoma. Radiology, 7:119–20, 130.

With William P. Murphy. Treatment of pernicious anemia by a special diet. J. Am. Med. Assoc., 87:470–76.

With William P. Murphy. A special diet for patients with pernicious anemia. Boston Med. Surg. J., 195:410–11.

Pernicious anemia: treatment by a special diet. Discussion of Case 12342, case records of the Massachusetts General Hospital. Boston Med. Surg. J., 195:429–34.

Anemia. In: *Principles of Medical Treatment,* ed. by George C. Shattuck, 6th ed., pp. 145–54. Cambridge, Mass., Harvard University Press.

With Raphael Isaacs. Lymphoblastoma: aspects concerning abdominal lesions, especially their production of early symptoms. Am. J. Med. Sci., 172:157–73.

1927

With Donald N. Medearis. Studies on red blood cell diameter. II. In pernicious anemia, before and during marked remission, and in myelogenous leukemia. J. Clin. Invest., 3:541–53.

With William P. Murphy. Liver diet in pernicious anemia, and the distinction between aleukocythemic myeloid leukemia and pernicious anemia. Med. Clin. N. Am., 10:1093–1102.

With William P. Murphy. Modern treatment of pernicious anaemia. The Alumnae Journal, 7:17–19. Peter Bent Brigham Hospital, Boston, Mass.

With Thomas E. Buckman. Chapters on purpura, hemorrhagic disease of the newborn and hemophilia. In: *A Text Book of Medicine,* ed. by Russell L. Cecil, pp. 950–61. Philadelphia, W. B. Saunders Company.

Chapter on erythremia. In: *A Text Book of Medicine,* ed. by Russell L. Cecil, pp. 962–66. Philadelphia, W. B. Saunders Company.

With Edwin J. Cohn, John F. Fulton, Hermann F. Ulrichs, Florence C. Sargent, John H. Weare and William P. Murphy. The nature of the material in liver effective in pernicious anemia. I. J. Biol. Chem., 74:69–72.

With William P. Murphy. A diet rich in liver in the treatment of pernicious anemia: study of one hundred and five cases. J. Am. Med. Assoc., 89:759–66.

Clinical discussion of the anemias. (Revision of section on treat-

ment.) Chapter XVI. In: *The Oxford Medicine,* ed. by Henry A. Christian, Vol. 2, pp. 646–72. New York, Oxford University Press.

With William P. Murphy, Edwin J. Cohn, Richard P. Stetson and Herman A. Lawson. The feeding of whole liver or an effective fraction in pernicious anemia: the response of the reticulocytes. Trans. Assoc. Am. Physicians, 42:81–86.

With William P. Murphy. Treatment of pernicious (Addisonian) anaemia with a diet rich in liver. Brit. Med. J., 2:674–76.

The treatment of pernicious anemia with liver on an effective fraction of liver. (The Mary Scott Newbold Lecture XVIII) Transactions of the College of Physicians of Philadelphia, 49:144–53.

1928

A familial hemorrhagic condition associated with prolongation of the bleeding time. Am. J. Med. Sci., 175:301–6.

With Edwin J. Cohn, Gordon A. Alles and William T. Salter. The nature of the material in liver effective in pernicious anemia. II. J. Biol. Chem., 77:325–58.

With William P. Murphy and Richard P. Stetson. The response of the reticulocytes to liver therapy; particularly in pernicious anemia. Am. J. Med. Sci., 175:581–99.

With Edwin J. Cohn, William P. Murphy and Herman A. Lawson. Treatment of pernicious anemia with liver extract: effects upon the production of immature and mature red blood cells. Am. J. Med. Sci., 175:599–622.

The treatment of pernicious anemia. In: *The Harvey Lectures,* 23:151–53. Baltimore, Williams & Wilkins Company. (Synopsis)

With William P. Murphy and Edwin J. Cohn. Le traitement de l'anémie pernicieuse par un régime riche en foie ou par un extrait de foie. Annales de Médecine, 23:319–27.

1929

A non-fatal case simulating acute leukemia with anemia and thrombopenic purpura. Med. Clin. N. Am., 13:1–9.

Recent progress: treatment of pernicious anemia. In: *Nelson Loose Leaf Living Medicine,* Vol. 4, pp. 59A–H. New York, Thomas Nelson & Sons.

Some fundamental clinical aspects of deficiencies. Ann. Internal Med., 3:216–29.

Presentation of the Kober Medal to George R. Minot, M.D., for research in scientific medicine: remarks by George R. Minot, M.D. Trans. Assoc. Am. Physicians, 44:11–12.

Treatment of pernicious anemia. In: *The George Blumer Edition of Billings and Forchheimer's Therapeusis of Internal Diseases,* Suppl., pp. 423–34. New York, D. Appleton & Company.

Treatment of anemia, other than pernicious anemia, with diet. In: *The George Blumer Edition of Billings and Forchheimer's Therapeusis of Internal Diseases,* Suppl., pp. 435–42. New York, D. Appleton & Company.

With Edwin J. Cohn and Thomas L. McMeekin. The nature of the material effective in pernicious anemia. III. Am. J. Physiol., 90:316–17. (A)

1930

With Janet M. Vaughan and Gulli Lindh Muller. The response obtained in healthy pigeons by the administration of substances effective in pernicious anaemia. Lancet, 218:1062; also in J. Clin. Invest., 9:3–4. (A)

With Edwin J. Cohn and Thomas L. McMeekin. The nature of the substance effective in pernicious anemia. Trans. Assoc. Am. Physicians, 45:343–49.

With Edwin J. Cohn and Thomas L. McMeekin. The nature of the material effective in pernicious anemia. IV. J. Biol. Chem., 87:49–52.

The treatment of pernicious anemia and the importance of an optimal diet for man. Journal of the National Institute of Social Sciences, 15:28–32.

With Stacy R. Mettier and Wilmot C. Townsend. Scurvy in adults: especially the effect of food rich in vitamin C on blood formation. J. Am. Med. Assoc., 95:1089–93.

With Raphael Isaacs. Pernicious anemia: synopsis of literature from North America during 1928. Folia Haematologica, 41: 179–88.

1931

With Henry Jackson, Jr. The medical care of the cancer patient. American Journal of Cancer, 15:6–11.

With Stacy R. Mettier. The effect of iron on blood formation as influenced by changing the acidity of the gastroduodenal contents in certain cases of anemia. Am. J. Med. Sci., 181:25–36.

The treatment of anemia. New Engl. J. Med., 204:1104–5. (A)

Review of *A Brief History of Medicine in Massachusetts* by Henry R. Viets. Boston and New York, Houghton Mifflin Company, 1930. In: New England Quarterly 4:362–65.

With William B. Castle. The adequate treatment of anemia. Ann. Internal Med., 5:159–69.

With Clark W. Heath. The response of the reticulocytes to iron and some aspects of iron therapy. Trans. Assoc. Am. Physicians, 46:290–95.

The treatment of anemia: with comments on food deficiency and its relation to the nervous system. Transactions of the American Neurological Association, 57:329–32.

1932

With Clark W. Heath. The response of the reticulocytes to iron. Am. J. Med. Sci., 133:110–21.

Chronic arthritis: remarks concerning prevention and treatment. Med. Clin. N. Am., 15:797–804.

Idiopathic hypochromic anemia. In: *Emanuel Libman Anniversary Volumes,* Vol. 2, pp. 831–45. New York, International Press.

The importance of the treatment of pernicious anemia on a quantitative basis. Trans. Am. Clin. Climat. Assoc., 48:31–38; also in J. Am. Med Assoc., 99:1906–8.

1933

Three cases of chronic dietary deficiency: features are chronic fatigue, anemia and prolonged coagulation time of the blood. Med. Clin. N. Am., 16:761–71.

With Soma Weiss. Nutrition in relation to arteriosclerosis. In: *Arteriosclerosis: A Survey of the Problem,* pp. 233–48. Publication of the Josiah Macy, Jr., Foundation. New York, The Macmillan Company.

James Jackson, 1812–1836. Harvard Med. Alumni Bull., 7(Jan.): 25–29.

James Jackson as a professor of medicine. New Engl. J. Med., 208: 254–58.

Deficiency disease from lack of specific gastric reaction: the etiology of pernicious and related macrocytic anemias. (Editorial) New Engl. J. Med. 208:556–57.

James Jackson and alcoholic neuritis: a correction. Harvard Med. Alumni Bull., 7(April):54–55.

William Sidney Thayer. Harvard Med. Alumni Bull., 7(April): 55–56.

With Maurice B. Strauss and Stanley Cobb. "Alcoholic" polyneuritis: dietary deficiency as a factor in its production. New Engl. J. Med., 208:1244–49.

General aspects of the treatment of chronic arthritis. New Engl. J. Med., 208:1285–90.

President's address: The importance of art and the general principles of treatment in chronic arthritis. Trans. Am. Clin. Climat. Assoc., 49:50–58; also in J. Am. Med. Assoc., 101:1266. (A)

With Thomas E. Buckman. Chapters on purpura, hemorrhagic disease of the newborn and hemophilia (revised). In: *A Text Book of Medicine,* ed. by Russell L. Cecil, 3d ed., pp. 1043–55. Philadelphia, W. B. Saunders Company.

Chapter on erythremia (revised). In: *A Text Book of Medicine,* ed. by Russell L. Cecil, 3d ed., pp. 1055–59. Philadelphia, W. B. Saunders Company.

1934

Anemia: etiology and treatment. (First Jessie Horton Kessler Lecture) Proceedings of the Institute of Medicine of Chicago, 10: 2–5.

Thoughts concerning the teaching of medical social conditions. Journal of the Association of American Medical Colleges, 9: 147–49.

Medical social aspects in practice. Arch. Internal Med., 54:1–10.

With Arthur J. Patek, Jr. Bile pigment and hemoglobin regeneration: the effect of bile pigment in cases of chronic hypochromic anemia. Am. J. Med. Sci., 188:206–15; also in J. Clin. Invest., 13:717. (A)

The interpretation of reticulocyte responses in pernicious anemia. Trans. Assoc. Am. Physicians, 49:287–98.

Nutrition in relation to mental disorders. In: *The Problem of Mental Disorder,* a study by the Committee on Psychiatric Investigations, National Research Council, pp. 255–65. New York, McGraw-Hill Book Company, Inc.

Animal experimentation: its importance and value to scientific

medicine. Bulletin of the American College of Surgeons, 18: 17–18.

The clinical investigative laboratory. In: *Lilly Research Laboratories—Dedication,* pp. 42–45. Indianapolis, Indiana.

Some aspects of anaemia. Medical reporter's notes of lecture to the Royal Society of Medicine, London. Lancet, 227:1281–83.

1935

Some aspects of the diagnosis of pernicious anemia. Med. Clin. N. Am., 18:935–44.

The development of liver therapy in pernicious anaemia: a Nobel lecture delivered before the Caroline Institute at Stockholm, December 12, 1934. Lancet, 1:361–64; also in *Les Prix Nobel en 1934,* pp. 1–10. Stockholm, P. A. Norstedt & Soner.

Remarks at dinner of Nobel Foundation, December 10, 1934. In: *Les Prix Nobel en 1934,* pp. 58–59. Stockholm, P. A. Norstedt & Soner.

With William B. Castle. The interpretation of reticulocyte reactions: their value in determining the potency of therapeutic materials, especially in pernicious anaemia. Lancet, 2:319–30.

Clinical investigation: physician and patient. (The Ninth Alpha Omega Alpha Annual Lecture) J. Am. Med. Assoc., 105:641–45.

The anemias of nutritional deficiency; etiology, diagnosis, treatment and prevention. J. Am. Med. Assoc., 105:1176–79.

1936

With William B. Castle. Pathological physiology and clinical description of the anemias. Chapter XVI in: *The Oxford Medicine,* ed. by Henry A. Christian, Vol. 2, pp. 589–680. Also reprinted as book, *Pathological Physiology and Clinical Description of the Anemias.* New York, The Oxford University Press.

Pernicious anaemia: the latest word on the etiology and treatment of pernicious anaemia–by a Nobel prize-winner. In: *The World Today,* Vol. 3, pp. 11–13. Chicago, Encyclopaedia Britannica, Inc.

Foreword. Instruction of medical students in the social aspects of medicine. Bull. Am. Assoc. Med. Social Workers, 9:34.

Purpura hemorrhagica with lymphocytosis: an acute type and an intermittent menstrual type. Am. J. Med. Sci., 192:445–56.

Discussion of talk by Arlie V. Bock, "The use and abuse of blood transfusions." New Engl. J. Med., 215:425.

Anemia and the gastro-intestinal tract: a synopsis. American Journal of Digestive Diseases and Nutrition, 3:643–46.

Harvard and nutrition. New Engl. J. Med., 215:1147–49.

1937

Människan Är Vad Hon Äter: Framtidens Medicin (Medicine and the Future). Svenska Dagbladet (Stockholm, Sweden), p. 5, January 10; reprinted in Olösta Gåtor; Actuella Problem. *Svenska Dagbladets Naturvetenskapliga Enquête 1937,* pp. 179–81. Stockholm, Wahlström & Widstrand.

Some aspects of the anemias of nutritional deficiency. Journal of the American Dietetic Association, 12:522–26.

Investigation and teaching in the field of the social component of medicine. Bull. Am. Assoc. Med. Social Workers, 10:9–18; reprinted in Anniversary volume: *Scientific Contributions in Honor of Joseph Hersey Pratt on His Sixty-fifth Birthday,* pp. 940–51. Lancaster, Pennsylvania, Lancaster Press.

Discussion of paper by M. M. Wintrobe, E. M. Hanrahan and Caroline Bedell Thomas, "Purpura hemorrhagica with special reference to course and treatment." J. Am. Med. Assoc., 109: 1176.

Notes concernant les troubles du sang. Bulletin et mémoires de la société de médecine de Paris, 141:800–801.

Chapter on pernicious anemia (revised). In: *A Text Book of Medicine,* ed. by Russell L. Cecil, 4th ed., pp. 996–1004. Philadelphia, W. B. Saunders Company.

With Thomas E. Buckman. Chapters on purpura, hemorrhagic disease of the newborn and hemophilia (revised). In: *A Text Book of Medicine,* ed. by Russell L. Cecil, 4th ed. pp. 1025–37. Philadelphia, W. B. Saunders Company.

Chapter on erythremia (revised). In: *A Text Book of Medicine,* ed. by Russell L. Cecil, 4th ed., pp. 1037–41. Philadelphia, W. B. Saunders Company.

1938

Discussion of paper by C. P. Rhoads and W. Halsey Barker, "Refractory anemia: analysis of 100 cases." J. Am. Med. Assoc., 110:795.

Progress on anaemia. In: *Britannica Book of the Year, 1938,* p. 43. Chicago, Encyclopaedia Britannica, Inc.

With Clark W. Heath, Frederick J. Pohle and Gunnar Alsted. The influence of mucin upon the absorption of iron in hypochromic anemia. Am. J. Med. Sci., 195:281–86.

The President's address. Trans. Assoc. Am. Physicians, 53:1–6.

Nutritional deficiency. Ann. Internal Med., 12:429–42.

Foreword to *Medicine in the Out-Patient Department,* by Winthrop Wetherbee, Jr. New York, Paul B. Hoeber, Inc.

Clinical Investigation. Science, 88:413–16; also in The Diplomate, 11:48–52 (1939); J. Am. Med. Assoc., 112:1210–13 (1939). (A)

The etiology, diagnosis and treatment of the anemias of nutritional deficiency. Bulletin of the New England Medical Center, 1:4–5. (Synopsis)

Discussion of paper by Claude E. Forkner, "An attempt to consolidate and to clarify present views concerning the anemias and the hemorrhagic disorders." In: *Abstracts of the Proceedings of the Forty-ninth Annual Meeting of the Life Insurance Medical Directors of America,* Vol. 25, pp. 279–81. Printed for private circulation, New York City, Press of Recording and Statistical Corporation.

Doctor a day: liver extract treatment in pernicious anemia. Published under auspices of the Massachusetts Medical Society and the Massachusetts Department of Health. Boston Evening Transcript, February 5, p. 13.

Discussion of paper by Frank H. Krusen, "Physical therapy in arthritis." New Engl. J. Med., 220:469–70.

The activities of the Children's Hospital. Harvard Med. Alumni Bull., 14:9–12.

Anemias of nutritional deficiency. In: *A Symposium on the Blood Forming Organs,* pp. 52–56. Madison, University of Wisconsin Press. (A)

1940

Anemias of nutritional deficiency. (The Gordon Wilson Lecture) Trans. Am. Clin. Climat. Assoc., 55:175–80.

Chapter on pernicious anemia (revised). In: *A Text Book of Medicine,* ed. by Russell L. Cecil, 5th ed., pp. 1076–85. Philadelphia, W. B. Saunders Company.

Chapters on purpura, hemorrhagic disease of the newborn, hemophilia and erythremia (revised). In: *A Text Book of Medicine,* ed. by Russell L. Cecil, 5th ed., pp. 1111–26. Philadelphia, W. B. Saunders Company.

1941

Foreword to *Chinese Lessons to Western Medicine: A Contribution to Geographical Medicine from the Clinic of Peiping Union Medical College,* by I. Snapper. New York, Interscience Publishers, Inc.

1942

Soma Weiss. In: *In Memoriam, Soma Weiss, 1899–1942,* pp. 14–19. Peter Bent Brigham Hospital, Boston, Mass. (Remarks at a memorial ceremony in honor of Soma Weiss, held March 19, 1942)

With E. P. Jordan and others. Primer on arthritis. Prepared by a committee of the American Rheumatism Association. J. Am. Med. Assoc., 119:1089–1104.

Some problems of nutritional deficiencies. Journal of Home Economics, 34:477–78.

Rest. 1942 Proceedings of the Interstate Postgraduate Medical Assembly of North America, pp. 207–8.

1943

The problem of nutritional deficiencies. Chapter III in: *The Role of Nutritional Deficiency in Nervous and Mental Disease.* Research Publications of the Association for Nervous and Mental Disease, 22:29–32. Baltimore, Williams & Wilkins Company. (A)

With Maurice B. Strauss. Physiology of anti-pernicious anemia material. Vitamins and Hormones, 1:269–91.

Chapters on pernicious anemia, purpura, hemorrhagic disease of the newborn, hemophilia and erythremia (revised). In: *A Text Book of Medicine,* ed. by Russell L. Cecil, 6th ed., pp. 970–90. Philadelphia, W. B. Saunders Company.

Introduction to chapter on hemorrhagic diseases and conditions. In: *Nelson Loose Leaf Living Medicine,* Vol. 4, p. 103. New York, Thomas Nelson & Sons.

With F. H. L Taylor and Charles S. Davison. Chapter L. The physiology of blood coagulation. In: *Nelson Loose Leaf Living Medicine,* Vol. 4, pp. 105–115D. New York, Thomas Nelson & Sons.

1944

Foreword to *Atlas of the Blood in Children,* by Kenneth D. Blackfan and Louis K. Diamond. New York, Commonwealth Fund.

1945

Review of *Atlas of the Blood in Children,* by Kenneth D. Blackfan and Louis K. Diamond. New York, Commonwealth Fund. In: Harvard Med. Alumni Bull., 19:101.

With F. H. L. Taylor, C. S. Davidson, H. J. Tagnon, M. A. Adams and A. H. MacDonald. Studies in blood coagulation: the coagulation properties of certain globulin fractions of normal human plasma *in vitro.* J. Clin. Invest., 24:698–703.

With C. S. Davidson, Jessica H. Lewis, H. J. Tagnon and F. H. L. Taylor. The coagulation defect in hemophilia: the effect, in hemophilia, of the parenterol administration of a fraction of the plasma globulins rich in fibrinogen. J. Clin. Invest., 24:704–7.

1946

Foreword to first issue of *Blood, The Journal of Hematology.* Blood, 1:1–2.

With Geneva A. Daland and Clark W. Heath. Differentiation of pernicious anemia and certain other macrocytic anemias by the distribution of red blood cell diameters. Blood, 1:67–75.

With Jessica H. Lewis, Henry J. Tagnon, Charles S. Davidson and F. H. L. Taylor. The relation of certain fractions of the plasma globulins to the coagulation defect in hemophilia. Blood, 1: 166–72.

With Jessica H. Lewis, C. S. Davidson, J. P. Soulier, H. J. Tagnon and F. H. L. Taylor. Chemical, clinical and immunological studies on the products of human plasma fractionation. XXXII. The coagulation defect in hemophilia: an *in vitro* and *in vivo* comparison of normal and hemophilic whole blood, plasma and derived plasma protein fractions. J. Clin. Invest., 25:870–75.

With C. S. Davidson, Jessica H. Lewis, J. P. Soulier, H. J. Tagnon and F. H. L. Taylor. Les protéines plasmatiques et le problème de l'hémophilie. Le Sang, 17:293–302.

David Linn Edsall, 1869–1945. Trans. Assoc. Am. Physicians, 59: 9–10.

With M. B. Strauss. Fisiologia do principio antipernicioso. Resehna clin.-cient., 15:101–12.

1947

With F. H. L. Taylor. Hemophilia: the clinical use of antihemophilic globulin. Ann. Internal Med., 26:363–67.

The hospital—a look ahead: some aspects of clinical investigation. New Engl. J. Med., 236:563–66.

The diagnosis and treatment of the macrocytic anemias. Transactions and Studies of the College of Physicians of Philadelphia, 15:1–6.

Chapters on pernicious anemia, purpura, hemorrhagic disease of the newborn, hemophilia and erythremia (revised). In: *A Text Book of Medicine,* ed. by Russell L. Cecil, 7th ed., pp. 1091–1111. Philadelphia, W. B. Saunders Company.

Nutrition and health. Nutrition Reviews, 5:321–22.

Pernicious anemia. In: *American People's Encyclopedia,* 1:858–62. New York, Grolier, Inc.

1948

The modern management of macrocytic anaemias. Brit. Med. J., 2:153–54.