G E O R G E  R I C H A R D S  M I N O T

1885—1950

A Biographical Memoir by
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Biographical Memoir

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George Richards Minot.
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 indispensable 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 B₁₂: 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-Robsbins, 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 hemo-
globin. Whipple confirmed this finding with intravenous in-
jections 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 re-
missions” 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 Hos-
pital it had been his custom to cross-question such patients as to
the details of their dietary history. In this way he came to be-
lieve that pernicious anemia patients often had lived on un-
balanced diets for many years and sometimes developed a dis-
taste 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 im-
mediately thereafter by E. Lester Smith at Glaxo Laboratories
in England.

Happily for the treatment of patients, Cohn and his associ-
ates 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 Perni-
cious 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 suc-
cessive 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 in-
sulin, 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 pro-
duced, 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<sub>1</sub>, 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 Throndike, 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 Throndike 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-
Precipitates 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:

"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'Hemato-
logie
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 Asso-
ciation
1949 George R. Minot Symposium on Hematology
KEY TO ABBREVIATIONS

Ann. Internal Med. = Annals of Internal Medicine
Arch. Internal Med. = Archives of Internal Medicine
Boston Med. Surg. J. = Boston Medical and Surgical Journal
Entomol. News = Entomological News
J. Biol. Chem. = Journal of Biological Chemistry
J. Exp. Med. = Journal of Experimental Medicine
J. Ind. Hyg. = Journal of Industrial Hygiene

1902


1903


1909


1912


1914


1915


1916


1917

370 BIOGRAPHICAL MEMOIRS


1918

1919

1920

1921


1922


1923


1924


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


1925


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.


1926


1927


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


1928


1929


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.


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


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.


1931


1932


1933

GEORGE RICHARDS MINOT


1934


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


Animal experimentation: its importance and value to scientific
1935


1936


1937


1938


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


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


(Synopsis)


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.


1940


1941


1942


1943


1944

1945


1946


1947


1948