James B. Herrick's 1910 article presenting the case of an anemic West Indian student with peculiar-shaped red blood cells was the first description of sickle cell anemia in Western medical literature. However, he told only part of the story. Records in Chicago, Washington, DC, and Grenada, West Indies, reveal more information about the events surrounding Herrick's discovery and help put them in historical perspective. Herrick's intern, Ernest E. Irons, abreast of the latest developments in medicine, actually performed the blood work and alerted Herrick about the odd-looking cells. Changing patterns in American race relations allowed the patient, Walter Clement Noel, to study dentistry in Chicago. He continued to receive care from Irons for 2½ years, then returned to Grenada to practice dentistry. Noel died nine years after his return to Grenada, at age 32.

(JAMA 1989;261:266-271)

WHEN THE SS Cearense docked in New York on Sept 15, 1904, after an eight-day voyage from Barbados, one of its passengers had a medical problem. A sore on the ankle of a 20-year-old Grenadian, Walter Clement Noel, had become quite painful. He sought help from a physician after clearing customs and immigration. Within a week, time and the iodine applied by his physician healed the wound, leaving a scar similar to others on his limbs. He continued his journey, now over land, to Chicago.

Around Thanksgiving Day, Noel, now a first-year dental student at the Chicago College of Dental Surgery (CCDS), developed severe respiratory problems. He coped with these symptoms until the day after Christmas, when he walked, weak and dizzy, across the street from his lodgings to Presbyterian Hospital (Fig 1). There Dr Ernest E. Irons, a 27-year-old intern, obtained a history and performed routine physical, blood, and urine examinations (Fig 2). He noticed that Noel's blood smear contained "many pear-shaped and elongated forms—some small," and alerted his attending physician, James B. Herrick, of the unusual blood findings. In his next blood examination report, on Dec 31, Irons drew a rough sketch of these erythrocytes (Fig 3).

For the next 2½ years Herrick and Irons followed Noel through several episodes of severe illness as he continued his dental studies. Though the two physicians performed numerous tests, consulted with colleagues, and searched the medical literature for similar cases, they never could confirm a diagnosis for Noel's illness. Finally in May 1910, three years after losing track of their patient, Herrick presented the case to the Association of American Physicians in Washington, DC, and published it, still undiagnosed, in the November 1910 issue of the Archives of Internal Medicine. Following time-honored medical tradition, the patient's name was not revealed. Noel's was the first recorded, documented case of sickle cell anemia in Western medicine.

Within months of this report, a physician at the University of Virginia Hospital in Charlottesville, having read Herrick's article, reported a similar case. Two more articles describing patients with like problems appeared in medical journals in 1915 and 1922. By the mid-1920s enough patients with this distinctive form of anemia had been studied for physician-researchers to note the disease's hereditary pattern and natural history. All authors cited Herrick's 1910 article as the first on the subject.

That brief 1910 paper has also served, until now, as historians' sole source of information about the discovery of sickle cell anemia. However, information recently located in Chicago, Washington, DC, and Grenada, West Indies, permits embellishment of the story and its placement in a broader medical and social context. The discovery took place during a time of change in medicine and in American race relations. The main characters of the story represent well this important transitional period in US history.

CHICAGO MEDICINE, 1904

At the time of the actual discovery, December 1904, Chicago was a growing center of medicine and of medical education. The city boasted some nationally known practitioners, medical educators, and researchers, including Frank Billings, Nicholas Senn, Ludvig Hektoen, John B. Murphy, Daniel Hale Williams, Christian Fenger, and Arthur Dean Bevan. The American Medical Association made its headquarters there. Just west of the downtown area stood a "medical district" of several square blocks housing a number of medical and dental schools and hospitals (Fig 1).

Both James Bryan Herrick (1861-1954) and Ernest Edward Irons (1877-1959) were living and working in that medical district. Herrick, who had already earned a reputation for his teaching, publications, and medical skills, served as an attending physician at both Presbyterian and Cook County hospitals and as professor of medicine at Rush Medical College. A native of nearby Oak Park, Ill, and an 1888 graduate of Rush, Herrick practiced internal medicine in Chicago after his internship at Cook County Hospital. During the 1890s and early 1900s, he published numerous articles, often case reports based on his wide experience in medical practice. Throughout those years, he maintained a keen interest in diagnostic

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techniques and wrote a short textbook in 1895, *Handbook of Medical Diagnosis for Students*. Always a student himself, Herrick was studying chemistry every morning that fall and winter of 1904 in courses at the University of Chicago. In later years, his research into angina pectoris and coronary occlusion would win him national attention and a number of awards.\(^2,^{10,11,14-21}\)

Irons, a native of Council Bluffs, Iowa, had graduated from Rush Medical College in 1903 and was now completing his internship under Herrick at Presbyterian Hospital. His primary interests were infectious diseases and bacteriology. He earned a PhD in bacteriology at the University of Chicago in 1912 and national recognition for his studies on focal infections. From 1923 to 1936, Irons served as dean of his medical alma mater and in 1949-1950 as president of the American Medical Association.\(^22\)

The two men were quite close\(^24,25\) (oral communications, E. Barton, MD, June 30, 1987, and S. A. Friedberg, MD, July 2, 1987). Irons took a room in the Herrick's home, just a few blocks from the medical district, and, from 1904 to 1909, shared Herrick's downtown private office.\(^22\)

Herrick had an interest in blood and blood disorders. In 1892, asked by Dean C. W. Earle of Northwestern University to head the school's medical clinic, Herrick insisted first on a "good microscope" and the latest hemocytometer and hemometer.\(^7\) At the May 1896 meeting of the Illinois State Medical Society, an organization in which he was active,\(^22\) Herrick heard a paper reinforcing his belief in the usefulness of microscopic blood examinations.\(^22\) Two years later he presented a paper in Philadelphia on lymphatic leukemia, attracting the attention of Richard C. Cabot, the famous Boston physician. Cabot even asked Herrick for the names of Chicago's experts on blood and for Herrick's comments on the hematologic aspects of Cabot's own writings. During the fall and winter of 1904, Herrick was again thinking about hematology. In October, he presented a talk to members of the West Side branch of the Chicago Medical Society, introducing a lecture series on diseases of the blood. He titled his discussion, "The Practical Value of Blood Examinations."\(^8\) Both he and his intern, Irons, knew how to prepare their own blood specimens for microscopic studies and how to interpret the results.

Fifty years earlier the two could not have performed such procedures. Knowledge of blood disorders based on red blood cell counts, altered red blood cell morphology, and changes in hemoglobin content grew rapidly during the latter half of the 19th century. Discussions by Rudolph Virchow and others on the significance of blood cells as well as subsequent discoveries by Robert Koch and Paul Ehrlich of effective methods of staining tissues on microscopic slides offered physicians a variety of ways to measure and observe blood components.\(^40\) In the first decade of the 20th century medical writers were recommending, for every newly hospitalized patient, a routine hematologic examination, including a blood cell count, microscopic study of both fresh and fixed blood stained with Ehrlich's triacid stain, and measurement of hemoglobin content.\(^45,46\) These textbooks and articles discussed several types of anemias and leukemias, disturbances in blood's appearance and measurement due to infection or foreign substances, and the use of special stains to demonstrate hidden blood disorders. Hematology, though not a specialty, had become an integral part of medicine.

Integration had begun to occur on another medical front as well. Walter Clement Noel could not have come to
The Presbyterian Hospital, Chicago, Ill.

EXAMINATION OF BLOOD.

Case Number: "Noel"
Date: 12/31
Room or Ward: 7

MACROSCOPICAL AND QUANTITATIVE.
Appearance: 2
Conglobulation: 50%
Erythrocytes per cu. mm. (Thomas Ziehl): 2,840,000
Leucocytes per cu. mm. (Thomas Ziehl): 18,450
Hemoglobin (Van Tienhich): 15,500
Specific gravity: 1036
Color index: 9

MICROSCOPICAL.

FRESH SPECIMEN.

Shape: nuculear- Vacuolated- many "clumps". Figure not assessed.
Leucocytes: apparent increase in number.
Ratio of granular to nongranular:
Fibrin: Blood-plalets
Plasmodium malarias

Fig. 3.—Ernest Irons' blood examination report on Walter Clement Noel, Dec 31, 1904, describing and depicting the oddly shaped red blood cells.

the United States to study dentistry in 1904 had not race relations begun to change around the nation. Emancipation of blacks from slavery after the Civil War had posed terrible medical problems but also opened great opportunities for blacks. With a large, generally impoverished, rural black population in great need of medical care and a white Southern medical profession reluctant to provide that care without payment, the call for black health professionals grew steadily. In answer to that call, a few medical schools in the North occasionally admitted black students, and Northern missionary associations dedicated to providing a basic education for the newly freed slaves established a handful of medical schools including Howard and Meharry. Within a generation, some newly minted black physicians founded private (proprietary) medical schools similar to those proliferating in white America during those pre-Flexner Report days. Schools for training black nurses, dentists, and pharmacists also opened their doors. By the turn of the century, black health professionals were practicing not just in the South, but, in increasing numbers, in the North.

Chicago drew its share of these practitioners, along with many black workers attempting to escape the racism and poverty of the rural South. Black America's most renowned physician and surgeon, Daniel Hale Williams, lived in Chicago and operated Provident Hospital with several other black physicians, staffing it with black nurses and black nursing students. Between 1900 and 1910, the black professional population of Chicago was growing, in part because several of the local white medical schools accepted blacks as students in this unregulated era of keen competition for pupils. It was this magnet of educational opportunities for blacks that attracted Walter Clement Noel to Chicago from his West Indian home.

WHO WAS WALTER CLEMENT NOEL?

Some 4000 km from Chicago and about 160 km from Venezuela lies the island of Grenada. In 1904, the colony, just 19 km wide by 32 km long, belonged to Great Britain; the British and French had traded ownership several times since Grenada's first white settlement in 1650. Though quite English in government, language, and customs, Grenada retained evidence of its French and African heritages, including an abundance of families with French surnames and people of mixed racial background. Census takers in 1901 counted 63,486 citizens, most living in rural areas. Tropical agricultural crops grown on numerous estates throughout the island were the mainstay of the economy. Most business people and professionals lived and worked in St. George's, the capital (population 5184).

Born and raised on Duquesne Estate in the mountainous bush country of St. Patrick's Parish at the north end of the island, Walter Clement Noel grew up in an agricultural setting. His boyhood home, the foundations of which may still be seen, sat atop a hill overlooking the plantation lands in an area of the estate aptly known as Prospect (P. Alexis, oral communication, July 29, 1987). Noel's family was wealthy. His mother, Mary Justina Noel, owned the estate, inherited with other property from her father, who had migrated from Dominica, British West Indies (P. Alexis, oral communication, July 29, 1987). Noel's father, John Cornelius Noel (1849 or 1850-1886), came from a landholding family on the eastern side of Grenada, near Grenville. The family could well afford to pay for Noel's education, when, in June or July of 1904, after completing studies at Harrison College in Barbados, he decided to become a dentist and to study in the United States.

He was not alone in this desire. Other black West Indians also enrolled in American dental and medical schools, especially at those founded in the South to provide professional education for blacks. Such one man, Oliver Charles Arthur, had returned to Grenada in 1901 or 1902, after studying for three years at Howard University Dental School. Arthur opened offices in St. George's and Grenville as the only licensed and professionally educated dentist on the island. Five years older than Noel, Arthur may have encouraged the younger man to pursue a career in dentistry. He wrote letters and sent college transcripts on Noel's behalf, not to one of the Southern black institutions, but first to an unidentified dental school in Pennsylvania and then, when Noel decided on Chicago, to Truman Brophy, dean at CCDS, one of the leading dental schools in the nation. Once the final arrangements had been made, Noel's mother also wrote a note to Dean Brophy from Duquesne, just three weeks before her son's departure: "I will be very glad if you would take an interest in him, and see that he does his work, especially as he is a stranger."

On arriving in Chicago, Noel, with less than $70 in his pocket, found rooms at 618 W Congress St, just one block and around the corner from school, in the heart of the medical district (Fig 1). On Wednesday evening, Oct 5, 1904, he first saw his classmates and faculty, assembled for opening exercises. Though other blacks were studying medicine, dentistry, and nursing in Chicago at the time, he was probably the only black person at CCDS, and one of several foreign students (others came from Europe, Asia, and Canada).

Less than three months later Noel was admitted to Presbyterian Hospital. After intern Irons reported the unusual findings in Noel's blood to Dr Herrick, the two physicians performed and repeated tests on the patient's sputum, stool, urine, and blood, searching for an explanation. Their differential diagnosis included hookworm disease, yaws, syphilis, ground itch, malaria, intestinal...
Fig 4.—Ernest Irons' notes on two 1906 visits to Walter Noel at Frances Willard Hospital and 534 Monroe St.

parasites, and the effects of coal tar medicinal preparations. None fit the clinical picture. Noel slowly recovered his strength and overcame the respiratory infection. His physicians discharged him on Jan 22, 1905, still without a clear diagnosis.

Noel returned to school. A full year elapsed before he again sought Irons' and Herrick's medical attention. He had two admissions to nearby Frances E. Willard National Temperance Hospital (Fig 1): a few days in January 1906 for bronchitis, and two months (Dec 26, 1906 to Feb 26, 1907) for a bilious and muscular attack. He probably participated in the "Students' Sick Benefit Fund," a medical care program sponsored by CCDS that permitted students, for $1 per year, to obtain medical attendance at one of four nearby hospitals [Fig 1]: Presbyterian [affiliated with Rush Medical College], Homeopathic, West Side, and Frances E. Willard National Temperance [sponsored by the Chicago-based Women's Christian Temperance Union]. He traveled for both occasions and, between those hospitalizations, visited the young man twice (in March 1906, for bronchitis, and in May, for knee joint problems) at his new lodging, 534 Monroe St, not far from Irons and Herrick's residence. Irons kept clinical notes each time (Fig 4) and always passed them on to Herrick for his file. Irons saw Noel one last time, in April 1907, to discuss progress made since his February discharge from Frances Willard Hospital. Noel reported feeling much better at that time, except for some lingering shortness of breath.

And then he disappeared. Herrick wrote in 1910, "Since then I have never seen or heard from him."

DISCUSSION

During the 2½ years they knew Noel, Herrick and Irons remained interested in his case. They made extra efforts to determine the root of the young man's problem, followed the course of his disease after discharging him from Presbyterian Hospital, and visited him at home when he was sick. Several possible factors, in addition to the medical uniqueness of the case, help explain Herrick and Irons' concern.

In his article Herrick twice commented about Noel's race and his mental abilities, calling him "an intelligent Negro" and "bright and intelligent." His use of those two phrases suggests that he found Noel different from other black patients he had encountered. Blacks whom Herrick treated at Cook County Hospital, the large charity institution in Chicago where he served as attending physician, often had only recently migrated from the South and had poor financial and educational backgrounds. He likely saw few blacks in his private practice. So the well-educated and well-heeled Noel, a dental student with a West Indian English accent, differed from Herrick's previous experience with black patients. The man gave a good, clear history, and answered medical questions easily. Furthermore, Herrick and Irons were in a private hospital rather than the busy and crowded public facility (Cook County Hospital), so they could make extra efforts to help him.

And the blood findings were interesting. So interesting that, in late 1905 or early 1906, Herrick read articles cited in JAMA's Current Literature section and in German medical journals (he had just spent several months studying in Germany), on yaws, hookworm disease, and alterations in red blood cell morphology. He scribbled down on several pieces of loose paper (one of which was the back side of a daily calendar sheet for Sept 10, 1905) references to four medical journal articles that seemed promising. Though none of the articles satisfactorily answered Herrick's questions about Noel's condition, one of them, written in German, apparently gave him a descriptive term he later applied to the odd cells present in the patient's blood smear: sickle-shaped. The references to these articles sat in Herrick's file, along with Irons' notes from visits to the patient through 1907 and with key documents from Noel's Presbyterian Hospital visit.

For several more years, amid their other activities, Irons and Herrick thought about the strange case. Neither met other physicians who had encoun-
tered similar cases. In a 1954 obituary notice about his mentor, one of the only direct references to the discovery besides Herrick's 1910 case report, Irons stated: "We had never seen anything like this before and Dr. Herrick delayed his report until all sorts of tests to exclude artefacts [sic] were repeated again and again." Herrick even consulted with his highly regarded colleague, Ludvig Hektoen, and tried some experiments to produce sickled cells in vitro, but to no avail. Ultimately stumped by the case, Herrick presented it unsolved in 1910.

Irons played a crucial but less visible role than Herrick in the story. He noticed the strange blood cells after doing the initial blood smear, sketched them, and brought the findings to his attending physician's attention. He followed the patient's course over the next two years, visiting him at home and in the hospital, and turned his notes over to Herrick. Herrick described some of these activities in his 1910 presentation and article, but Irons received none of the subsequent recognition for helping to discover sickle cell anemia. Herrick appears to have directed the handling of the case, performed the search for references, and worked through and written up the results. He therefore has received the credit.

The paper he published was a case study like many of Herrick's other previous writings. By the time he wrote it, his interests had begun to focus on angina pectoris and coronary occlusion, and Irons' interests had turned to his PhD studies on focal infections. Though neither man pursued the case or its implications for hematology, both physicians and their patient had already made their marks on history.

Herrick and Irons were men of their time, open to the new ideas and techniques of medicine being taught in the classroom, described in medical journals, and discussed at medical conventions and local medical society meetings. They applied this new knowledge and technology as best they could in their pursuit of an explanation for Noel's unusual blood problem, even searching the world medical literature for pertinent articles. The end product of their work, publication of a case study, stimulated other physicians to notice similar instances in their own practices and to publish that information. These case studies triggered enough information and curiosity about the sickling phenomenon for physicians to begin conducting full-blown clinical and laboratory studies. By the late 1920s, sickle cell anemia had become a recognized medical entity. By the 1950s it had great importance for medicine as the first identified molecular genetic disease.

Noel, though unusual in national background (West Indian), was an English-speaking black man studying dentistry with whites in the United States. He may have been the only black at CCDS, but others attended integrated or all-black dental, medical, nursing, and pharmacy schools in Chicago and elsewhere. Noel's experience exemplified the racial changes occurring in American society and American medicine.

Epilogue: What Happened to Noel?

Herrick's comment in 1910, "Since then [April 1907] I have never seen or heard from him," seems odd in light of what he and Irons knew of their West Indian patient. Perhaps Noel failed to tell them in April 1907 that he was to graduate from dental school at the end of the following month. But Herrick and Irons could have assumed that his disappearance was related to his student status and inquired at CCDS, directly across the street from Rush Medical College (Fig 1).

Despite his serious and lengthy illnesses between December 1904 and February 1907, Noel completed his work sufficiently well to graduate with his class on May 28, 1907. He returned to Grenada and opened an office in the heart of St George's on the ground floor of a building his mother owned (corner of Young and Government streets, presently occupied by a pharmacy). He lived upstairs (oral communications, E. MacLeish, July 28, 1987; E. Alexis, July 29, 1987; and C. St. Bernard, July 37-31, 1987). Lillie is known of Noel's life during these years. One of his former patients, a 16-year-old schoolgirl at the time, recalls leaving her convent school one day with an escort and walking the few steps to Noel's office, where he pulled her aching tooth. She described Noel as smartly dressed, healthy looking, and plump, with dark coffee-colored skin, a "round, fat face and a good body" (E. MacLeish, oral communication, July 28, 1987). He owned his own dental equipment and, by 1915, had hired a young man in the office as his assistant. Noel never married.

On May 2, 1916, some nine years after his return to Grenada, Walter Clement Noel died in his home/office at age 32. Eldon Marksman, his assistant, reported the death, which Dr G. W. Paterson certified as having been caused by "asthenia from pneumonia." According to family members, Noel, who enjoyed going out, had gone to a "race meeting" (horse race) in Grenville, across the mountains on the other side of the island, and returned, all in one day. He had then taken a bath, caught a chill, developed pneumonia, and died (C. St. Bernard, oral communications, July 27-31, 1987).

Noel could not have been a healthy man. He had suffered several bouts of illness before he left home for Chicago in 1904 and again during his stay there. He died young of pneumonia, a disease not uncommon in those with sickle cell anemia. Furthermore, Noel wrote a will a year before his death, indicating that he had some concern over impending death.

Noel was buried in the Catholic cemetery behind the church in Sauteurs overlooking the Caribbean. He and his sister, Jane, who had died at age 24 ("asthenia from pulmonary tuberculosis"), shared a grave next to their father, who had died some 30 years earlier at age 36 ("disease of the kidney" [Noel told Herrick he had lived off "accidentsltraumatic]). Could each of them (as well as a deceased sister born in 1875) have been victims of sickle cell anemia? Noel never knew that his former physician, Herrick, had presented and published his case history or that he was the first patient with a recorded, documented case of sickle cell anemia.

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The name of Walter Clement Noel is used with permission of Noel's step-grandnephew, Cosmore St. Bernard, St George's, Grenada.
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