This Week's Citation Classic®
CC/NUMBER 49
DECEMBER 9, 1985

Finch S C & Finch C A. Idiopathic hemochromatosis, an iron storage disease. A. Iron metabolism in hemochromatosis. *Medicine* **34**:381-430, 1955.
[Depts. Med., Harvard Med. Sch. and Peter Bent Brigham Hosp., Boston, MA, Univ. Washington Sch. Med., Seattle, WA, and Yale Univ. Sch. Med., New Haven, CT]

This paper combined a presentation of experimental data concerning internal iron metabolism with a comprehensive clinical analysis of idiopathic hemochromatosis. Also included was information concerning the hereditary nature of this disorder and evidence that repeated phlebotomies could remove excess tissue iron with resultant clinical improvement. [The SCI® indicates that this paper has been cited in over 420 publications since 1955.]

Stuart C. Finch
Department of Medicine
Cooper Hospital/University Medical Center
Rutgers Medical School
Camden, NJ 08103

October 14, 1985

The pathology curriculum at the University of Rochester School of Medicine and Dentistry in the 1930s and early 1940s was heavily influenced by the interest in iron metabolism of its eminent dean and Nobel laureate, George Hoyt Whipple.[1] He had demonstrated that most excess tissue iron of dogs could be depleted by chronic phlebotomy.

Paul Hahn, working in that department, wondered whether the tissue iron in idiopathic hemochromatosis might also be removed and repeatedly bled a patient with that disease. His attempt to mobilize iron through creating anemia appeared to be unsuccessful and phlebotomies were abandoned. In retrospect, the patient had a hepatoma that undoubtedly prevented iron mobilization.

A few years earlier, my cousin, Clement Finch, had been a student fellow in Whipple's laboratory. There he developed an interest in the field of iron metabolism, which subsequently became his lifetime major line of investigation. In the mid-1940s, while at the Peter Bent Brigham Hospital in Boston, he undertook iron loading of experimental animals and successfully mobilized the iron by phlebotomy. On the basis of these various studies, he and a research fellow, Charles E. Rath, cautiously initiated a series of phlebotomies on a patient with hemochromatosis. The patient was an employee of the Internal Revenue Service who was of importance to us in more ways than one. It proved possible to bleed him 500 ml weekly without significant anemia developing.

At about that time, I joined the team, and in the course of the next few years, a number of other patients with hemochromatosis were phlebotomized. Some family studies were carried out and additional observations were made in man and experimental animals.[2,3] In the phlebotomized patients, the lack of progression of their diseases and even improvement in clinical status gave credence to the belief that the tissue damage seen in idiopathic hemochromatosis was simply the result of excessive iron stores.

In late 1948, our laboratory was fortunate to have a visit from J.H. Sheldon, a practicing country physician in England who in 1936 had written a classic monograph on hemochromatosis. He urged us to write a comprehensive summary of both our experimental studies and clinical observations. It was not until 1955 that all clinical hemochromatosis papers were reviewed and the paper was finished.

There are probably several reasons the article has been frequently cited. It was a comprehensive article in which differences between excess tissue iron and clinical hemochromatosis due to long-standing tissue iron deficiency were emphasized. Perhaps the most appealing aspects of the paper were 1) the experimental information on storage iron and its mobilization, 2) a comprehensive summary of the various clinical presentations and complications of idiopathic hemochromatosis, 3) information concerning therapeutic phlebotomy and the laboratory changes that occur, and 4) the demonstration that the disease was potentially reversible through the removal of excess iron. The genetic information summarized was more provocative than conclusive, but it may have set the stage for subsequent clinical studies that have clearly defined the genetics and additional clinical aspects of familial hemochromatosis.[4]

1. **Whipple G H.** The hemoglobin of striated muscle. I. Variations due to age and exercise. *Amer. J. Physiol.* 76:693-707. 1926.
2. **Finch C A, Hegsted M, Kinney T D, Thomas E D, Rath C E, Haskins D, Finch S C & Fluharty R G.** Iron metabolism: the pathophysiology of iron storage. *Blood* 5:983-1008. 1950. (Cited 120 times since 1955.)
3. **Haskins D, Stevens A R, Jr., Finch S C & Finch C A.** Iron metabolism: iron stores in man as measured by phlebotomy. *J. Clin. Invest.* 31:543-7. 1952. (Cited 120 times since 1955.)
4. **Milder M S, Cook J D, Stray S & Finch C A.** Idiopathic hemochromatosis, an interim report. *Medicine* 59:34-9. 1980.

