

# This Week's Citation Classic®

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**Bothwell T H, Pirzolo-Birolli G & Finch C A.** Iron absorption. I. Factors influencing absorption. *J. Lab. Clin. Med.* 51:24-36, 1958.  
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The regulation of the absorption of iron was studied in animals and in man. Both the size of iron stores and the rate of erythropoiesis were shown to influence absorption. The larger the iron stores, the less iron was absorbed, whereas the greater the red-cell production, the greater the amount of iron absorbed. [The SCJ<sup>®</sup> indicates that this paper has been cited in over 280 publications.]

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The Fifth Congress of the International Society of Hematology was held in Paris in 1954, and it was at breakfast in a sidewalk café at that Congress that I met Clem Finch for the first time. Out of this meeting came the offer of a job in his hematology laboratory at the University of Washington.

At the time, I was working as a Nuffield Travelling Fellow at the University of Oxford and was pursuing an interest in iron metabolism that had started while I was training as a medical resident in South Africa. The reason for the interest was not difficult to explain, since a large proportion of the adult black population in the country suffered from various degrees of iron overload as a result of drinking fermented beers prepared in iron containers. My own initial studies had, therefore, been directed toward comparing external and internal iron exchange in the local variety of iron overload with the other forms that were recognized elsewhere. It was a field in which Finch's pathophysiological studies had already made a major impact.<sup>1</sup>

When I arrived in Seattle in 1955, a major objective of the iron program was to define

those factors responsible for controlling iron transport, and, during the 18 months I spent there, the particular areas of interest included not only iron absorption but also iron transport to the erythroid marrow<sup>2</sup> and to the fetus.<sup>3</sup>

Insofar as internal iron exchange was concerned, the field had been revolutionized by the availability of radioiron of high specific activity and by the pioneering ferrokkinetic studies of Rex Huff and his colleagues.<sup>4</sup> These techniques were refined and extended in Seattle, and the dominant role of erythropoietic activity in dictating plasma iron turnover was clearly defined.<sup>2</sup>

The same approach was applied to iron absorption. By combining animal and human studies, it was possible to show that the absorptive process was responsive to two major influences—it was inversely related to the size of the iron stores and directly related to the rate of erythropoiesis. In addition, the intraluminal effects of iron dosage and of valency on absorption were also defined in quantitative terms. In a companion investigation, the absorption of food iron was measured in a large number of subjects with various hematologic disorders.<sup>5</sup> In this latter study, the size of the iron stores seemed to be more important in modifying iron absorption than did the rate of erythropoiesis.

The article has probably been frequently cited because it provided a framework for future studies. Any explanation of the control of iron absorption at a molecular level would have to be compatible with the observed effects of storage iron status and erythropoietic activity. Thus far, no really satisfactory explanation has been forthcoming.

From a personal standpoint, it has been an ongoing privilege to continue to work with Finch over the years in collaborative ventures, the most recent of which was the production of a book that covers many aspects of iron metabolism, including absorption.<sup>6</sup>

1. **Finch C A, Hegsted M, Kinsey T D, Thomas E D, Rath C E, Haskins D, Finch S & Fluharty R G.** Iron metabolism. The pathophysiology of iron storage. *Blood* 5:983-1008, 1950. (Cited 120 times since 1955.)
2. **Bothwell T H, Hurtado A V, Donohue D M & Finch C A.** Erythrokinetics. IV. The plasma iron turnover as a measure of erythropoiesis. *Blood* 12:409-27, 1957. (Cited 215 times.)
3. **Bothwell T H, Pribilla W F, Mebus W & Finch C A.** Iron metabolism in the pregnant rabbit. Iron transport across the placenta. *Amer. J. Physiol.* 193:615-22, 1958. (Cited 115 times.)
4. **Huff R L, Hennessy T G, Austin R E, Garcia J F, Roberts B M & Lawrence J H.** Plasma and red cell iron turnover in normal subjects and in patients having various hematopoietic disorders. *J. Clin. Invest.* 29:1041-52, 1950. (Cited 360 times since 1955.)
5. **Pirzolo-Birolli G, Bothwell T H & Finch C A.** Iron absorption. II. The absorption of radioiron administered with a standard meal in man. *J. Lab. Clin. Med.* 51:37-48, 1958. (Cited 145 times.)
6. **Bothwell T H, Charlton R W, Cook J D & Finch C A.** *Iron metabolism in man.* Oxford: Blackwell Scientific, 1979. 588 p.