Technical Papers

Protein Apoferritin and Ferritin in Iron Feeding and Absorption[1]

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The level of iron in the body is relatively constant. Recent studies have indicated that iron, once taken into the body, remained there, the normal rate of iron excretion being negligibly small (*3*). The level of iron then had to be governed by an absorption process in the gastrointestinal tract. Studies by Hahn, Bale, Ross, Balfour, and Whipple (*2*) showed that the gastrointestinal mucosa was indeed the seat of such a regulatory process. The mucosa was found to become "saturated" within a few hours after feeding a dose of iron, and further absorption of iron was prevented for several days. The depletion of body stores of iron resulted in a five- to fifteenfold increase above normal in the rate of absorption of iron. These authors suggested that the "block" of iron absorption might be due to a temporary storage of iron in the mucosal cells, perhaps in the form of ferritin. This storage iron would be in equilibrium with serum iron, and only when the storage iron had been depleted below a certain level would more iron be absorbed.

Recently we have tested this hypothesis in the guinea pig. Advantage has been taken of the great tendency for ferritin to crystallize even in tissue juices. By immersing scrapings of the gastrointestinal mucosa in 10-per cent $CdSO_4$ solution, crystals of ferritin could be observed to form, and the concentration of ferritin in a particular region of the tract could be related to the number and size of the ferritin crystals. In the guinea pig, the two tissues which were found to contain the most ferritin were the liver and the gastrointestinal tract. In these normal, growing animals ferritin in the gastrointestinal tract was found only in the duodenal region, and here only in traces.

When 10-mg. doses of ferrous iron were fed per day, a marked increase in the content of ferritin was noted all along the tract. During the first 24 hours it was mainly found in the upper part of the small intestine. On continued daily feeding of iron it could be found after several days in the walls of the small and large intestines and in smaller amounts in the stomach and even the caecum.

The discovery of ferritin along the gastrointestinal tract, its increase in this tissue in response to iron feeding, and the relatively high content of ferritin in this tissue lends significance to the hypothesis of its regulatory role in iron absorption. The following modification of the hypothesis of Hahn, *et al.* is suggested: Iron is assumed to be absorbed into the mucosal cells in the ferrous form (Fig. 1). Here it is

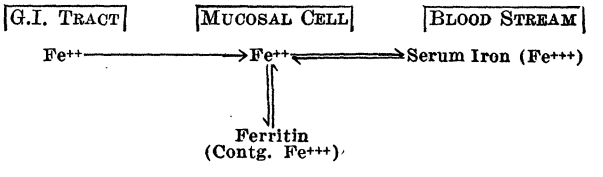

FIG. 1

stored in the form of ferritin, which is a combination of the protein apoferritin with ferric hydroxide (*1*). In the cell there is postulated to be an equilibrium between ferrous iron and the ferric iron stored in ferritin, the cell being in a state of "physiological saturation" with respect to ferrous iron. A lowering of the concentration of serum iron in the blood stream would lead to the removal of ferrous iron from the mucosal cell, resulting in a diminution of ferritin iron in the mucosa. Only when the ferritin iron had diminished to a point where the cell was no longer "physiologically saturated" with respect to ferrous iron would more iron be absorbed by the cell.

The protein apoferritin crystals themselves (*i.e.* ferritin free from iron) could not be detected in the gastrointestinal tract, either in the normal or in the iron-fed animals. In response to iron feeding a great increase in ferritin was observed, which signifies a great increase in the protein apoferritin. Here, then, is the curious phenomenon: The feeding of iron leads to an increase in the concentration of a particular protein which combines with iron to form a storage compound for the iron.

Details of these experiments will be published later.

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References

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