Humans have evolved to expend at least as much physiological effort in excluding dietary iron as in acquiring it

Clinical Implications of New Insights into Hepcidin-Mediated Regulation of Iron Absorption and Metabolism

by Andrew M. Prentice

Key insights
A deeper understanding of the pathways involved in iron homeostasis have overthrown the old paradigm that the human gut is poorly designed for iron absorption. Instead, the normal physiological status in humans is one where iron absorption is constantly suppressed in order to maintain stable iron levels in the absence of active mechanisms for iron excretion. To this end, the central role of hepcidin is to balance the physiological need for iron against the threat of infection.

Current knowledge
Hepcidin is a hormone that functions as the master regulator of iron homeostasis. It interacts mainly through the cellular iron exporter ferroportin. Ferroportin transports iron from cellular stores (i.e., enterocytes, macrophages, and hepatocytes) into the blood, thereby raising the levels of circulating iron. Hepcidin induces degradation of ferroportin, resulting in a net lowering of iron concentrations. Upregulation of hepcidin even at very low levels of inflammation underscores the importance of curtailing iron levels when there is danger of infection. Addressing iron deficiency in poor populations therefore needs to combine hygiene and infection control alongside iron supplementation in order to be safe and effective.

Practical implications
Hepcidin, ferroportin, and their regulators are potential targets for the treatment of iron disorders and anemias. Iron overload could be modulated by artificially enhancing hepcidin. To this end, mini-hepcidins that can perpetuate hepcidin action are being explored. Conversely, the use of hepcidin antagonists could be useful for the treatment of anemia related to chronic disease or cancer chemotherapy. However, when designing interventions that affect iron levels, great care should be taken not to exceed safe iron thresholds.

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