The urge to know: What does iron have to do with infection?

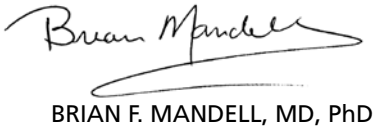
Reading the 1-Minute Consult article by Daoud et al on iron therapy in the setting of infection (page 168 in this issue of the *Journal)* got me thinking about how concepts get incorporated into practice and about the urge and challenge to stay aware of advances in pathophysiology.

If you are one who avoids giving iron to patients with infection, you will be interested in knowing why Daoud et al argue that giving iron is OK. If you hadn't thought about it recently, this is an excellent opportunity to consider why there has been concern. And why *does* the serum iron level drop with infection?

Patients with hemochromatosis, characterized by total body overload of iron, are reported to be at risk of overwhelming infection from *Vibrio vulnificus*. This may well hold true for patients with chronic severe liver disease of other etiologies as well. *Vibrio* and certain other bacteria (*Listeria, Yersinia, Legionella*) can demonstrate rapid growth and increased intracellular resistance to killing in the setting of excess iron. Macrophages, in the setting of chronic infection or inflammation, retain excess iron, which may reduce their bactericidal functions. Thus, there has been concern about iron supplementation (including transfusion) in the setting of infection, even in patients with low iron levels and anemia.

The circulating level of the liver protein hepcidin increases as part of the acute-phase response to infection, perhaps with the physiologic "goal" of reducing the availability of free iron to microbial invaders. Hepcidin binds and blocks the function of the membrane iron exporter ferroportin, and iron is functionally trapped within intestinal enterocytes (reducing its absorption) and macrophages (reducing its availability to erythrocyte precursors).

For some of us out of medical school for more than 10 years, the work of Ganz and others[1,2] describing the seminal role of hepcidin in iron metabolism may be only partially known. The short article by Daoud and colleagues may urge us to read more about the pathophysiologic foundation of a clinical conundrum. I hope so, for it is that urge to understand that helps define our professional identity as physicians.



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1. **Ganz T, Nemeth E**. Hepcidin and disorders of iron metabolism. Annu Rev Med 2011; 62:347–360.
2. **Lee PL, Beutler E**. Regulation of hepcidin and iron-overload disease. Annu Rev Pathol 2009; 4:489–515.

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