To the Editor:

Means and Krantz2 assert that the importance of iron metabolism in the anemia of chronic disease has been controversial. We agree and wish to point out that there is overwhelming evidence that the sequestration of iron in the RE system is an epiphenomenon unrelated to the anemia.

The diversion of red blood cell (RBC) iron to the RE system cannot explain the anemia in chronic disease, because the anemia does not respond to oral iron.2-5 A recent study of the anemia associated with adjuvant arthritis in the rat found that there is no response to parenteral iron6 in this circumstance as well.

Orally administered iron is absorbed normally in the anemia secondary to uremia,7,9 and normally or almost normally in the anemia secondary to rheumatoid arthritis. In comparison to normal controls, it is sometimes slightly decreased,9 sometimes unchanged,10 and sometimes slightly increased.11

Iron absorbed from the gastrointestinal tract binds to transferrin and transferrin-bound iron (when the tracer is administered intravenously) is incorporated efficiently into the erythron in the anemia of chronic disease.3,12 It cannot be argued that absorbed iron follows some other route in chronic disease because, when the tracer is administered orally, iron is incorporated into the erythron in uremia12 and in rheumatoid arthritis13 just as well as in the normal control.

Why then is there hypochromia and increased free erythrocyte protoporphyrin in chronic disease? It is probably because the iron taken up by the RBCs in chronic disease is not used normally. The iron goes possibly, instead of to hemoglobin, to intracellular ferritin and hemosiderin.14 Indeed, siderocytes (ie, circulating RBCs with iron inclusions) are seen in azotemia.15,16 Moreover, there is increased ferritin in bone marrow erythroblasts17,18 in chronic disease, further suggesting a utilization defect. Although the ferritin in the circulating RBCs in chronic disease is normal,19,20 suggesting that the utilization defect is not complete, nevertheless, there remains a sharp contrast with iron deficiency, in which RBC ferritin is decreased.21

A decrease in marrow sideroblasts in the anemia of chronic disease (claimed in some studies)22 is seemingly inconsistent with the conclusion that iron does not limit erythropoiesis. But even where a decrease is claimed, the sideroblast count is still much greater than that in iron deficiency. It must also be noted that some investigators23 have found the sideroblast count in the marrow of the anemia of chronic disease to be the same as that in the normal.

The failure of the RBC to use iron could be secondary to a mitochondrial lesion, a block in heme synthesis, or failure of the mitochondria to take up iron or transport it into the mitochondria from their receptors.24,25

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REFERENCES

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Iron and the anemia of chronic disease [letter; comment]
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