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TO THE EDITOR:

Heterozygous Hemochromatosis is Not Benign

The superb study by the Salt Lake City group¹ of 1058 heterozygotes for hemochromatosis delineates that the phenotype differs from persons who lack this HLA-linked gene defect^{2,3} in having elevated serum iron concentrations, transferrin-saturation, and ferritin protein.

The study delineates that this genetically determined heterozygous abnormality in the regulation of iron absorption usually produces only a modest increase in food iron uptake across the gut wall with a slow progressive build-up of body iron with age manifested in the serum only by a rise with age in serum ferritin, with no concomitant rise with age in either serum iron or transferrin-saturation values. Our own data suggests there is also a rise with age in serum ferritin saturation with iron.⁴

While one can agree with the conclusion that "complications due to iron overload alone in those heterozygotes are extremely rare,"¹ one must caution that the increased body load of stored iron (including that stored on circulating ferritin) means that the triggers

of free radical generation from storage iron, such as the supplements of vitamin C taken by over 40% of Americans daily, produce excessive free radical generation from this excess iron.⁵

When the gene for iron overload is accompanied by the gene for elevated LDL cholesterol, the extra free radical generation converts the harmless LDL cholesterol to vasculotoxic lipoxidized LDL cholesterol, resulting in twice as many coronary occlusions in persons with high LDL cholesterol who also have the gene for iron overload (manifested by a serum ferritin > 200 $\mu\text{g/liter}$) as compared to persons who just have high LDL cholesterol.⁵

Because elevated iron stores are not benign when we let them get higher every year,⁵ we recommend that heterozygotes for hemochromatosis with serum ferritin > 150 $\mu\text{g/liter}$ be voluntary blood donors⁵ often enough (about 3 times a year) to keep their serum ferritin < 150 $\mu\text{g/liter}$.

Since serum ferritin protein is an acute phase reactant, one must rule out that a serum ferritin > 150 $\mu\text{g/liter}$ is due to inflammation rather than iron overload. The classic way to do this is indirectly, by measuring serum iron and percent saturation of iron binding capacity, since iron binding capacity (transferrin) is a reverse acute phase reactant.⁵ One can more directly separate high ferritin protein due to inflammation from that due to iron overload by our new test, measurement of ferritin-iron (i.e., the number of atoms of iron in each molecule of ferritin) (low in inflammation, high in iron overload).^{4,5}



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