Ferritin: *an important part of the iron panel*

Ferritin is protein produced by nearly every cell of the body. Ferritin molecules are large; each molecule can hold 4,500 atoms of iron.

One function of ferritin is to serve as the primary iron reservoir from which iron can be mobilized and used in the production of hemoglobin. Another function of ferritin is to contain iron as part of the Iron Withholding Defense System. Free iron, a powerful oxidant, can severely damage healthy tissues and alter DNA. Functioning in a defensive mode, ferritin keeps iron away from invading cancer and pathogenic microorganisms. These invaders need iron in order to multiply and grow. For this reason, ferritin rises when inflammation is present even though hemoglobin or serum iron might drop slightly. Were it not for this sequestering function, iron would be free to nourish and increase the growth of cancer cells as well as harmful and opportunistic bacteria.

Serum ferritin is a good measure of iron stores, especially for someone who is iron-deficient. Serum ferritin can be elevated in people with iron overload: hemochromatosis, Wilson's disease (copper overload; aceruloplasminemia), porphyria cutanea tarda (PCT), African siderosis, fatty liver disease (non-alcoholic steatohepatitis [NASH]), alcoholic liver disease or from excessive consumption of supplemental iron. SF can also be elevated in conditions where both iron overload and anemia are present generally seen in patients with red blood cell production abnormalities (thalassemia, sickle cell disease, sideroblastic anemia). Often these individuals require long term red blood cell transfusions to correct anemia and to sustain life. Additionally, ferritin can be elevated in chronic renal (kidney) insufficiencies, infections, chronic inflammation, some forms of leukemia and cancers.

Elevated SF can also be seen in patients as a response to medication or hormone replacement therapy or in chronic users of nicotine gums or alcohol. Serum ferritin can be highly elevated in conditions not categorized as iron overload: inflammatory bowel disease, thyroid disease, rheumatoid arthritis or hereditary hyperferrintinemia-cataract syndrome (HFCS). HFCS is a disorder that results in early onset cataracts; SF will be dramatically increased in these individuals. Phlebotomy is not warranted and could actually do harm if performed therapeutically to lower serum ferritin.

Transferrin-iron saturation percentage (TS%) is a sensitive method for determining whether elevated serum ferritin is due to iron overload or inflammation. TS% is an indirect measure of transferrin the protein that carries iron to ferritin, bone marrow, liver and spleen. An elevated TS% > 60% in males or >50% in females is highly predictive for iron overload. When SF is elevated but TS% is not, further investigation is needed. The C-reactive protein (CRP) or tests for specific diseases can more clearly define the underlying cause of abnormal serum ferritin.

Presently normal ranges for serum ferritin vary from lab to lab. Such variations limit the consistency with which patients iron levels can be determined abnormal. Standardizing ranges for serum ferritin is a slow process but one which may soon be achieved. In 2010, the Iron Disorders Institute's Scientific & Medical Advisory Board issued an Opinion Statement that the ideal adult serum ferritin range is 50-150ng/mL. This range applies to those who are healthy or whose iron reduction therapy has achieved a one time target of SF ≤50ng/mL on one occasion.

KEY RESOUCES:

—McLaren CE, Barton JC, Eckfeldt JH, McLaren GD, Acton RT, Adams PC, Henkin LF, Gordeuk VR, Vulpe CD, Harris EL, Harrison BW, Reiss JA, Snively BM. Heritability of serum iron measures in the hemochromatosis and iron overload screening (HEIRS) family study. *American Journal of Hematology.* 2010 85(2):101-5.

—Bacon BR, Olynyk JK, Brunt EM, Britton RS, Wolff RK HFE genotype in patients with hemochromatosis and other liver diseases. *Annals of Internal Medicine*. 1999 130(12):953-62.

—Phatak P, Brissot P, Wurster M, Adams PC, Bonkovsky HL, Gross J, Malfertheiner P, McLaren GD, Niederau C, Piperno A, Powell LW, Russo MW, Stoelzel U, Stremmel W, Griffel L, Lynch N, Zhang Y, Pietrangelo A. A phase 1/2, dose-escalation trial of deferasirox for the treatment of iron overload in HFE-related hereditary hemochromatosis. *Hepatology.* 2010 52(5):1671-779.

—Ghaziani T, Alavian SM, Zali MR, Shahraz S, Agah M, Jensen KP, Ansari S, Sendi H, Lambrecht RW, Covault J, Bonkovsky HL. Serum measures of iron status and HFE gene mutations in patients with hepatitis B virus infection. *Hepatology Research* 2007 37(3):172-8.

—Olynk J, Cullen D, Aquilia S, Rossi E, Summerville L, Powell L. A Population-based study of the clinical expression of the hemo - chromatosis gene. *New England Journal of Medicine* 1999; 341:718–724.

—McLaren C, McLachlan G, Halliday J. Distribution of transferrin saturation in an Australian population: relevance to the early diagnosis of hemochromatosis. *Gastroenterology* 1998; 114:543–549.

—Fargion S, Mattioli M, Fracanzani A, et al. Hyperferritinemia, iron overload, and multiple metabolic alterations identify patients at risk for nonalcoholic steatohepatitis. *American Journal of Gastroenterology* 2001; 96:2448–2455.

—Lim M, Lee C, Ju Y, et al. Serum ferritin as a serologic marker of activity in systemic lupus erythematosus. *Rheumatology International* 2001; 20:89–93.

—Harrison, S.A, B. R. Bacon. Hereditary hemochromatosis: Update for 2003. *Journal of Hepatology* 38 (2003): S14-S23.

Important Ferritin Reference Ranges

ferritin	Adult Males	Adult Females
Ideal Range	50-150 ng/mL	50-150 ng/mL
Induction Phase*	50-75 ng/mL	50-75 ng/mL
Serum ferritin decreases ~30ng/mL per 500cc phlebotomy		

Adolescents, Juveniles, Infants & Newborns
of normal height and weight for their age and gender

Male ages 10-19 23-70 ng/mL	Infants 7-12 months 60-80 ng/mL
Female ages 10-19 6-40 ng/mL	Newborn 1-6 months 6-410 ng/mL
Children ages 6-9 10-55 ng/mL	Newborn 1-30 days 6-400 ng/mL
Children ages 1-5 6-24 ng/mL	

**Induction applies only to patients with ihemochromatosis undergoing therapeutic phlebotomy*

BOOST FERRITIN

—consume meals rich in vitamin C and lean cuts of red meat
—avoid calcium supplements, coffee or tea 2 hours before & after meat meals
—if iron supplements are recommended take them with vitamin C-rich foods or beverages

LOWER FERRITIN

—blood donation, for some: iron chelation therapy
—consume calcium rich foods, coffee and tea at mealtime
—limit supplemental vitamin C at mealtime

December nanograms: iron avidity update—For more articles about iron visit: www.irondisorders.org