

Phlebotomy Guidelines

for Patients with Hereditary Hemochromatosis

NOTE: these guidelines are intended to reduce the risk of under-bleeding or over-bleeding a patient. Each patient is unique. Clinicians may need to adjust phlebotomies accordingly.

Hgb*	SF*	TS%*	Action Employed	MCV*	Comments
Normal	Elevated** 1,000 ng/mL or greater	Elevated greater than 45%	Aggressive	Normal	With few exceptions, pre-treatment Hgb should be 12.5g/dL or greater. SF and TS% should be checked once a month during iron reduction phase. CBC may also be done at this time to determine MCV, etc. MCV will drop by 3% of baseline without causing anemia, when iron reduction reaches ideal SF (see chart below) and TS% levels. DRCA: double red cell apheresis. Well tolerated by many patients; requirements are different; advantages: smaller needle and fewer extractions. Some patients may need fluid replacement. Diet during iron reduction should include restriction of red meat; no raw shellfish or alcohol. Once ideal ranges are achieved, providing limitations of disease consequences (diabetes, mellitus, etc) the diet may resume without restriction. Single Topic Handouts for your patients: Hemochromatosis Diet, Hemochromatosis Genetics, Iron Avidity, DIOS, How Much Alcohol is Safe?
Important: Serum ferritin (SF) >1,000ng/mL is CRITICAL and requires aggressive treatment. (double red cell apheresis) The risk of cirrhosis is <1% in patients whose SF has not been elevated above 1,000ng/mL.					
Normal	Elevated** above normal up to 1,000 ng/mL	Elevated greater than 45%	Aggressive to Moderate	Normal	One unit (500cc) per week depending upon patient, may need to adjust to one unit every other week.
Normal	High Normal**	Elevated greater than 45%	Standard Therapeutic Phlebotomy	Normal	One unit (500cc) monthly.
Normal	Normal**	Normal 25-35%	Routine Blood Donation	Normal	One unit (500cc) every 8 weeks, to maintain SF 50-150 ng/mL with TS% <40%
Normal	Elevated**	Normal	Rule out NASH, dysmetabolic iron overload syndrome (DIOS) chronic liver disease (alcohol, hepatitis) or hyperferritinemia cataract syndrome (HFC). NASH: diagnosis includes: hyperinsulinemia + hepatic index >1.9 HFC: diagnosis: ophthalmologist confirms early onset cataracts. HFC is not a condition of iron overload		Normal
Normal	Normal**	Elevated	Common phenomenon for patients with classic hemochromatosis, possibly caused by abnormal shuttling of iron into plasma due to genetic makeup of the patient. Discontinue phlebotomy until SF rises to ideal range. Read about Iron Avidity www.irondisorders.org or www.hemochromatosis.org		Normal to slightly decreased
Below or low normal (10.5 to 12.0g/dL)	Elevated**	Below Normal	Rule out anemia of chronic inflammation	Check for fever Treat underlying condition: infection, arthritis, irritable bowel disease, etc.	Normal to slightly decreased
Below or low normal (10.5 to 12.0g/dL)	Elevated or normal**	Elevated or normal	Rule out B12/folic acid deficiency	Serum or urine methylmalonic acid (MMA) and homocysteine B12 injections/folic acid supplements	Elevated See maintenance below

*Hgb=hemoglobin; SF=Serum Ferritin; TS%=transferrin-iron saturation percentage; MCV=mean corpuscular volume

**See reference ranges in Ferritin Chart

The therapy for the majority of hemochromatosis patients is blood donation or phlebotomy. Most patients are candidates for standard phlebotomy. With few exceptions, patients should have a pretreatment hemoglobin of 12.5g/dL. Quantities removed by phlebotomy can vary from minimal extraction of 250cc up to large volume extraction of 600cc or more with double red cell apheresis (DRCA). Extraction continues until ferritin reaches 25ng/mL on one occasion but hemoglobin does not drop below normal range for age, weight or gender.

Alcohol consumption or concurrent disease: will influence a patient's unloading pattern and phlebotomy frequency may need to be adjusted. Patients whose initial serum ferritin is above 1,000ng/mL should be advised to abstain from alcohol. A patient's liver health and risk of alcohol consumption should be determined by the physician.

Maintenance: Once iron reduction is achieved (ideal SF and TS% ranges are reached) the patient may require as few as 3 or four phlebotomies a year. Patients can be advised of diet and techniques to help reduce the amount of iron absorbed, which may lessen the frequency of phlebotomy during maintenance.

Minimal extraction: used for youths, persons who are frail, small in stature or weight, or who have coexistent illness such as heart problems. Blood is extracted from vein in the arm using a 20-22 gauge butterfly needle with vacuum bottle. Duration is about 15-20 minutes. The amount extracted is about 250-300 cc (about 125 mg of iron). The frequency can be adjusted depending on patient tolerance. Other patients who may benefit from this method of blood removal are those with small, inaccessible, scarred or rolling veins or those who cannot tolerate a standard phlebotomy.

Sample Phlebotomy Order

"Phlebotomize 500 cc once a week*** if Hgb > 12.5g/dL" (Approximate hematocrit of 38%)

***period of time should reflect frequency desired

Note: For patients whose initial ferritin is greater than 1,000ng/mL, SF should be evaluated every 4-6 weeks until lowered to ~200 ng/mL. Otherwise, SF and TS% can be checked every two bleeds until SF reaches 75ng/mL

Treatment Centers: Iron Disorders Institute maintains two websites that provide information about the National Network of HHC Donor Centers. Many of these centers have a variance from the FDA to use HHC blood for transfusion, and do not charge the patient for phlebotomy, regardless of the frequency. A physician's order is necessary for the patient to participate. Any HHC patient who lives near Bethesda, MD may wish to contact The Warren Magnuson Clinical Center, Hemochromatosis Protocol Coordinator, Yu Ying Yau, RN, at 301-496-1430. YYau@mail.cc.nih.gov www.irondisorders.org or www.hemochromatosis.org

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



Iron Disorders Institute

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www.irondisorders.org

Key References:

- Witte D, Crosby W, Edwards C, Fairbanks V, Mitros F, Hereditary Hemochromatosis *Clinica Chimica Acta* 1996, 245:139-200
- Stephen A. Harrison and Bruce R. Bacon Hereditary hemochromatosis: update for 2003 *Journal of Hepatology*, 38 (2003): 14-238.
- Bolan CD, Conry-Cantilena C, Mason G, Rouault TA, Leitman SF. MCV as a guide to phlebotomy therapy for hemochromatosis. *Transfusion*. 2001 41(6): 819-27.
- Leitman SF, Browning JN, Yau YY, Mason G, Klein HG, Conry-Cantilena C, Bolan CD. Hemochromatosis subjects as allogeneic blood donors: a prospective study. *Transfusion*. 2003 Nov; 43(11): 1538-44.