IRON REIGN™

IMPORTANT TERMS & DEFINITIONS

Hereditary Hemochromatosis • Iron Overload • Diagnosis • Treatment • Genetics

A patient-friendly reference glossary for understanding the language commonly used in hereditary hemochromatosis and iron overload.

A-C

Anemia - A condition in which the blood does not have enough healthy red blood cells or hemoglobin to adequately carry oxygen. It is different from iron overload, although anemia can occasionally complicate treatment decisions.

Arthropathy - Joint disease or joint damage. Hemochromatosis can cause characteristic joint pain and arthritis, particularly involving the knuckles, hips, knees, and other joints.

C282Y - The HFE gene variant most strongly associated with classic HFE hereditary hemochromatosis. People who inherit two copies of C282Y have an increased risk of developing iron overload, although not everyone does.

Carrier - A person who has one copy of a genetic variant associated with a hereditary condition. In HFE hemochromatosis, a carrier usually has one altered HFE copy and one normal copy.

Cirrhosis - Advanced scarring of the liver. Long-standing, severe iron overload can damage liver tissue and eventually contribute to fibrosis and cirrhosis.

Compound Heterozygote - A person who has two different variants in the same gene. In HFE hemochromatosis, the common example is inheriting one C282Y variant and one H63D variant.

D-H

Decompensated Liver Disease - Advanced liver disease in which the liver can no longer adequately perform its normal functions.

DNA (Deoxyribonucleic Acid) - The genetic material containing the biological instructions used in the development and functioning of the body.

Ferritin - A protein that stores iron. A serum ferritin blood test helps estimate the body's iron stores. Elevated ferritin can occur with iron overload but can also rise because of inflammation, infection, liver disease, metabolic conditions, and other causes.

Fibrosis - The formation of scar tissue. Chronic iron accumulation in the liver can contribute to progressive fibrosis.

Gene - A segment of DNA containing biological instructions. Variations in certain genes can affect how the body absorbs and regulates iron.

Genetic Testing - Laboratory testing that looks for genetic variants associated with inherited conditions. HFE testing commonly evaluates variants such as C282Y and H63D.

H63D - A common HFE gene variant. By itself, it is generally much less strongly associated with clinically significant iron overload than C282Y.

Hematocrit (Hct) - The percentage of blood volume composed of red blood cells. It is commonly checked before or during therapeutic phlebotomy treatment.

Hematologist - A physician specializing in diseases and disorders involving blood and blood-forming tissues.

Heme Iron - Iron found primarily in meat, poultry, seafood, and other animal-derived foods. Heme iron is generally absorbed more efficiently than non-heme iron.

Hemochromatosis - A group of disorders characterized by inappropriate accumulation of iron in the body. Hereditary forms result from genetic abnormalities affecting iron regulation.

Hemoglobin (Hgb) - The oxygen-carrying protein in red blood cells. Hemoglobin is routinely monitored during therapeutic phlebotomy.

Hepatologist - A physician specializing in diseases of the liver.

Hepcidin - A hormone produced mainly by the liver that serves as a major regulator of iron balance. In classic HFE hemochromatosis, inadequate hepcidin activity contributes to excessive intestinal iron absorption.

Hepatocellular Carcinoma (HCC) - The most common primary liver cancer. People who develop cirrhosis from hereditary hemochromatosis can have an increased risk of HCC.

Hereditary Hemochromatosis (HH) - An inherited disorder in which the body's regulation of iron absorption is impaired, potentially allowing excessive iron to accumulate over time.

HFE Gene - A gene involved in regulation of iron metabolism. Variants in HFE - especially C282Y - are responsible for the most common form of hereditary hemochromatosis.

Homozygous - Having two copies of the same genetic variant. C282Y homozygous means a person inherited a C282Y HFE variant from each biological parent.

I-M

Iron - An essential mineral needed to produce hemoglobin and support many cellular processes. Too little iron can cause health problems, but excessive iron can also damage tissues and organs.

Iron Overload - Accumulation of more iron in the body than it needs or can safely store.

Iron Studies / Iron Panel - A group of blood tests used to evaluate iron status. Depending on the laboratory, these can include serum iron, transferrin, TIBC, transferrin saturation, and ferritin.

Liver Biopsy - A procedure in which a small sample of liver tissue is removed for examination. It was historically important in evaluating hemochromatosis. Modern blood testing, genetic testing, elastography, and MRI-based iron measurement have substantially reduced the need for biopsy in many patients.

Liver Iron Concentration (LIC) - An estimate or measurement of the amount of iron stored in liver tissue. MRI techniques can now provide noninvasive estimates of LIC.

MRI (Magnetic Resonance Imaging) - A noninvasive imaging technique. Specialized MRI methods can quantify or estimate iron accumulation in organs such as the liver and, in selected circumstances, the heart.

N-S

Non-Heme Iron - Iron primarily found in plant foods and iron-fortified foods. Its absorption is generally more variable than heme iron and is strongly influenced by other components of a meal.

Organ Damage - Injury to tissues or organs resulting from prolonged excessive iron accumulation. Potentially affected organs include the liver, heart, pancreas, endocrine glands, and joints.

Phlebotomy - Removal of blood from the body. Regular blood removal is the standard first-line treatment for most people with HFE hereditary hemochromatosis who require iron depletion.

Secondary Iron Overload - Excess iron caused by something other than classic hereditary hemochromatosis, such as repeated blood transfusions, certain blood disorders, or other medical conditions.

Serum Ferritin - The laboratory measurement of ferritin circulating in blood. It is commonly used with transferrin saturation and other clinical information when evaluating iron overload.

Serum Iron - A measurement of iron circulating in the bloodstream bound primarily to transferrin. It can fluctuate and generally should not be interpreted by itself.

T-Z

Therapeutic Phlebotomy - Medically prescribed removal of blood to lower excessive body iron stores. Each treatment removes red blood cells containing iron, requiring the body to use stored iron to make replacement cells.

Total Iron-Binding Capacity (TIBC) - A blood test that indirectly measures the blood's capacity to bind iron with transferrin. It is used with serum iron to help calculate transferrin saturation.

Transferrin - The principal protein responsible for transporting iron through the bloodstream.

Transferrin Saturation (TSAT or TS%) - The percentage of transferrin's available iron-binding sites occupied by iron. It is one of the most important screening measurements when evaluating suspected iron overload.

Unsaturated Iron-Binding Capacity (UIBC) - A measurement of the portion of transferrin's iron-binding capacity that is not currently occupied by iron.

Variant - A difference in a DNA sequence. Genetic variants can be harmless, influence disease risk, or cause disease depending upon the gene and specific variant.

Venesection - Another term for phlebotomy, commonly used outside the United States.

Vitamin C and Iron Absorption - Vitamin C can increase intestinal absorption of non-heme iron. This is particularly relevant when considering high-dose vitamin C supplementation in people with iron overload.

KEY IRON REIGN PRINCIPLE

No single laboratory result should be used by itself to diagnose hereditary hemochromatosis.
Transferrin saturation, ferritin, clinical history, genetic testing when appropriate, and evaluation for other causes of abnormal iron studies should be considered together.

Educational information only. Laboratory reference ranges and clinical decisions vary by laboratory, patient, and medical situation. Patients should review abnormal results and treatment decisions with a qualified healthcare professional.