DR. JEFF C.H. DONOVAN

DERMATOLOGIST, SPECIALIZING IN HAIR LOSS

4370 Lorimer Road
Suite 334B
Whistler, BC, Canada
V8E 1A6

Tel: 604.283.1887
Fax: 604.648.9003
Email: office@donovanmedical.com
Web: www.donovanmedical.com

HEMOCHROMATOSIS

Ferritin levels are commonly ordered as part of a standard work up for many patients with hair loss. Although low ferritin levels are commonly thought to be associated with hair loss, one must not simply skim over the lab results too quickly if the ferritin levels return back showing that the patient has extremely high ferritin. Although there are many, many causes of elevated ferritin, it is important for all hair specialists to immediately recognize the possibility that a patient with elevated ferritin might have a diagnosis of hemochromatosis.

Consideration must be given to the possibility of hemochromatosis in all patients with both of the following two criteria:
a) an elevated transferrin saturation above 0.45 (45 %) and
b) an elevated ferritin level above 200 ng/mL in women and 300 ng/mL in men

What is " hemochromatosis"?

- This is a condition whereby the body absorbs and stores too much iron. Normally, the job of the intestines is to absorb iron. In hemochromatosis, the intestines do this too effectively and iron accumulates to harmful levels in the body.
- Iron accumulates in many organs and may cause injury to those organs.
- The heart, liver and pancreas (and rarely thyroid) are the main organs that are likely to be damaged by iron overload in patients with hemochromatosis

What is primary hemochromatosis and what is secondary hemochromatosis?

- Primary hemochromatosis is the hereditary form. The affected patient inherits one gene (called the HFE gene) from his or her mother and one gene from the father. These genes tend to increase the ability of the intestine's to absorb iron from the diet. This form occurs commonly in those of European descent and men are 5 times more likely to be affected than women.
- Secondary hemochromatosis is a form of hemochromatosis where iron overload occurs from liver disease (hepatitis C, fatty liver disease), kidney dialysis, or too many blood transfusions in the past

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How common is "primary" (hereditary) hemochromatosis?

- About 0.5 % of those with European ancestry have hereditary hemochromatosis. That works out to 1 in 1000 people.

What symptoms might a person have?

- Often patients have no symptoms. In fact, about ¾ of people who are diagnosed are asymptomatic because they get tested long before they develop symptoms. Many get tested because they learn of a family member who was affected.
- In men, symptoms start appearing sometime between ages of 30 and 50. In women, symptoms don't often appear until menopause.
- Symptoms may be vague in some, which delays the diagnosis. These symptoms include
    - Fatigue and lethargy
    - Weight loss
    - Erectile dysfunction in men
    - Loss of sex drive
    - Joint pain (knuckles – especially 2nd and middle fingers)
    - Abdominal pain
    - Jaundice
    - Bronze or grey color to skin (late finding)
    - Memory problems
    - Heart rhythm disturbances
    - Early menopause
    - Depression
    - Diabetes
    - Testicular atrophy
    - Hypothyroidism

How is hemochromatosis diagnosed?

- A full history and physical examination will be performed by the doctor. Questions pertaining to fatigue, weight loss, jaundice, abdominal pain, sexual dysfunction, prior blood transfusion, family history, alcohol use, iron supplements, and other questions will be asked. An examination will be done including heart and liver and joint examination.
- In terms of diagnostic tests, a blood test is a good starting point after the history and physical is performed. An elevated level of TRANSFERRIN SATURATION (RATIO OF SERUM IRON/TIBC) is a potential indicator that something is not quite right. Ideally these tests and all blood tests in this particular work up should be done fasting (this is still controversial)
- In general, anyone with a transferrin saturation above 45 % should be investigated further. That's a pretty low cut off but helpful in screening people who might benefit from a proper work up
    - A transferrin saturation above 40 % in women is particularly abnormal
    - A transferrin saturation above 50 % in men is particularly abnormal

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- If TRANSFERRIN SATURATION is elevated, the next step is to measure FERRITIN levels
    - For patients with hemochromatosis, transferrin saturation is elevated and ferritin levels are generally above 300 ng/mL in men and 200 ng/mL in women. Ferritin can be elevated for many other reasons so it's important not to conclude that everyone with elevated ferritin to these levels has hemochromatosis. However, patients with elevated ferritin and elevated transferrin saturation need to have the proper work up to rule out hemochromatosis.
- Liver enzymes
    - AST, ALT, bilirubin, ALP
    - If liver enzymes levels are abnormal (or ferritin above 1000), a liver biopsy might be considered if hemochromatosis is suspected or confirmed.
- Other tests are often ordered
    - including fasting blood glucose, hemoglobin A1c, triglycerides, TSH and vitamin B12
- Gene mutations
    - The C282Y gene mutation is most common gene mutation but others including the H63D HFE gene mutation are also found. Patients with the C282Y mutation are the most likely to be symptomatic
    - It's important to discuss the pros and cons of being tested for the hemochromatosis gene mutations.
    - If positive, referral should be made to an expert in hemochromatosis (often a hematologist but this varies from center to center)
    - About 10 % of patients of European ancestry have ONE HFE gene mutation. But it normally takes two genes (one from each parent) for patients to develop iron overload and the clinical findings of hemochromatosis
- Liver biopsy
    - If hemochromatosis is confirmed, a patient may undergo a liver biopsy to see how much iron has accumulated and how healthy the liver is. This is often done with significantly high ferritin levels and in those with elevated liver enzyme results or abnormal liver ultrasound or MRI findings.
- MRI scans
    - In some centers, patients may have an MRI scan to see how much iron has accumulated in various parts of the body.

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What conditions besides hemochromatosis can give elevated ferritin and elevated transferrin saturation?

In addition to hemochromatosis, the following conditions can be associated with elevated transferrin saturation

- Porphyria cutanea tarda (normal HGB)
- Sideroblastic anemia (low HGB)
- Thalassemia (low HGB)
- B12 deficiency (low HGB)

What complications can arise from having hemochromatosis?

Several diseases can occur in patients with hemochromatosis including :

- Liver problems (including cirrhosis and liver cancer).
- Diabetes
- Heart arrhythmias
- Cardiomyopathy
- Heart failure
- Arthritis
- Osteoporosis or osteopenia
- Erectile dysfunction (men)
- Early menopause (women)
- Predisposition to certain types of infections

What is the treatment for hemochromatosis?

- The main treatment for most cases is phlebotomy or "bloodletting". The goal of removing blood from the body is to reduce iron levels. Red blood cells are packed full of iron and so removing blood provides a simple way to lower the iron levels in the body. Iron supplements should be stopped.
- Phlebotomy is started right away if ferritin levels are less than 1000 and the liver enzymes are normal. In general, the goal is to bring ferritin to levels between 50 and 150 ng/mL and keep hemoglobin above 125 g/L (12.5 g/dL**)** If ferritin levels are above 1000 or liver enzymes are elevated generally a liver biopsy will be considered.
- Some physicians recommend waiting to start phlebotomy until it is clear that iron has started to accumulate in one or more organs.
- With phlebotomy, the hope is to bring the ferritin and transferrin levels back to normal. Patients will have their hemoglobin, ferritin and transferrin saturation measured every 4-12 weeks. If the hemoglobin drops too fast and the patient now starts to develop an anemia, the phlebotomy will be done slower.

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- The actual amount of blood removed will depend on the patient, his or her age and the severity of the iron overload. For many patients, 500 mL is removed every week or even twice per week until levels normalize. Thereafter, phlebotomy occurs every 2-4 months (rarely monthly). Some patients do not require ongoing phlebotomy after an initial session or two.
- Phlebotomy is helpful to prevent complications provided the hemochromatosis is diagnosed before complications have set in. If there are already complications that have occurred, phlebotomy can help slow the progression of the complications (such as joint pain and liver cirrhosis).
- For those who cannot tolerate phlebotomy, therapies to chelate iron may be prescribed
- Other recommendations are commonly given including:
    - Avoiding addition iron supplements or multivitamins containing iron
    - Avoiding taking extra vitamin C
    - Avoiding alcohol as it may further damage the liver. The incidence of cirrhosis is markedly increased in those who consume alcohol
    - Avoiding eating undercooked seafood, shellfish and raw fish as patients with hemochromatosis are at increased risk to develop serious infections from eating these foods. Many of these seafoods contain bacteria that thrives in iron rich environments. In addition, iron accumulates in certain immune cells and reduces the ability to fight certain infections.

In addition to phlebotomy, screening tests will be done for patients with hemochromatosis to assess the liver (liver ultrasound), heart (EKG, ECHO), and endocrine system (hormone testing). Other tests may be done as well as mentioned above including fasting blood glucose, hemoglobin A1c, triglycerides, TSH

Do the patient's family members need to be tested if a patient has hemochromatosis?

- It is often recommended that the first-degree relatives of people with hemochromatosis undergo testing. This includes the patient's parents, siblings, and children.