What is Iron Overload?

Iron overload occurs when you have too much iron in your body. This can be a problem for people who get lots of red blood cell transfusions. Red blood cells contain iron. Each time you get a red blood cell transfusion you are putting more iron in your body. Your body doesn't have a good way to get rid of the extra iron you get from blood transfusions. This iron can build up in your vital organs and may injure them over time.

This section helps you understand iron overload and how to treat iron overload. Also visit our Online Learning Center to view a webcast on iron overload.

1. What actually happens to cause iron overload?

With each red blood cell transfusion, your body receives more iron. As red cells break down over time, the iron in the hemoglobin is released. Your body has no natural way to rid itself of excess iron, so extra iron is stored in body tissues. That's why patients receiving transfusions are at risk for iron overload.

Your body normally stores up to 3 or 4 grams of iron. On average, a person receives 2 units of blood during a red blood cell transfusion, and each unit of blood has 200 to 250 milligrams of iron. So each 2 unit blood transfusion adds an extra 400 to 500 milligrams of iron to your body. If you get one blood transfusion of 2 units each month, you would accumulate about 5 to 6 grams (5000-6000 milligrams) of extra iron in one year.

Your body doesn't know how to get rid of excess iron. But it does know how to store it. A protein called transferrin carries iron through your blood and to your organs where it is stored. Extra iron that is not immediately needed to make new blood cells is normally stored in the liver, spleen, and bone marrow. This excess iron can lead to injury of the organs in which it is deposited.

Excess iron may accumulate in these 3 normal storage sites and also in other organs that don't normally store iron, such as the:

- Pancreas
- Joints (especially in the hands)
- Skin
- Pituitary gland
- Adrenal glands
- Thyroid gland
- Sex organs
- Heart

What are the symptoms of iron overload?

Early on, iron overload can cause no symptoms, or it can cause non-specific symptoms that are also seen in other conditions. Many patients may not experience any symptoms of iron overload. Your doctor may use blood tests to monitor your iron levels if you are receiving lots of red blood cell transfusions. Some of these symptoms include:

- Tiredness or weakness
- Loss of sex drive
- Weight loss
- Abdominal pain
- Joint aches or pain
- Young people might not grow or go through puberty normally.
- Women might stop getting their periods.

With severe iron overload, you may experience:

- Gray-colored or bronze-colored skin
- Shortness of breath
- Arthritis
- Liver disease, including cirrhosis or liver cancer
- Enlarged spleen that may cause abdominal pain or difficulty eating a normal-sized meal
- Diabetes
- Shrunken testicles
- Heart problems, including both heart failure and heart rhythm problems

About 1 in 300 Americans naturally absorb and store increased iron. This is caused by a hereditary condition called hemochromatosis. Hereditary hemochromatosis is most common in people whose ancestors came from Northern Europe. Patients with this condition may get symptoms of iron overload very quickly. They may also develop a condition that needs blood transfusion.

What tests are used to detect iron overload?
High levels of iron can be detected through two simple blood tests. These tests tell doctors how much iron is stored in your body.

- **Serum transferrin saturation.** A serum transferrin saturation test measures the amount of iron attached to transferrin in your blood. Transferrin is a protein that attaches to iron and carries it in your blood. Transferrin levels greater than 45 percent are generally considered too high.

- **Serum ferritin.** Ferritin is a protein inside of cells that stores iron for later use by your body. For unknown reasons, a small amount of ferritin is released into your blood. The ferritin level in your blood is called your serum ferritin level. By testing serum ferritin levels, doctors can determine the total amount of iron that is being stored in your cells. Serum ferritin levels are generally considered high when they are above 1000 ng/mL.

There are a number of conditions other than iron overload that can affect your serum ferritin. These can make diagnosing iron overload difficult. Some patients have a high ferritin level, but no signs of iron overload when special tests are done. You may need to have the blood tests repeated to get the most accurate results.

Normal serum ferritin level is in the range of 12 to 350 ng/mL for men and 12 to 300 ng/mL for women (there is variability in normal ranges between different laboratories). Since ferritin levels are an imperfect measure of the degree of iron overload, there is uncertainty among doctors about at what serum ferritin level treatment for iron overload should begin.

Some doctors will want to begin treatment for iron overload when the patient's serum ferritin is in the range of 1,000-1,500 ng/mL. Others may recommend beginning treatment after 20 or more red cell units have been transfused, even if the ferritin hasn't quite reached 1,000 ng/mL.

To get a more exact measure of iron overload, there are some other tests your doctor may want to perform:

- **Liver Biopsy.** In a liver biopsy, a needle is inserted into your liver and a small amount of tissue is removed to determine how much iron is present. Having a biopsy also allows your doctor to tell whether the organ is being damaged by iron. There are some risks of this procedure, including a risk of bleeding (especially for patients with low platelets) and infection. Also, liver biopsies don't tell you if you have any iron in your heart.

- **SQUID (Superconducting Quantum Interference Device).** This imaging test uses a very low-power magnetic field with very sensitive detectors to measure the presence of iron in your body with a high degree of accuracy. However, the complexity, cost, and technical requirements of this technology have limited its use for measuring iron. Only a handful of SQUID **machines are available in the United States.**

- **MRI (Magnetic Resonance Imaging).** A special MRI test – sometimes called T2 MRI, R2 MRI or quantitative MRI – uses the magnetic properties of the body to provide detailed three-dimensional images and an estimate of how much iron there is in different organs. MRIs can let doctors see how much iron is in the heart and liver without the risk of bleeding and infection associated with biopsy. This technology is relatively new and not all centers have access to it, but the number of places where it is available is growing.

How quickly does iron overload happen?
The answer is different for each person. It is difficult to predict the rate at which iron will accumulate in a given patient. For some people, it can take many transfusions over many years for the buildup of iron to cause problems. But, for others it can happen very quickly—after as few as 10 to 15 transfusions (20 to 30 units of red blood cells). This is why it is important to talk to your doctor about any symptoms you are having and get your iron levels tested regularly.

Does iron overload make you sick right away?

Iron overload affects each person differently. And there is no definitive set of symptoms that tells you whether or not you have iron overload. Some of the symptoms are like those of many other diseases. These include tiredness, weakness, abdominal pain, low sex drive, and joint pain. This can make it difficult for a doctor to recognize and diagnose. If left untreated, iron overload can cause organ damage in some people. If this happens, you can become sick very quickly.

When should I worry about iron overload?
In general, you should start being screened for iron overload at the time of your diagnosis. After you have received about 20 units of blood, you should be tested again. It is important to keep track of how many units of blood you receive each time you get a blood transfusion. You may get 2 or more units each time you get a blood transfusion. You might need to get tested for iron overload after only 10 blood transfusion episodes. If you don't know how many units you get during your blood transfusions, ask your doctor or nurse to help you find out.

Can anything make iron overload worse?
Patients with iron overload should not take iron supplements or multivitamins with iron. Patients with hereditary hemochromatosis may develop iron overload after a very small number of transfusions. Alcohol use also can increase iron overload in the liver and can also damage the liver. Also, some viral infections such as Hepatitis C can cause the liver to be damaged by iron more quickly and seriously.

Check with your doctor to see if you should make any changes to your diet. Because the typical iron absorption from our diets is low (1 to 4 milligrams of iron per day) compared to the amount of iron in a single unit of blood cells (200 to 250 mg per day), some doctors will counsel you to eat a generally healthy diet and not to worry. Other doctors may recommend a diet that is low in iron-rich foods, avoiding such items as:

- Red meat
- Tuna
- Salmon
- Iron-fortified cereals
- Eggs

How can iron overload be treated?

- **Iron chelation** is a drug therapy for iron overload. This therapy uses drugs called iron chelators to remove extra iron from your body. There are two iron chelators that are approved by the U.S. Food and Drug Administration (FDA) for use in the United States. If you are considering iron chelation, you should discuss possible side effects with your doctor. You will require extra laboratory tests to monitor for side effects that you may not feel.

- **Deferoxamine (Desferal®)** is usually administered by subcutaneous (under the skin) infusion using a small portable pump about the size of a CD player. Patients using the pump are instructed how to sterilize the skin, insert the needle, and operate the pump. The pump is worn for 8-12 hours a day, usually at night while sleeping. Patients who are severely iron overloaded may need a continuous infusion through a central venous catheter. Deferoxamine works by binding with the excess iron so that it can be excreted. Many patients find it hard to tolerate Deferoxamine because of the discomfort and inconvenience of using the pump. However, many studies have demonstrated that Deferoxamine is very effective at reducing iron overload.

- **Deferasirox (Exjade®)** is a newer iron chelating medication that comes in a tablet form. It is dissolved in juice or water and taken (by mouth) once a day. Most patients tolerate it very well, but side effects can include nausea, diarrhea, rash, and more serious effects such as kidney or liver injury. Once the body gets used to the drug, side effects usually go away. Your doctor should monitor your liver and kidneys for potentially serious side effects while you are taking Deferasirox. *When taking either Deferoxamine or Deferasirox, you should:*

1. Have your vision and hearing tested prior to starting therapy, with re-testing every 6-12 months. Both Deferoxamine and Deferasirox can cause damage to the eyes and ears.

2. Avoid taking Vitamin C unless it is prescribed by your doctor. Under your doctor's specific orders, Vitamin C can be added at a later time to iron chelation therapy and may improve results for some patients. Vitamin C should only be taken in a moderate dose, such as 100 mg daily.

Deferiprone or L1 (FerriproxTM)—currently being used in Europe, Asia and Canada, but is not yet approved by the FDA for use in the United States—comes in a pill form and is taken three times a day. It is generally well tolerated by patients, but it can cause a drop in white blood cell counts, so patients need to have their blood checked weekly while taking this drug (white blood cells protect you against infections).