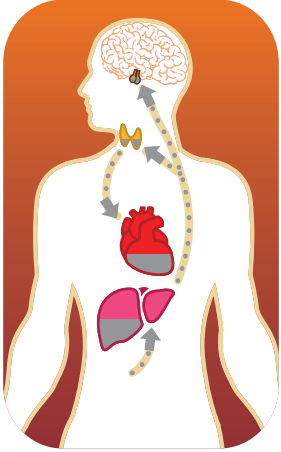


Chronic Iron Overload



When the body's iron capacity is exceeded and the body cannot get rid of it, iron builds up—first in the liver, and then in hormonal organs like the thyroid and pituitary glands, and eventually in the heart. This condition is called chronic iron overload.³

Iron is an essential element in the human body mostly found in red blood cells. Iron helps cells “breathe” by carrying oxygen to cells and tissues, and is essential to giving the body energy and having a properly functioning immune system.¹ Most people get iron from the food they eat, including animal products, plants and iron-fortified foods.²

In a healthy person, most of the iron within the body is found in red blood cells as part of the protein called hemoglobin. Iron circulates through the body continuously and any unused iron is stored in cells of the liver, the bone marrow and the spleen for future use.¹

A condition called chronic iron overload develops when the body's limited iron storage capacities are exceeded. Since there is no natural mechanism to remove excess iron from the body, iron builds up – first in the liver, and then in hormonal organs like the thyroid and pituitary glands, and eventually in the heart.³

The major cause of chronic iron overload is regular blood transfusions, which can be required for managing many chronic health conditions such as sickle cell disease, thalassemia, and myelodysplastic syndromes.^{3,4} One unit of blood contains on average 200 mg iron.⁵ As the iron level in the body rises, it can be detected in the level of the iron storage protein in the blood, the serum ferritin, which also rises. Serum ferritin levels can be tested using a simple blood test. Chronic iron overload occurs when the serum ferritin level consistently rises above 1,000 µg/L. The normal level of serum ferritin ranges from 12-300 µg/L for men and 12-150 µg/L for women.³

Transfusions of only 20 units of blood over time (10 in children) can lead to chronic iron overload.³ The consequences of iron overload include organ dysfunction and organ damage.³

Causes and Consequences

In addition to blood transfusions, accumulation of excess iron in the body can result from increased iron absorption in the stomach and intestines. A healthy person absorbs and releases about 1-2 mg of iron each day, or about 10-15% of the iron in a normal diet.^{1,2} People with certain blood disorders such as non-transfusion-dependent thalassemia (NTDT) absorb about 3-4 mg of iron each day or up to 20% of the iron in a normal diet.^{1,6}

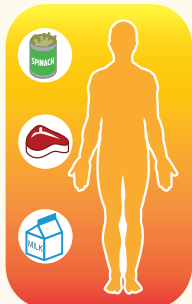
In these patients, the body absorbs more iron in order to produce more healthy blood cells, but because these patients' bodies are unable to produce healthy blood cells, the iron accumulates in their bodies instead.



Blood cells in a vein

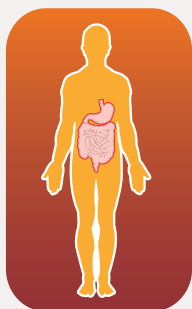
How iron enters the body

FOOD



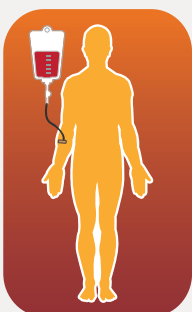
A **healthy person** absorbs and releases about 1-2 mg of iron each day, or about 10-15% of the iron in a normal diet.^{1,2}

Intestinal Absorption



A **person with non-transfusion-dependent thalassemia (NTDT)** absorbs about 3-4 mg of iron each day, or up to 20% of the iron in a normal diet.^{1,6}

Blood Transfusion



A **person who receives blood transfusions** absorbs an average of 200 mg of extra iron from each unit of blood transfused.⁵ As few as 20 transfusions in a lifetime (10 in children) can lead to chronic iron overload.³

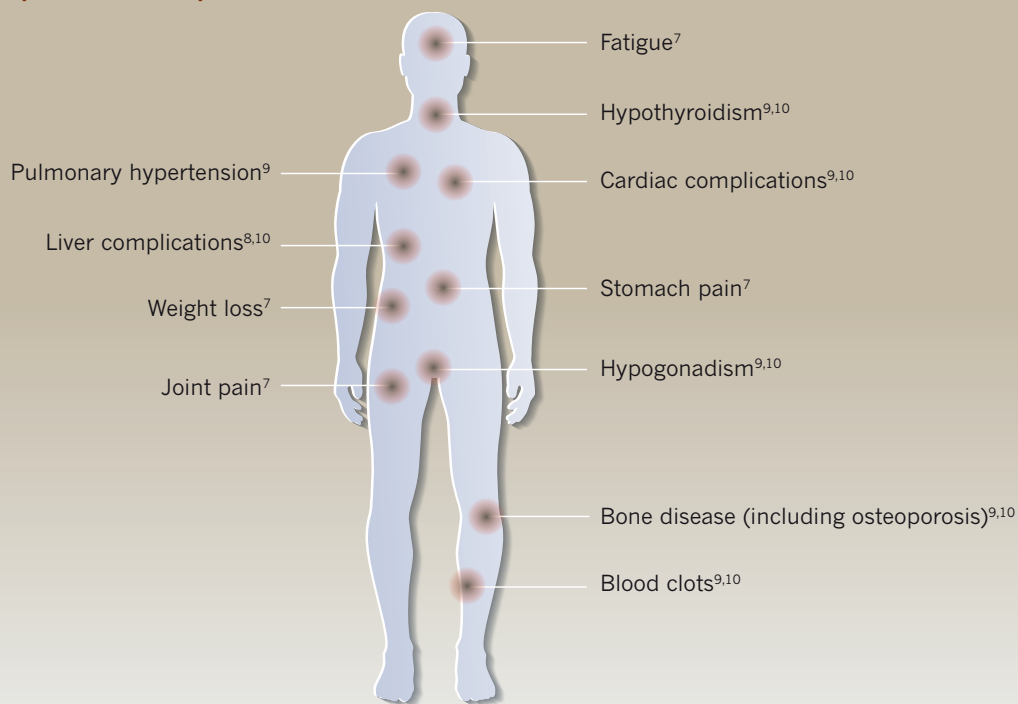
Symptoms and Complications

Symptoms of chronic iron overload may not appear until substantial organ damage has occurred. Therefore, a high degree of awareness is necessary to identify patients at risk.

Early symptoms are typically non-specific, and include symptoms commonly seen in primary care, such as fatigue, joint pain, weight loss and stomach pain.^{3,7}

Later complications of chronic iron overload vary with the underlying disease in transfusion-dependent anemias, and may include blood clots, bone disease (including osteoporosis), pulmonary hypertension, hypothyroidism, and damage to organs including the reproductive system and the liver.^{8,9} In non-transfusion-dependent anemias, the clinical consequences of iron overload include liver disease, bone disease, blood clots, endocrine disorders and sometimes cardiac complications.¹⁰

Symptoms and Complications



When chronic iron overload is detected, patients can work with their doctors to monitor iron levels as part of their overall treatment plan.

References

- Muñoz M, Villar I, García-Erce JA. An update on iron physiology. *World J Gastroenterol.* 2009 Oct 7; 15(37):4617-4626.
- National Institutes of Health. Dietary Supplement Factsheet: Iron. Accessed July 7, 2014 from <http://ods.od.nih.gov/factsheets/Iron-HealthProfessional/>.
- Shander A, Cappellini MD, Goodnough LT. Iron overload and toxicity: the hidden risk of multiple blood transfusions. *Vox Sanguinis* 2009; 97, 185-197.
- Andrews NC. Disorders of iron metabolism. *N Engl J Med* 1999; 341:1986-1995.
- Thalassemia International Federation. Guidelines for the clinical management of thalassemia. Nov. 2008.
- Cappellini MD, Cohen A, Eleftheriou A, et al. Guidelines for the clinical management of thalassemia. Nicosia, Cyprus: Thalassemia International Federation; 2008.
- Yen AW, Fancher TL, Bowlus CL. Revisiting Hereditary Hemochromatosis: Current Concepts and Progress. *The American Journal of Medicine* 2006; 119, 391-399.
- Kohgo Y, Ikuta K, Ohtake T, Torimoto Y, Kato J. Body iron metabolism and pathophysiology of iron overload. *Int J Hematol.* 2008 Jul; 88(1):7-15.
- Musallam et al. Elevated liver iron concentration is a marker of increased morbidity in patients with beta thalassemia intermedia. *Haematologica.* 2011, 96(11): 1605-1612.
- Musallam, KM. Iron overload in non-transfusion-dependent thalassemia. *Thalassemia Reports.* 2013; 3(1): 34-36.