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**Iron metabolism, iron deficiency anemia**

**Human iron metabolism** is the set of chemical reactions that maintain [human homeostasis](https://en.wikipedia.org/wiki/Human_homeostasis) of [iron](https://en.wikipedia.org/wiki/Iron) at the systemic and cellular level. Iron is both necessary to the body and potentially toxic. Controlling iron levels in the body is a critically important part of many aspects of human health and disease. [Hematologists](https://en.wikipedia.org/wiki/Hematologist) have been especially interested in systemic iron [metabolism](https://en.wikipedia.org/wiki/Metabolism) because iron is essential for [red blood cells](https://en.wikipedia.org/wiki/Red_blood_cells), where most of the human body's iron is contained. Understanding iron metabolism is also important for understanding diseases of [iron overload](https://en.wikipedia.org/wiki/Iron_overload), such as [hereditary hemochromatosis](https://en.wikipedia.org/wiki/Hereditary_hemochromatosis), and [iron deficiency](https://en.wikipedia.org/wiki/Iron_deficiency), such as [iron-deficiency anemia](https://en.wikipedia.org/wiki/Iron-deficiency_anemia).

**Cellular respiration**

Human cells require iron in order to obtain energy as ATP from a multi-step process known as cellular respiration, more specifically from oxidative phosphorylation at the mitochondrial cristae. Iron is present in the iron–sulfur cluster and heme groups of the electron transport chain proteins that generate a proton gradient that allows ATP synthase to synthesize ATP (chemiosmosis). Heme groups are part of hemoglobin, a protein found in red blood cells that serves to transport oxygen from the lungs to other tissues. Heme groups are also present in myoglobin to store and diffuse oxygen in muscle cells.

**Oxygen transport**

The human body needs iron for oxygen transport. Oxygen (O2) is required for the functioning and survival of nearly all cell types. Oxygen is transported from the lungs to the rest of the body bound to the heme group of hemoglobin in red blood

**1**

cells. In muscles cells, iron binds oxygen to myoglobin, which regulates its release.

**Toxicity**

Iron is also potentially toxic. Its ability to donate and accept electrons means

that it can catalyze the conversion of hydrogen peroxide into free radicals. Free radicals can cause damage to a wide variety of cellular structures, and ultimately kill the cell. Iron bound to proteins or cofactors such as heme is safe. Also, there are virtually no truly free iron ions in the cell, since they readily form complexes with organic molecules. However, some of the intracellular iron is bound to low-affinity complexes, and is termed labile iron or "free" iron.

To prevent that kind of damage, all life forms that use iron bind the iron atoms to proteins. This binding allows cells to benefit from iron while also limiting its ability to do harm. Typical intracellular labile iron concentrations in bacteria are 10-20 micromolar, though they can be 10-fold higher in anaerobic environment, where free radicals and reactive oxygen species are rare,In mammalian cells, intracellular labile iron concentrations are typically smaller than 1 micromolar, less than 5 percent of total cellular iron.

**Mechanisms of iron regulation**

Human iron homeostasis is regulated at two different levels. **Systemic iron levels are balanced by the controlled absorption of dietary iron by enterocytes, the cells that line the interior of the intestines,** and **the uncontrolled loss of iron from epithelial sloughing, sweat, injuries and blood loss**. In addition, systemic iron is continuously recycled. Cellular iron levels are controlled differently by different cell types due to the expression of particular iron regulatory and transport proteins.

**2**

**Systemic iron regulation**

**Dietary iron uptake**

Like most mineral nutrients, the majority of the iron absorbed from digested food or supplements is absorbed in the duodenum by enterocytes of the duodenal lining. These cells have special molecules that allow them to move iron into the body. To be absorbed, dietary iron can be absorbed as part of a protein such as heme protein or iron must be in its ferrous Fe2+ form. A ferric reductase enzyme on the enterocytes’ brush border, duodenal cytochrome B (Dcytb), reduces ferric Fe3+ to Fe2**+.** A protein called divalent metal transporter 1 (DMT1), which can transport several divalent metals across the plasma membrane, then transports iron across the enterocyte’s cell membrane into the cell. If the iron is bound to heme it is instead transported across the apical membrane by heme carrier protein 1 (HCP1) Start with absorption from the intestine, and end with its distribution to the body.

These intestinal lining cells can then either store the iron as ferritin, which is accomplished by Fe2+ binding to apoferritin (in which case the iron will leave the body when the cell dies and is sloughed off into feces), or the cell can release it into the body via the only known iron exporter in mammals, ferroportin. Hephaestin, a ferroxidase that can oxidize Fe2+ to Fe3+ and is found mainly in the small intestine, helps ferroportin transfer iron across the basolateral end of the intestine cells. In contrast, ferroportin is post-translationally repressed by hepcidin, a 25-amino acid peptide hormone. The body regulates iron levels by regulating each of these steps. For instance, enterocytes synthesize more Dcytb, DMT1 and ferroportin in response to iron deficiency anemia. Iron absorption from diet is enhanced in the presence of vitamin C and diminished by excess calcium, zinc, or manganese.

The human body’s rate of iron absorption appears to respond to a variety of interdependent factors, including total iron stores, the extent to which the bone marrow is producing new red blood cells, the concentration of hemoglobin in the

**3**

blood, and the oxygen content of the blood. The body also absorbs less iron during times of inflammation, in order to deprive bacteria of iron. Recent discoveries demonstrate that hepcidin regulation of ferroportin is responsible for the syndrome of anemia of chronic disease.

**Iron recycling and loss**

Most of the iron in the body is hoarded and recycled by the reticuloendothelial system, which breaks down aged red blood cells. In contrast to iron uptake and recycling, there is no physiologic regulatory mechanism for excreting iron. People lose a small but steady amount by gastrointestinal blood loss, sweating and by shedding cells of the skin and the mucosal lining of the gastrointestinal tract. The total amount of loss for healthy people in the developed world amounts to an estimated average of 1 mg a day for men and 1.5–2 mg a day for women with regular menstrual periods. People with gastrointestinal parasitic infections, more commonly found in developing countries, often lose more. Those who cannot regulate absorption well enough get disorders of iron overload. In these diseases, the toxicity of iron starts overwhelming the body's ability to bind and store it.

**Iron deficiency**

Iron is an important topic in prenatal care because women can sometimes become iron-deficient from the increased iron demands of pregnancy.Functional or actual iron deficiency can result from a variety of causes. These causes can be grouped into several categories:

\*Increased demand for iron, which the diet cannot accommodate.

\*Increased loss of iron (usually through loss of blood).

\*Nutritional deficiency. This can result due to a lack of dietary iron or consumption of foods that inhibit iron absorption. Absorption inhibition has been observed caused by phytates in bran , calcium from supplements or dairy products, and tannins

**4**

from tea, although in all three of these studies the effect was small and the authors of the studies cited regarding bran and tea note that the effect will probably only have a noticeable impact when most iron is obtained from vegetable sources.

\*Acid-reducing medications: Acid-reducing medications reduce the absorption of dietary iron. These medications are commonly used for gastritis, reflux disease, and ulcers. Proton pump inhibitors (PPIs), H2 antihistamines, and antacids will reduce iron metabolism.

\*Damage to the intestinal lining. Examples of causes of this kind of damage include surgery involving the duodenum or diseases like Crohn's or celiac sprue which severely reduce the surface area available for absorption. Helicobacter pylori infections also reduce the availability of iron.

\*Inflammation leading to hepcidin-induced restriction on iron release from enterocytes .

\*Is also a common occurrence in pregnant women, and in growing adolescents due to poor diets.

\*Acute blood loss or acute liver cirrhosis creates a lack of transferrin therefore causing iron to be secreted from the body.

**5**