



Iron Deficiency Anemia

The word anemia comes from Greek roots meaning “without blood” because it occurs when an individual has insufficient red blood cells to carry oxygen throughout the body. There are many potential causes of this, including genetic diseases (such as sickle cell anemia) and nutritional deficiencies (including iron, folic acid, and/or B12). Conditions such as celiac disease, Crohn’s disease, intestinal parasitic infections, and liver disease can interfere with the body’s ability to make use of nutrients from food. This typically occurs due to decreased absorption, which is the process of moving nutrients across the membrane of the gastrointestinal (GI) tract and into the bloodstream. When there is disruption or damage to the mucosal lining of the GI tract, such as in the conditions listed above, the body has a reduced ability to absorb many nutrients, including iron. This is known as malabsorption. Without enough iron, the body has trouble forming red blood cells in sufficient quantity or correctly, which leads to inadequate amounts of the iron-rich part of the blood (hemoglobin). This results in iron deficiency anemia, which is the most common form of anemia worldwide, accounting for 50% of anemia cases.

The average adult intake of iron is about 10-15 mg per day, of which we only absorb 1-2 mg, while the rest passes out of the body in stool. The recommended daily intake for adults aged 19-50 years is 8 mg for men and 18 mg for women (unless pregnant, in which case the recommendation increases to 27 mg); for those 50+ years of age, the recommendation is 8 mg for both men and women. Cells in the section of the small intestine located just after the stomach (duodenum) absorb iron after enzymes change the iron in food from ferric iron (Fe^{3+}) to a more easily absorbed ferrous iron (Fe^{2+}). An acidic environment, where there is low gastric pH, provides the best environment for this process. If you don’t ingest enough iron, or if your body has any problems with enzyme conversion or maintaining a low enough gastric

pH, then the body might not receive enough usable iron.

The body can also lose iron through conditions that cause chronic bleeding, such as Crohn’s disease and ulcerative colitis. Over time, if the loss of iron is greater than the body’s ability to absorb it, then the body will use up its iron stores.

Symptoms and Complications

Individuals with iron deficiency anemia may frequently experience dizziness, extreme fatigue, headaches, shortness of breath, tiredness, and weakness. Other signs and symptoms of anemia include extreme paleness, brittle nails, cold hands and feet, restless legs syndrome, and cravings for things that are not food, such as ice and dirt (pica). If iron deficiency is not treated, it can lead to complications such as rapid or irregular heart rate, as the heart must pump more blood to compensate for lack of oxygen. This can also lead to heart enlargement or heart failure if continued over time. There have been reports of premature births and low birth weights for babies born to women with severe iron deficiency anemia, as well as delayed growth and development.

Signs and Symptoms of Iron Deficiency Anemia

- fatigue or tiredness
- feeling short of breath
- weakness
- dizziness or light-headedness
- headaches
- pale skin
- chest pain, fast heartbeat
- cold hands and feet
- brittle nails
- decreased appetite (often in young children and infants)
- cravings for non-food items (pica)

Causes

Malabsorption is a common cause of iron deficiency in those with digestive diseases. Low dietary iron intake, increased iron loss through bleeding, genetic conditions, or increased demand for iron by the body are other common causes. Women are particularly prone to developing iron deficiency anemia, as heavy menstrual bleeding and pregnancy increase the amount of iron that the body needs.

Causes of Iron Deficiency Anemia

Malabsorption

- celiac disease
- Crohn's disease
- diverticular disease
- hiatus hernia
- chronic hepatitis and liver conditions
- previous gastrectomy
- achlorhydria and hypergastrinemia (high antacid or proton pump inhibitor use)
- digestive system surgeries to lose weight (bariatric surgery)
- *Helicobacter pylori* infection
- a rare disease that occurs when an abnormal protein, called amyloid, builds up in your organs and interferes with their normal function (amyloidosis)
- other types of GI conditions that cause damaged or impaired absorption sites

Iron Loss

- inflammatory bowel disease (Crohn's disease, ulcerative colitis, ulcerative proctitis)
- peptic ulcer (gastric, duodenal, Cameron's)
- some types of colonic or gastric polyps
- cancer (gastric, oesophageal, small bowel, colonic)
- gastritis, esophagitis
- acute upper gastrointestinal bleeding
- use of non-steroidal anti-inflammatories (NSAIDs), such as ibuprofen, naproxen, and aspirin that can cause internal bleeding
- parasitic infections (hookworm)
- vascular abnormalities (angiodysplasia, gastric antral vascular ectasia, hereditary haemorrhagic telangiectasia)
- heavy menstruation (menorrhagia)
- recurrent nose bleeds (epistaxis)
- urinary blood loss
- abnormal breakdown of red blood cells (chronic intravascular haemolysis)
- regular blood donation, phlebotomy

Increased Demand for Iron

- adolescence
- pregnancy
- erythropoietin therapy

Inadequate Dietary Intake

- vegetarians and vegans
- low calorie diet
- highly processed diet
- some eating disorders

Diagnosis

General fatigue, tiredness, and shortness of breath cause most people with undiagnosed anemia to see their physician. To diagnose iron deficiency anemia, your physician will assess your symptoms and will likely send you for laboratory testing. This will usually include a blood sample to assess iron stores and to evaluate the size, colour, and abundance of your red blood cells as well as potentially providing a stool sample to see if you are losing blood (and iron). Typically, the hemoglobin level, percentage of the blood made up of red blood cells (hematocrit), and an indicator of iron storage in the body (ferritin) are low when you have iron deficiency anemia. If your physician suspects malabsorption, then you might have to undergo further tests. These can include ultrasound, endoscopy, and colonoscopy, which allow your physician to visualize any changes within the abdomen and digestive tract that might be causing malabsorption.

Management

Dietary Modifications

Many individuals with iron deficiency anemia will need to take supplements in order to adequately increase iron stores and improve the quantity and quality of their red blood cells. However, eating more iron-rich foods can still help.

There are two types of absorbable iron: heme and non-heme. Heme iron comes from the hemoglobin and myoglobin derived from animal food sources such as meat, seafood, and poultry, which is most easily absorbed. Shellfish, liver, and red meat are particularly good sources of heme iron, but most meat, seafood, and eggs are good options. Plants, iron-fortified foods, and most iron supplements contain non-heme iron, which is less well absorbed. Some good sources of non-heme iron include beans, lentils, tofu, spinach, fortified grains, nuts and seeds, and blackstrap molasses. You can increase the amount of non-heme iron your body absorbs by pairing iron-rich foods with those that have plenty of vitamin C. To learn more about increasing your iron levels through diet, contact a registered dietitian.

Oral Iron Supplements

Taking iron in the form of oral tablets is the simplest and most accessible way to replenish iron stores. There are many different iron supplements available. Over-the-counter iron supplements are the most common, but pharmacists keep some of these products behind the counter, as they require in-depth advice regarding their use, so ask your pharmacist about them.

Iron supplements come in various salts, strengths, and dosage forms. Pharmacists can help when it comes to interpreting the prescription from your physician or making recommendations about which product is best, depending on your individual needs. The pharmacist can also help select a dose, if your physician has not provided one for you.

The usual oral administration of iron supplements is one dose, two to three times daily, but experts have recently found alternate day therapy to have fewer side effects. Studies have evaluated the use of every other day dosing, so over two days a person consumes less product. A study looked at 200 mg of ferrous sulfate taken twice daily compared to 400 mg given once every other day. Although the twice-daily dosing resulted in faster increases in hemoglobin, there was an increased rate of side effects, particularly nausea. This study is helpful, since it provides guidance to help individualize treatment and allow a person to consider the risks and benefits of different therapeutic options and dosing regimens.

With oral non-heme iron supplements, the iron recovery is gradual, and it can take many months to replete iron levels and iron stores. Oral heme products do work more quickly than non-heme products.

Some Cautions

Some marketers claim their iron products to be better absorbed than others but there are no definitive product head-to-head clinical trials to substantiate these claims. Each person has his or her own unique digestive process and GI tract characteristics.

Be cautious of iron products that claim to have fewer side effects than other supplements, as this may simply be a result of the dose or amount of iron in that product being lower than in others. There are newer products on the market that bind iron molecules to different salts or sugars, and some are advertised as naturally derived and try to improve the side effect profile of iron. Studies of these products are not always robust and may not adequately compare the efficacy and safety of the product to the standard iron supplements used to treat IDA. For this reason, it can be difficult to determine if these naturally derived products claiming to be better absorbed and tolerated, or made of heme iron, are truly better than iron salts such as ferrous sulphate, ferrous gluconate, and ferrous fumarate. Some people

have reported that they have personally found them to be better, and feel it is worth the comparatively higher costs. Discuss with your physician or pharmacist the options available that are most suitable for you and avoid accepting marketing and side effect claims at face value.

Common side effects of oral iron supplements include stomach upset, dark stools, and constipation, as well as teeth staining with continued use of liquid products.

Intravenous (IV) Iron Infusion

For some individuals, it is not possible for the body to absorb the desired amount of iron through the digestive tract due to the high dose of iron needed, a malabsorption condition, or intolerable GI side effects with oral iron. Those who have experienced significant blood loss or those with very low iron levels may require high amounts of iron replenishment. IV administration is the most effective option for those who fall into these categories as it can supply a large amount of iron to the body. Those receiving IV iron recover from symptoms more quickly and can often feel an immediate improvement in anemia symptoms. However, a disadvantage with IV iron is the infusion itself and infusion related side effects. These include infections, headache, nausea, and vomiting, but rarely can include rash and allergic reactions.

Older IV iron products, e.g., ferric gluconate complex (Ferri-lecit®), and iron sucrose (Venofer®) generally require multiple (three or more) infusions of longer duration (2-3 hours) with 4-6 weeks in between sessions.

A newly introduced IV iron, approved by Health Canada for the treatment of iron deficiency anemia in adults who have intolerance or unresponsiveness to oral iron therapy, called iron isomaltoside 1000 (Monoferric®), typically requires one 30-minute infusion, with faster increases in hemoglobin count without any differences in side effects. Healthcare professionals who have been trained to manage associated side effects and allergic reactions, if they occur, administer iron infusions, typically in a hospital as an out-patient. Most reactions occur within 30 minutes of the infusion and you might be asked to stay in the patient care area after the infusion.

An iron infusion might not raise hemoglobin immediately and usually takes a few weeks, depending on the patient's condition, iron product, and the dose used. If iron supplementation is not effective or the situation requires an immediate response with increased hemoglobin and/or number of functional red cells, then a blood transfusion may be required, mainly administered in a hospital.

Having fewer iron infusions with shorter infusion durations could potentially reduce the frequency of side effects and save healthcare costs.

Outlook

While we can't always correct malabsorption, the resulting iron deficiency anemia can be treated, which will help manage related symptoms. Studies are ongoing to identify new agents that are better absorbed orally as well as IV versions that are more convenient to administer and are better tolerated. It might be beneficial to make IV iron more accessible as physicians are recognizing it as a more effective alternative to oral supplements in some patients.

Notes :

About the Gastrointestinal Society

The GI (Gastrointestinal) Society is a registered Canadian charity committed to improving the lives of people with gastrointestinal and liver conditions, supporting research, advocating for appropriate patient access to healthcare, and promoting gastrointestinal and liver health.

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