



Iron Deficiency Anemia

The word anemia comes from Greek roots meaning *without blood*. Anemia is a condition where you don't have enough red blood cells to carry oxygen to every cell and organ in your body. Cells can't work properly when they are short of oxygen.

People commonly report they feel tired all the time when they have anemia, but some don't even notice how tired they are, because it is mild, or it develops slowly and can worsen over time. Anemia progresses when there are fewer properly functioning red blood cells.

About 70% of the iron in our bodies is found in hemoglobin, a protein within red blood cells. Iron is also a key component of muscle tissue and an essential component of mitochondria, the energy factory of our cells.

Iron deficiency anemia occurs when your body does not have enough iron to produce hemoglobin, which is the important part of red blood cells and gives these cells their red colour.

Causes

Iron deficiency arises when our body loses iron from blood loss or bleeding, has problems absorbing enough iron in the gut, or has difficulty making normal red blood cells.

Common situations of blood loss which can lead to iron deficiency anemia are heavy menstrual periods, gastrointestinal bleeding (e.g., stomach ulcers, hemorrhoids, gallstones, inflammatory bowel disease), surgeries, pregnancy, childbirth, thyroid issues, and cancers.

Poor iron absorption is another reason for low iron levels in the body, and can occur from low iron diets, celiac disease, weight loss surgeries, heart failure, chronic kidney disease, inflammatory bowel disease, or connective tissue conditions.

Difficulty making normal red blood cells is a much less common cause of anemia. Some people are born with conditions with abnormal production of hemoglobin, called hemoglobinopathies, where they make different shaped red blood cells that break down faster and so they appear anemic in blood tests. Some people have trouble producing red blood cells because their bone marrow is not functioning properly, or they have severe kidney problems or cancers.

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. These conditions typically affect 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.

Causes of Iron Deficiency Anemia

Malabsorption

- celiac disease
- Crohn's disease
- ulcerative colitis
- diverticular disease
- hiatus hernia
- chronic hepatitis and liver conditions
- previous gastrectomy
- weight loss surgeries
- achlorhydria and hypergastrinemia (high antacid or proton pump inhibitor use)
- *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
- chronic diseases associated with inflammation (e.g., rheumatologic conditions, heart failure, chronic kidney disease, to an extent)
- medications (e.g., metformin, proton pump inhibitors)
- cancer

Blood Loss

- inflammatory bowel disease (Crohn's disease, ulcerative colitis, ulcerative proctitis)
- heavy menstruation (menorrhagia)
- hemorrhoids
- peptic ulcer (gastric, duodenal, Cameron lesions)
- some types of colonic or gastric polyps
- surgery
- childbirth
- cancer (gastric, esophageal, 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)
- 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
- menstruation
- pregnancy
- breast feeding or lactation
- erythropoietin therapy

Inadequate Dietary Intake

- vegetarian and vegan diet
- low calorie diet
- highly processed diet
- some eating disorders

Symptoms and Complications

Individuals with iron deficiency anemia may frequently experience dizziness, extreme fatigue, headaches, shortness of breath, tiredness, and muscle weakness. Other signs and symptoms of anemia include extreme paleness, brittle nails, cold hands and feet, restless legs syndrome, increased risk of infections, depression, and cravings for things that are not food (pica), such as ice and dirt, or having a poor appetite, especially in infants and children.

If iron deficiency is not treated, it can lead to complications as the body compensates for the lack of iron and oxygenation with rapid or irregular heart rate, as the heart must pump more blood,

and rapid breathing. Unborn babies can also be affected; there have been reports of premature births and low birth weights for babies born to women with severe iron deficiency anemia, as well as permanently delayed growth and development.

Signs and Symptoms of Iron Deficiency Anemia

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

Diagnosis

General fatigue, pale skin, 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, including hemoglobin level, as well as potentially providing a stool sample to see if you are losing blood (and iron).

Typically, hemoglobin level, the percentage of the blood made up of red blood cells (hematocrit), and an indicator of iron stores 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. Malabsorption is a common cause of iron deficiency in those with digestive diseases, particularly when iron is not easily absorbed by the body. Consuming coffee, tea, or calcium supplements with meals can also reduce iron absorption.

Management

Prevention

The Canadian recommendations for the adequate intake of iron varies by age, gender, and whether women are pregnant or

breastfeeding. Infants and children from 7 months to 8 years of age have a recommended adequate intake of 7-11 mg of iron per day. Males older than 9 years of age should get 8 mg per day, with 11 mg recommended daily for ages 14 to 18 during growth and development. Females are recommended to have a daily intake of 8-15 mg from 9 to 18 years of age, 18 mg from 19 to 50 years, and 8 mg daily for those 51 and older. During pregnancy, the recommended adequate intake increases to 27 mg daily. These recommendations are for individuals without any absorption issues or other conditions affecting iron in the body.

Dietary Modifications

Many individuals with iron deficiency anemia will need to take supplements 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 (See Canada's food guide for a list of foods).

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 or by taking vitamin C during meals, which helps your body absorb iron from your diet. 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 without the need for a prescription, and those with higher doses may be accessed by asking the pharmacist at your pharmacy.

To achieve an optimal balance of high dose with good iron absorption and minimal side effects, some experts recommend not taking more than 100 mg of elemental iron per day or 200 mg every other day. Your healthcare professional might recommend higher doses in some cases and it may be well tolerated by some. There are different iron salts which contain different amounts of elemental iron, (e.g., ferrous fumarate is 33%, ferrous sulfate is 20%, and ferrous gluconate is 12%). Depending on the formulation, high doses might not be absorbed completely, while still causing side effects (e.g., constipation, stomach upset,

nausea, vomiting, dark stools).

There are other forms of oral iron supplements in addition to the common iron salts. These include heme iron polypeptide (e.g., Proferrin®), iron complexed with polysaccharides (e.g., FeraMAX® polydextrose iron complex), and iron designed to be delivered by liposomes or phospholipids (e.g., Ferosom Forte LCE Liposomal™ Iron and Sucrosomial® Iron), which are becoming more popular and offer other options to normalize iron levels. These newer iron supplement formulations may improve absorption and have fewer side effects than the traditional iron salts. Some of these come in a flavoured powder to be diluted and drank or as flavoured chewable tablets. Discuss the options and dose with your pharmacist to find one best suited for your individual preferences and needs. Those that are better absorbed will lead to faster normalization of iron levels, and normally will take 3 to 6 months.

Some Cautions

With the abundance of iron supplements available from online vendors, health food stores, etc., there are various marketing claims. Supplements with clinical studies, quality products, and dependable manufacturers are the most trustworthy and your pharmacist or physician are the most reliable sources of information for these facts. Although you may have fewer side effects with one product over another, make sure they provide comparable amounts of elemental iron, otherwise, you may be comparing a lower dose, which is expected to have fewer adverse effects than one with a higher content of elemental iron.

Common side effects of oral iron supplements include stomach upset, dark stools, constipation, and nausea, as well as teeth staining with continued use of liquid iron 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 time constraints (e.g., surgery, pregnancy, childbirth), a malabsorption condition, an inflammatory condition (e.g., Crohn's disease, ulcerative colitis), heart failure, chronic kidney disease, cancer, or intolerable side effects with oral iron. Those who have experienced significant blood loss or those with very low iron levels may require IV iron to replenish stores faster than can be achieved with oral formulations.

High dose 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 without needing absorption in the gut. Those receiving IV iron recover from symptoms more quickly (i.e., within a matter of days to weeks) and can often feel an immediate improvement in anemia symptoms, although laboratory measurements should be done 4 to 6

weeks after the infusion.

However, a disadvantage with IV iron is the infusion itself and infusion-related side effects. Occasionally, these may include staining of the skin or veins with iron (may fade slowly over >6 months), mild aches and pains in the days after the infusion, pseudoallergy (i.e., muscle contractions, flushing), low blood pressure, or rare risk of a severe allergic or anaphylactic reaction (reported as less than 1 in 200,000) and is a theoretical risk of all IV medications.

Older IV iron products, e.g., sodium ferric gluconate complex (Ferrlecit®) 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 newer 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 ferric derisomaltose (Monoferric®), can be given at a higher dose and typically requires an infusion lasting 30 minutes, resulting in 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 outpatient clinic or at a private infusion clinic. Most reactions occur within 30 minutes of the infusion, and you might be asked to stay in the patient care area after the infusion.

Having fewer iron infusions with shorter durations could potentially reduce the frequency of side effects and reduce the related IV administration costs. Unfortunately, low dose IV iron preparations rarely have enough iron to achieve this goal. The use of IV iron will provide a more immediate repletion of iron stores in the body compared to oral supplements, but it still will take some time for the body to use the iron to make red blood cells. And for some individuals, maintenance dosing with an effective oral supplement after the IV iron top-up will prevent or delay another episode of iron deficiency anemia.

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.

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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