Iron deficiency anemia is a common anemia that occurs when iron loss (often from intestinal bleeding or menses) occurs, and/or the dietary intake or absorption of iron is insufficient. In such a state, hemoglobin, which contains iron, cannot be formed. Iron deficiency is the most common single cause of anemia worldwide, accounting for about half of all anemia cases. It is more common in women than men. Estimates of iron deficiency worldwide vary widely, but the number almost certainly exceeds one billion persons globally. Worldwide, the most important cause of iron deficiency anemia is parasitic infection caused by hookworms, whipworms, and roundworms, in which intestinal bleeding caused by the worms can lead to undetected blood loss in the stool. These are especially important problems in growing children. Malaria infections that destroy red blood cells (although the iron is recycled) and chronic blood loss caused by hookworms (where the iron is lost) contribute to anemia during pregnancy in most developing countries. In adults of post-menopausal age (over 50 years old) the most common cause of iron-deficiency anemia is chronic gastrointestinal bleeding from gastric ulcer, duodenal ulcer or a gastrointestinal cancer.

In the developed world, where intestinal worm parasite burden is less than in many undeveloped countries, about 20% of all women of childbearing age have iron deficiency anemia, compared with only 3% of adult men. The principal cause of iron deficiency anemia in these countries is blood lost during menses in premenopausal women, which is not compensated by intake from food and supplements. Iron deficiency anemia is one result of an advanced stage iron deficiency, which is even more common. When the body has sufficient iron to meet its needs (functional iron), the remainder is stored for later use, mostly in the bone marrow, liver, and spleen (although all cells store some iron) as part of a finely tuned system of human iron metabolism. The store of iron present in all animal cells is deposited mostly in ferritin complexes.

Iron deficiency ranges from iron depletion, which yields little physiological damage, to iron deficiency anemia, which can affect the function of numerous organ systems. Iron depletion causes the amount of stored iron to be reduced, but has no effect on the functional iron. However, a person with no stored iron has no reserves to use if the body enters a state in which it requires more iron than is being absorbed from the diet.
Symptoms and Signs
Iron deficiency anemia is characterized by pallor, fatigue and weakness. Because it tends to develop slowly, adaptation occurs and the disease often goes unrecognized for some time. In severe cases, dyspnea can occur. Unusual obsessive food cravings, known as pica, may develop. Pagophagia or pica for ice is a very specific symptom and may disappear with correction of iron deficiency anemia. Hair loss and lightheadedness can also be associated with iron deficiency anemia.

Diagnosis
Anemia may be diagnosed from symptoms and signs, but when anemia is mild it may not be diagnosed from mild non-specific symptoms. Pica, an abnormal craving for dirt, ice, or other "odd" foods occurs variably in iron and zinc deficiency, but is neither sensitive or specific to the problem so is of little diagnostic help. Anemia is often first shown by routine blood tests. Sufficiently low haemoglobin by definition makes the diagnosis of anemia, and a low haematocrit value is also characteristic of anemia. Further studies will be undertaken to determine the anemia's cause. If the anemia is due to iron deficiency, one of the first abnormal values to be noted on a CBC, as the body's iron stores begin to be depleted, will be a high red blood cell distribution width (RDW), reflecting an increased variability in the size of red blood cells (RBC). In the course of slowly depleted iron status, an increasing RDW normally appears even before anemia appears.

A low mean corpuscular volume (MCV) often appears next during the course of body iron depletion. It is the result of many red blood cells which are abnormally small. A low MCV, a low mean corpuscular hemoglobin (MCH) and/or Mean corpuscular hemoglobin concentration (MCHC), and the appearance of the RBCs on visual examination of a peripheral blood smear narrows the problem to a microcytic anemia. The blood smear of a patient with iron deficiency shows many hypochromic and microcytic RBCs and may also show poikilocytosis and anisocytosis. With more severe iron deficiency anemia the peripheral blood smear may show target cells, hypochromic pencil-shaped cells, and occasionally small numbers of nucleated red blood cells. Very commonly, there is mild thrombocytosis.

Body store iron deficiency is diagnosed by diagnostic tests as a low serum ferritin, a low serum iron level, an elevated serum transferrin and a high total iron binding capacity (TIBC). A low serum ferritin is the most sensitive lab test for iron deficiency anemia, however serum ferritin can be elevated by any type of chronic inflammation, and so is not always a reliable test of iron status if it is within normal limits.
Serum iron levels (i.e., iron not part of the hemoglobin in red cells) may be measured directly in the blood, but these levels increase immediately with iron supplementation and pure blood serum iron concentration in any case is not as sensitive as a combination of total serum iron, along with a measure of the serum iron-binding protein levels (total iron binding capacity or TIBC). The ratio of serum iron to TIBC (called iron saturation or transferrin saturation index or percent) is the most specific indicator of iron deficiency, when it is sufficiently low. The iron saturation (or transferrin saturation) of < 5% almost always indicates iron deficiency, while levels from 5% to 10% make the diagnosis of iron deficiency possible, but not definitive. Saturations over 12% (taken alone) make the diagnosis unlikely. Normal saturations are usually slightly higher for women (>12%) than for men (>15%), but this may simply indicate an overall slight poorer iron status for women in the "normal" population.

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<th>Change in lab values in iron deficiency anaemia</th>
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<tr>
<td>Change</td>
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<td>Decrease</td>
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Iron deficient anemia and thalassaemia minor present with many of the same lab results. It is very important not to treat a patient with thalassaemia with an iron supplement as this can lead to hemochromatosis (accumulation of iron in various organs especially liver). A hemoglobin electrophoresis would provide useful evidence in distinguishing these two conditions, along with iron studies.

**Gold standard**
Traditionally, a definitive diagnosis requires a demonstration of depleted body iron stores by performing a bone marrow aspiration, with the marrow stained for iron. Because this is invasive and painful, while a clinical trial of iron supplementation is inexpensive and non-traumatic, patients are often treated based on clinical history and serum ferritin levels without a bone marrow biopsy.

**Treatment**
If the cause is dietary iron deficiency, eating more iron-rich foods such as beans and lentils or taking iron supplements, usually with iron(II) sulfate, ferrous gluconate, or iron amino acid chelate ferrous bisglycinate, synthetic chelate NaFerredetate EDTA will usually correct the anemia. If anemia does not respond to oral treatments, it may be necessary to administer iron parenterally (e.g., as iron dextran) using a drip or haemodialysis. Parenteral iron involves risks of fever, chills, backache, myalgia, dizziness, syncope, rash and anaphylactic shock. A follow up blood test is essential to demonstrate whether the treatment has been effective.

**References**
1. Essential Haematology, edition 4, AV Hoffbrand, JE Petit, and PAH Moss

**Questions**
1. Discuss the causes of iron deficiency anaemia.
2. Discuss the lab findings in iron deficiency anaemia.
3. What is the Gold Standard used to diagnose iron deficiency anaemia?