Iron

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Iron

- In contrast to zinc, iron is an abundant element on earth representing about 5% of the earth's crust and is a biologically essential component of every living organism.
- However, despite its geologic abundance, iron is often a limiting factor for life. This apparent paradox is because in contact with oxygen, iron forms oxide, (most commonly seen as rust), which is highly insoluble and not readily available for uptake by organisms.
- In response, various cellular mechanisms have evolved to capture iron from the environment in biologically useful forms. Examples are siderophores secreted by microbes to capture iron in a highly specific complex or mechanisms to reduce iron from the insoluble ferric iron (Fe+3) to the soluble ferrous form (Fe+2) as in yeasts.

For thousands of years Uluru's surface has been exposed to the water and oxygen in the air. This exposure has slowly decayed the minerals in the rock, causing them to oxidise. The result of this has been that the iron minerals found inside the arkose surface is rusting which ultimately led to its red colour.

Iron

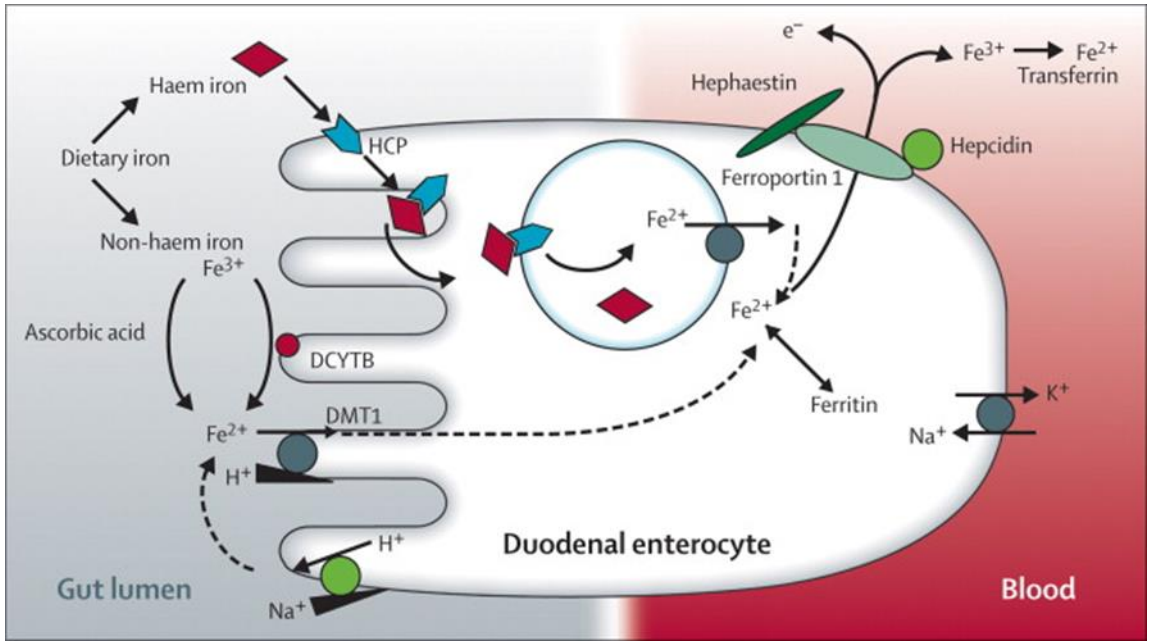
- Iron is the most abundant trace element in humans, a transition metal and an essential element for almost all living organisms as it participates in a wide variety of metabolic processes, including oxygen transport, forming part of the enzymes implicated in deoxyribonucleic acid (DNA) synthesis and cell respiration, and electron transport.
- Iron plays a vital role in the process by which cells make energy. Human cells require iron in order to convert energy from food into ATP (Adenosine Triphosphate) and this is the body's primary energy source.
- These physiological roles are carried out due to its ability to uptake and donate electrons, interchanging between its ferric (Fe3+) and ferrous (Fe2+) forms. This allows iron-containing proteins to participate in oxidation-reduction reactions, many of which are essential for fundamental biological processes in humans.
- Iron is necessary for immune cell creation and growth.
- Iron is important for healthy brain development and growth in children, and for the normal production and function of various cells and hormones.

Types of iron

- There are two types of absorbable dietary iron: haem and non-haem iron.
- Haem iron is contained in haemoglobin or myoglobin, and is derived almost exclusively from meat (veal, pork, lamb, chicken, turkey, and others), fish, and seafood.
- Non-haem iron (especially ferric salts) is most frequently found in vegetables (legumes, corn, wheat, barley, and others), but also in animal source foods, (as animals consume plant foods with non-haem iron) and fortified foods. Iron-fortified foods include rice, pasta, bread, and other cereals, cooked spinach, nuts, seeds and dry fruits, eggs, and dairy products.
- The absorption of iron in these two forms is different. Haem iron has a greater bioavailability, with absorption of 20%–30%. Thus, once the haem group of proteins containing it is released, it remains soluble and is taken up easily.

Iron absorption inhibition

- Non-haem iron, is the most abundant in the diet. Facilitated by gastric acidity, iron is reduced by an enzyme present in the enterocyte brush border, being absorbed at a rate of less than 10%. This absorption is maximised by ascorbic acid and foods with a substantial content of haem iron. Enterocytes are the key element in this absorption process.
- Inhibitors of iron absorption include phytate, found in plant-based diets that demonstrate a dose-dependent effect on iron absorption.
- Polyphenols which are found in black and herbal tea, coffee, wine, legumes, cereals, fruit, and vegetables.
- Unlike other inhibitors such as polyphenols and phytates, which prevent only non-haem iron absorption, calcium inhibits both haem and non-haem iron at the point of initial uptake into enterocytes.
- Animal proteins such as casein, whey, egg whites, and proteins from plants (soy protein) have been shown to inhibit iron absorption.
- Oxalic acid is found in spinach, chard, beans, and nuts and acts to bind and inhibit iron absorption.



Food sources

Sources of haem iron:

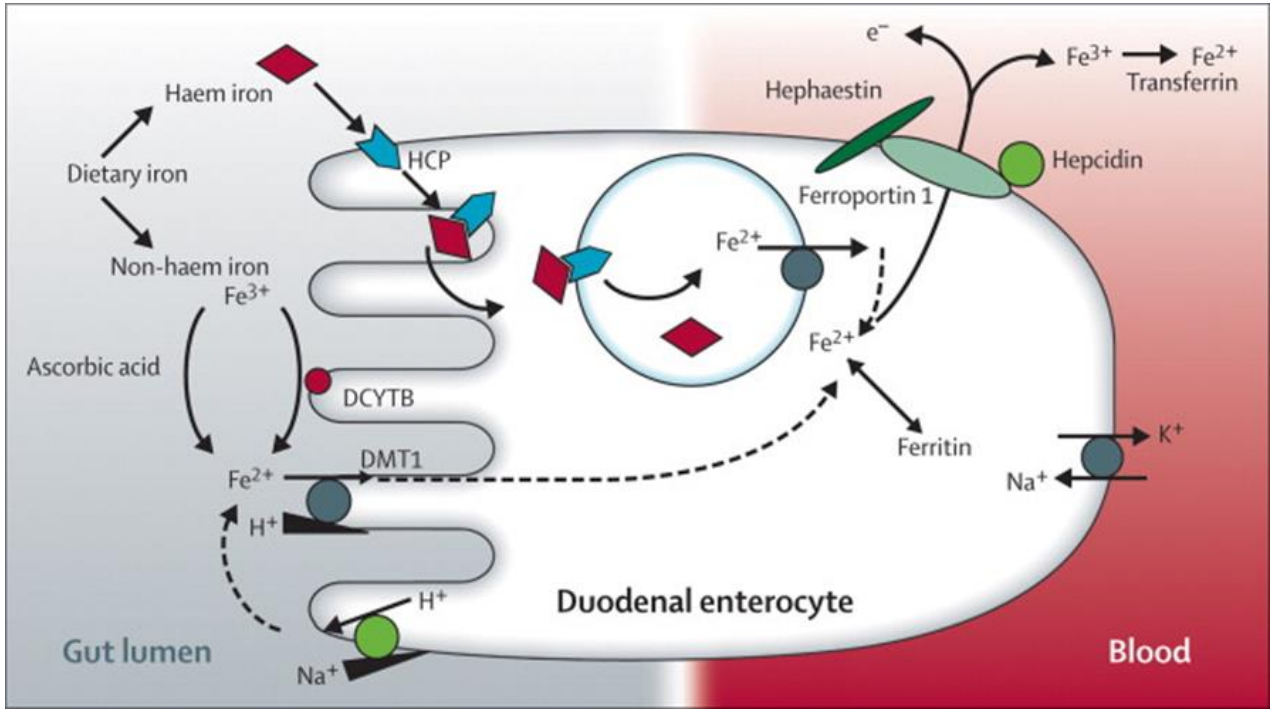
- Oysters, clams, mussels
- Beef or chicken liver
- Organ meats
- Canned sardines
- Beef
- Poultry
- Canned light tuna

Sources of non-haem iron:

- Fortified breakfast cereals
- Beans
- Dark chocolate (at least 45%)
- Lentils
- Spinach
- Potato with skin
- Nuts, seeds
- Enriched rice or bread

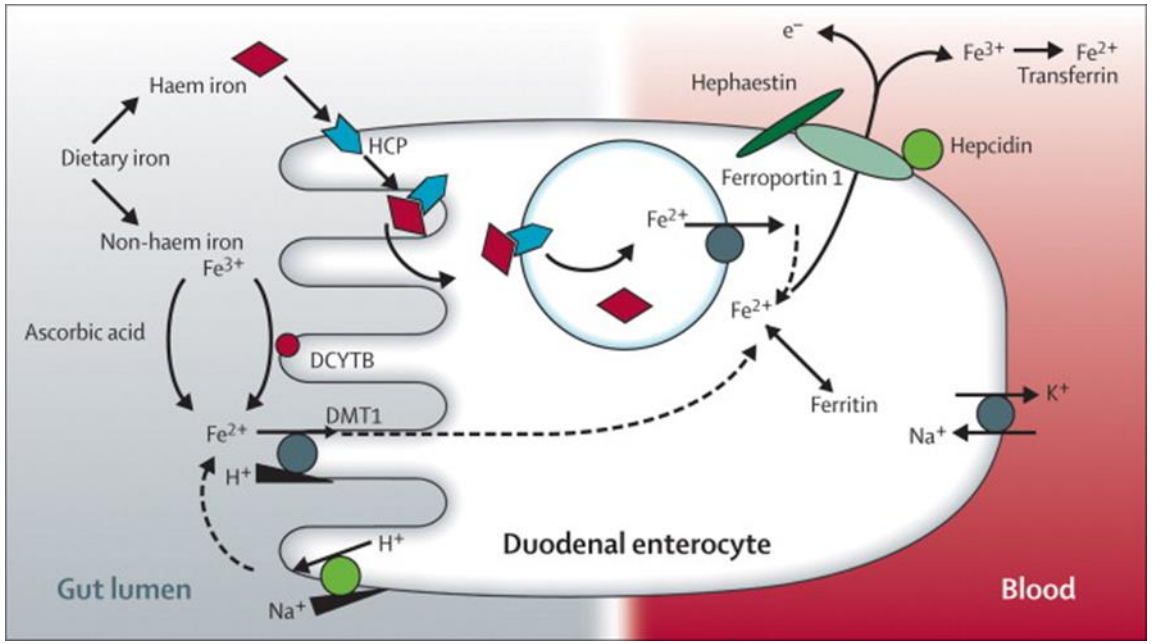
Iron absorption

- Iron in the form of haem, is readily absorbed. This reduced form, enters the enterocyte cytoplasm by means of a membrane transporter. This absorption takes place primarily in the duodenum and proximal jejunum, and it is complex and highly regulated, as the key point in iron metabolism.
- The intact haem is taken up by the small intestinal enterocyte by endocytosis. Once inside the enterocyte, iron is liberated and essentially follows the same pathway for export as absorbed inorganic iron. Some haem may be transported intact into the circulation.
- Once inside the enterocyte, iron follows one of two major pathways. Which path is taken depends on a complex programming of the cell based on both dietary and systemic iron loads.
- Iron metabolism is controlled at different levels and by diverse mechanisms.



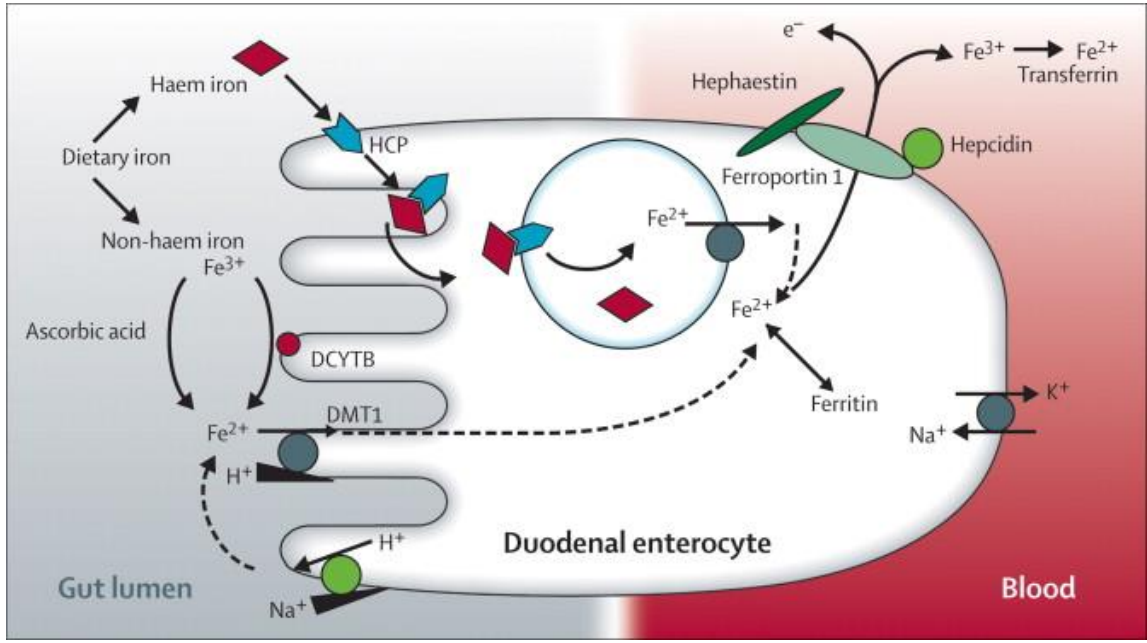
Iron-mechanisms of absorption

- At least three main mechanisms have been identified in the regulation of the absorption process.
- The most important is erythropoietic requirements, in such a way that absorption increases with increasing requirements. Thus, in anaemic individuals, absorption increases, although up to no more than 20–40 mg/day.
- The second mechanism is dietary iron content, so that absorption decreases as dietary content increases.
- The third main mechanism is a reduction in the iron pool, which increases its absorption.
- So, unlike other minerals, iron levels in the human body are controlled only by absorption.
- The mechanism of iron excretion is an unregulated process arrived at through loss in sweat, bleeding, menstruation, shedding of hair and skin cells, and rapid turnover and excretion of enterocytes.



Iron absorption

- Iron limiting states: where a feedback mechanism exists that enhances iron absorption in people who are iron deficient, in contrast, people with iron overload dampen iron absorption via hepcidin. It is now generally accepted that iron absorption is controlled by a transporter called ferroportin which allows or does not allow iron from the mucosal cell into the plasma.
- Ferroportin is a unique iron exporter, essential for dietary iron absorption, recycling of iron from senescent erythrocytes, mobilisation of stored iron, and iron transfer to the developing foetus. Iron is exported out of the enterocyte via ferroportin located in the basolateral membrane. Ferroportin is the only known receptor for the iron-regulatory hormone hepcidin that binds to it.
- Hepcidin, a key molecule in iron metabolism and mainly produced in the liver, is a central regulator of iron in the body, controlling absorption and iron transport.
- Hepcidin levels increase when there's too much iron in the body and decrease when there's not enough. modulates the passing of iron from cells (enterocytes, macrophages, and hepatocytes) to the plasma.



Hepcidin

Hepcidin is the master regulator of iron metabolism and plasma iron required to produce blood

- Plasma Iron is maintained normally at 10-30 µM
- Chronically >30 µM leads to iron deposition in tissues, injury, and organ damage
- Chronically <10 µM causes cellular dysfunction, and anaemia

Hepcidin Potential Diagnostic Utility

- Hepcidin can diagnose iron deficiency in non-anaemic patients
- Hepcidin can predict genetic disorders related to anaemia (e.g. IRIDA)
- Hepcidin can predict non-responsiveness to oral iron
- Hepcidin can distinguish iron deficiency anaemia (IDA) from anaemia of chronic disease (ACD)
- Hepcidin measurement may improve the prediction of acute kidney injury (AKI) after heart surgery or in critical illness
- Hepcidin may predict mortality in critically ill patients with AKI
- Hepcidin may predict mortality in coronary artery disease
- Anaemia defined by hepcidin is a risk factor for mortality post critical care discharge
- Hepcidin can predict iron deficiency in first-time blood donors

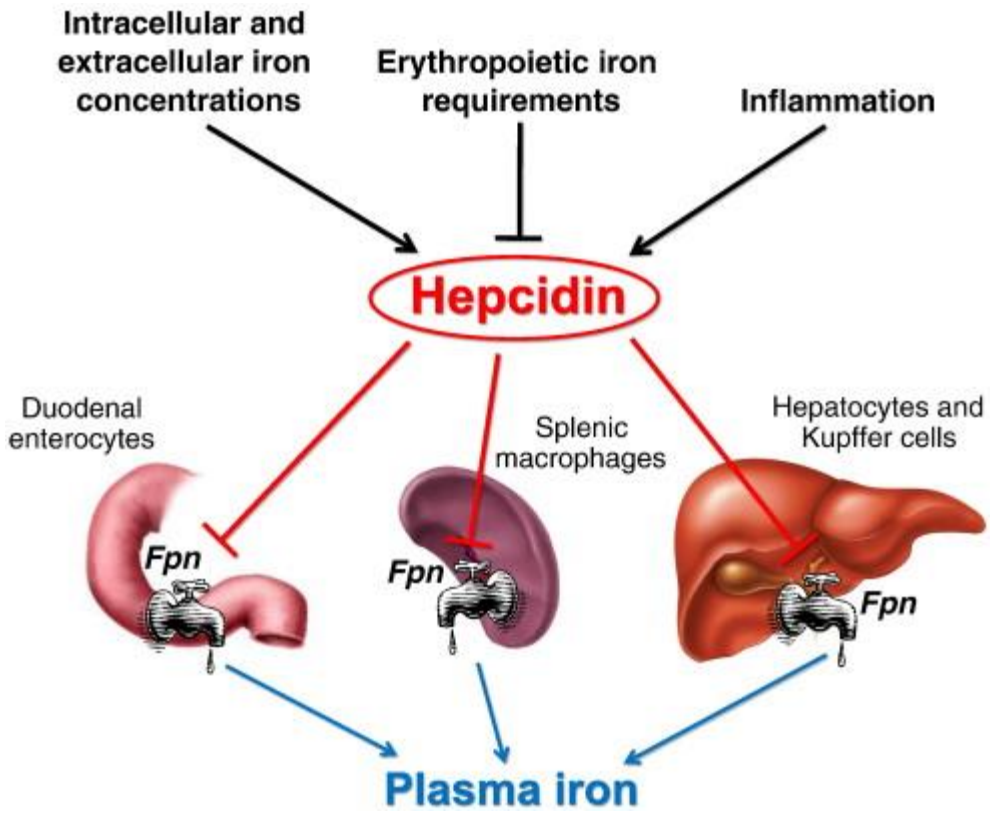
Hepcidin

Dysregulation of hepcidin expression results in iron disorders.

Overexpression of hepcidin leads to anaemia of chronic disease, while low hepcidin production results in hereditary haemochromatosis (HFE) with consequent iron accumulation in vital organs.

Most hereditary iron disorders result from inadequate hepcidin production relative to the degree of tissue iron accumulation.

Impaired hepcidin expression has been shown to result from mutations in any of 4 different genes: TfR2, HFE, haemochromatosis type 2 (HFE2), and hepcidin antimicrobial peptide (HAMP). Mutations in HAMP, the gene that encodes hepcidin, result in iron overload disease, as the absence of hepcidin permits constitutively high iron absorption.



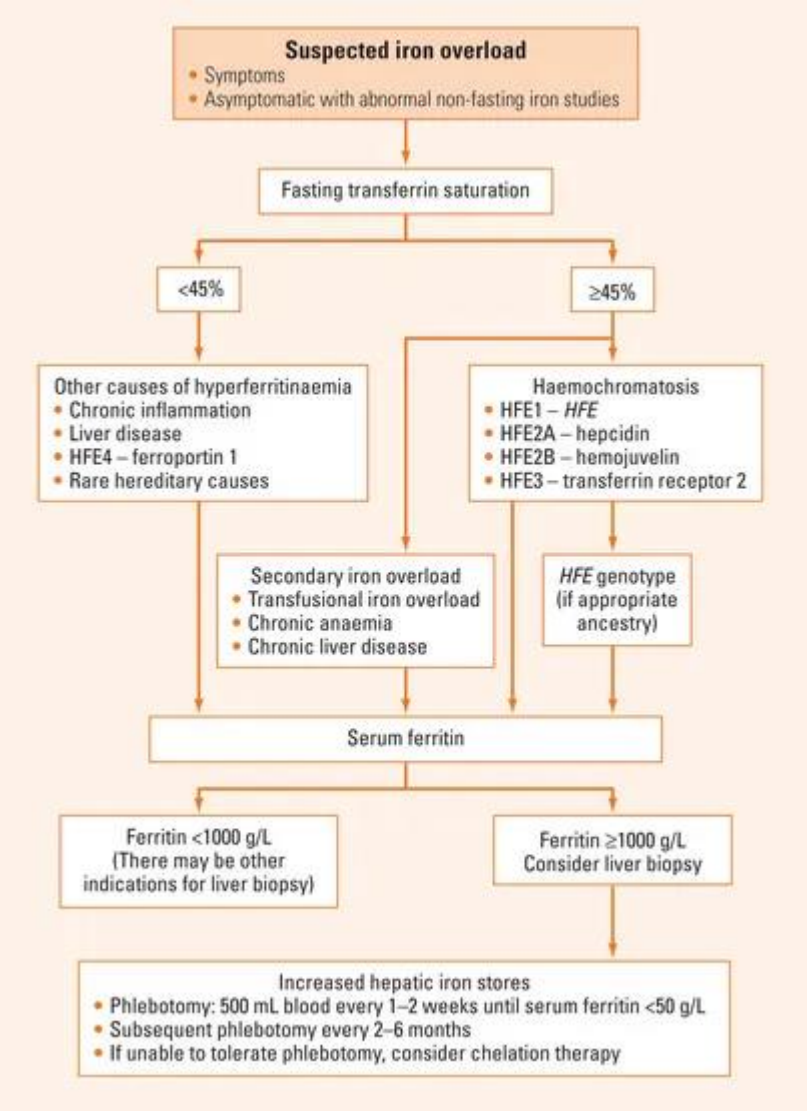
Serum hepcidin in various disease processes

Iron-refractory iron deficiency anemia	Genetic overproduction of hepcidin	High normal to high
Anemia of hepatic adenomas	Autonomous hepcidin production by tumor	High? (only tumor mRNA measured)
Hereditary hemochromatosis	Genetic hepcidin deficiency, varying severity	Undetectable, low, or low for iron load
Secondary iron overload	Transfusions, iron therapy	High
β-thalassemia intermedia (rare transfusions)	Ineffective erythropoiesis, high erythropoietic drive	Low
β-thalassemia major (regular transfusions)	Ineffective erythropoiesis, moderated erythropoietic drive, secondary iron overload	Low or low for iron load
Hepatitis C, alcoholic liver disease	Suppression of hepcidin by alcohol, virus or growth factors	Low
Infections, rheumatologic diseases, inflammatory bowel disease, cancer	Inflammation	High
Chronic kidney diseases	Decreased clearance of hepcidin, variable inflammation	High

Adapted from T Ganz and E Nemeth. Hepcidin and Disorders of Iron Metabolism. 2011. Ann Rev Med 62: 347-360.

Excess iron

- Some people have a hereditary condition called haemochromatosis that causes an excessive buildup of iron in the body.
- Genetic mutations in the haemochromatosis gene (HFE) are the most common genetic cause of elevated ferritin levels and are usually seen in people with northern European ancestry
- Treatments are given periodically to remove blood or excess iron in the blood.
- People with haemochromatosis are educated to follow a low-iron diet and to avoid iron and vitamin C supplements.
- If left untreated, iron can build up in certain organs so that there is a higher risk of developing conditions like liver cirrhosis, liver cancer, or heart disease.



Iron overload disorders

BOX

Etiological classification of iron overload disorders

Congenital causes

- **Various types of hereditary (primary) hemochromatosis (HH)**
  - Disordered hepcidin/ferroportin system
  - Disordered iron transport
- **Hereditary anemia with ineffective erythropoesis („iron loading anemias“)**
  - Increased intestinal iron absorption

Acquired causes

- **Ineffective erythropoesis (myelodysplastic syndrome)**
  - Increased intestinal iron absorption
- **Chronic transfusion therapy**
  - High iron supply from red cell concentrates

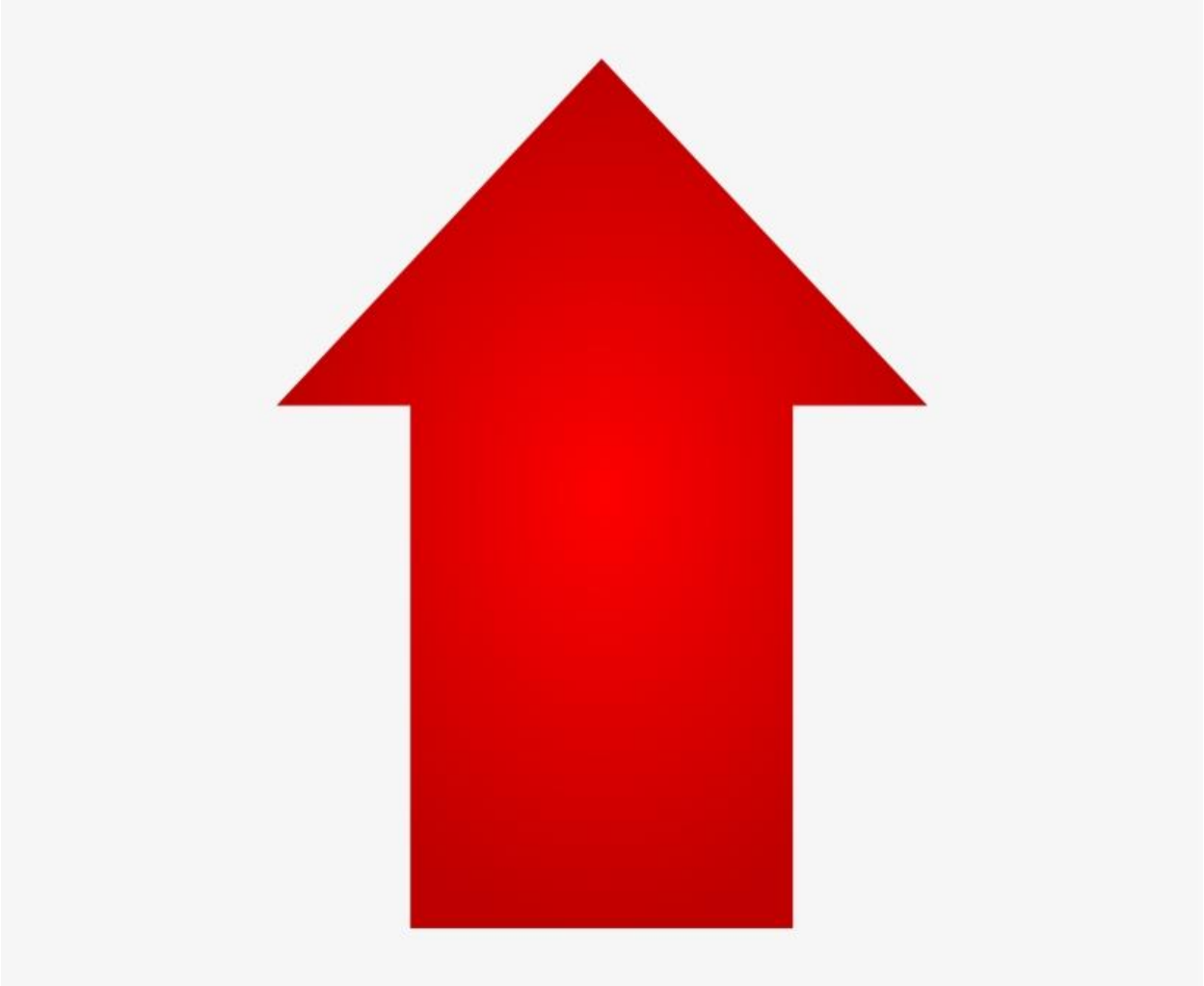
Secondary hemochromatosis

Excess iron

- Excessive iron occurs most often from taking high-dosage supplements when not needed or from having a genetic condition that stores too much iron.

Common signs:

- Constipation
- Upset stomach
- Nausea, vomiting
- Abdominal pain



Iron in excess

- Turmeric may reduce excess iron from both the bloodstream as well as the cells of the body.
- Curcumin is a biologically active iron chelator.
- Green Tea-polyphenols can bind to iron and inhibit iron absorption by the body.
- Quercetin-may help with iron overload by reducing intestinal iron absorption, chelating iron, and reducing oxidative stress

Cofactors-using the iron in our system

- Copper is a component of two plasma proteins, hephaestin and ceruloplasmin. Without these, haemoglobin could not be adequately produced. Located in intestinal villi, hephaestin enables iron to be absorbed by intestinal cells. Ceruloplasmin transports copper. Both enable the oxidation of iron from Fe2+ to Fe3+, a form in which it can be bound to its transport protein, transferrin, for transport to body cells. In a state of copper deficiency, the transport of iron for haem synthesis decreases, and iron can accumulate in tissues, where it can eventually lead to organ damage.
- Zinc functions as a co-enzyme that facilitates the synthesis of the haem portion of haemoglobin.
- The B vitamins folate and vitamin B12 function as co-enzymes that facilitate DNA synthesis. Thus, both are critical for the synthesis of new cells, including erythrocytes.
- Magnesium is a cofactor for enzymes that help synthesize haemoglobin.

Cofactors-using the iron in our system

Vitamin A and beta-carotene may form a complex with iron, keeping it soluble in the intestinal lumen and preventing the inhibitory effect of phytates and polyphenols on iron absorption. Studies have shown that carotenoids (such as beta-carotene, lycopene and lutein) can increase the uptake of non-haem iron.

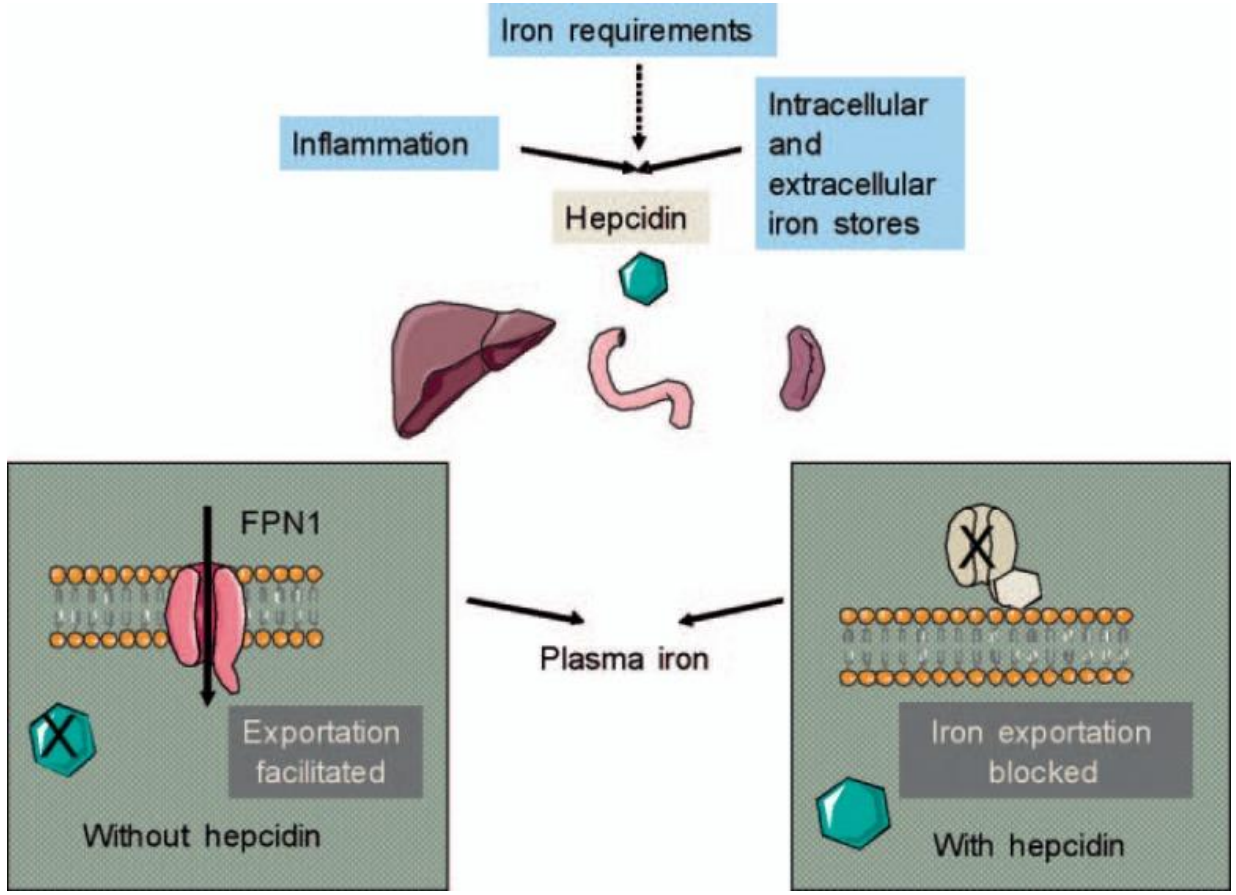
J Nutr. 1998 Mar;128(3):646-50. doi: 10.1093/jn/128.3.646.
Vitamin A and beta-carotene can improve nonheme iron absorption from rice, wheat and corn by humans

Hepcidin

"Anaemia of chronic inflammation"

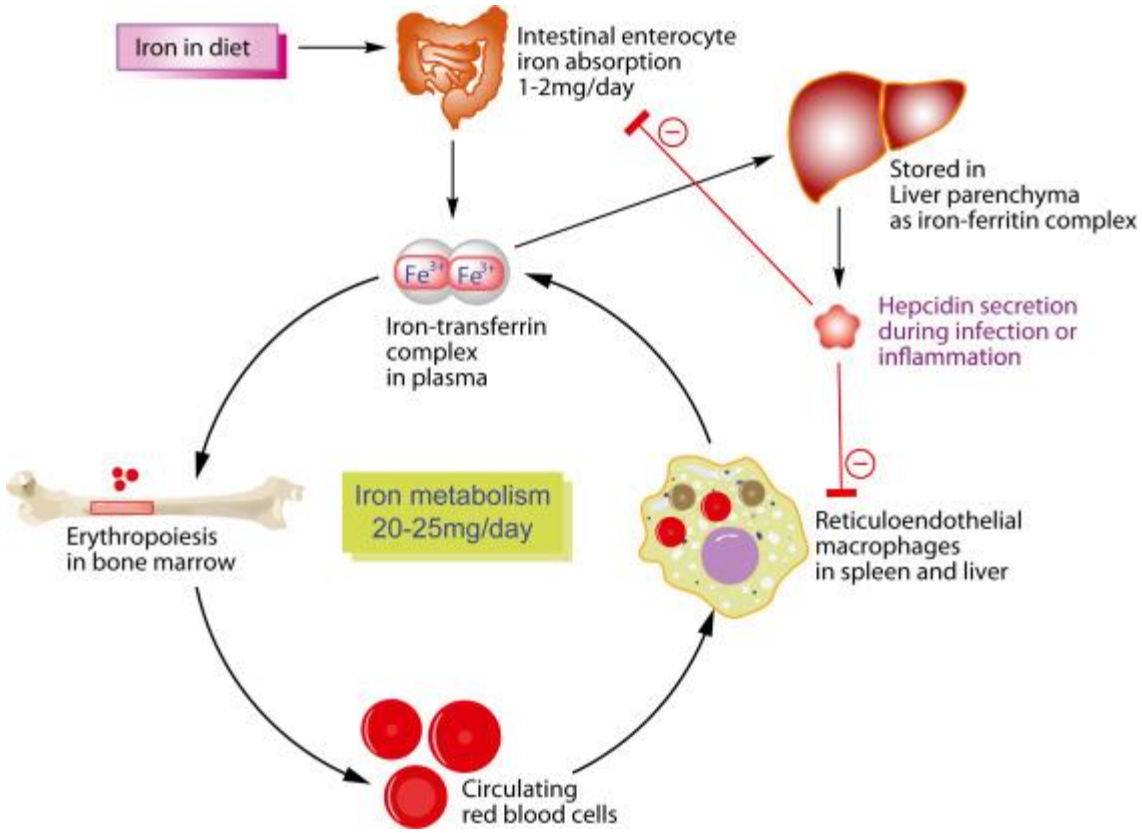
- Inflammation and iron are known extracellular stimuli for hepcidin expression leading to low iron.
- When you compare hepcidin to ceruloplasmin this relates to all facets of iron metabolism being ruled and regulated by copper.
- So, it is ceruloplasmin that is key and not higher levels of hepcidin being expressed disrupting the process of the sophisticated iron recycling programme.
- When ceruloplasmin is weak hepcidin is high which triggers inflammation.
- Iron gets stored so doesn't show on blood test.
- Copper metabolism compromised and iron metabolism chaotic.

Low rbc magnesium, aberrant ceruloplasmin, low serum iron, low % saturation (serum iron/TIBC), low or high ferritin. *IHCAN Jan 2025*



Iron absorption

- Iron binds to the iron-carrier transferrin in the plasma for transport and is responsible for moving iron to the different organs when needed.
- It is then transferred across the duodenal mucosa into the blood, where it binds to and is transported by transferrin to the cells or the bone marrow for erythropoiesis producing red blood cells (RBCs)
- Iron abundance states: the liver takes up non–transferrin-bound iron and stores it when not being used, in a storage protein called ferritin and hence not transported into blood. When the enterocyte dies and is shed, this iron is lost.

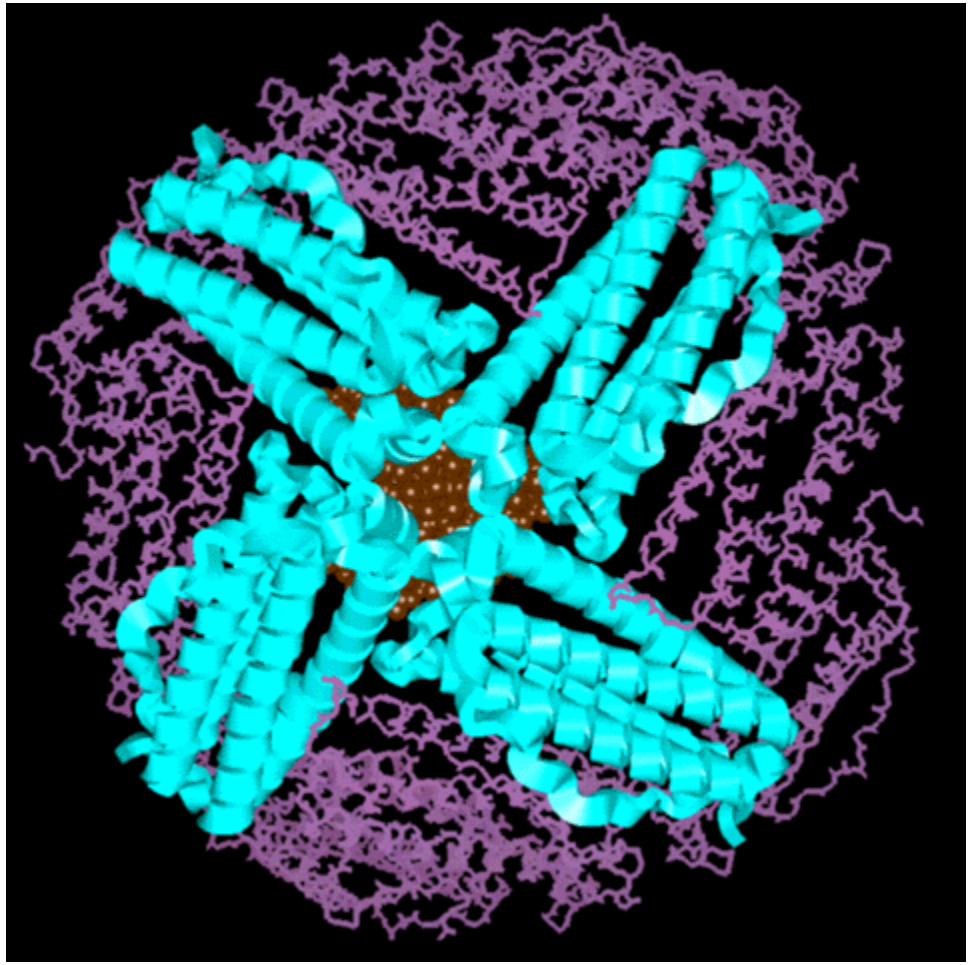


Iron-Fenton reaction

- This prevents significant amounts of iron from existing in its free form, which could damage proteins and cell membranes by free radical formation. its concentration in body tissues must be tightly regulated.
- Iron has been suggested as a risk factor for many cancers. (IHCAN Jan 2025)
- Iron can be toxic in the presence of oxygen as it generates free radicals: this is commonly known as the Fenton reaction.
- Fenton reactions can be harmful when they happen unintentionally; but some immune cells, known as neutrophils, use this reaction to generate free radicals that are toxic and lethal for pathogens.

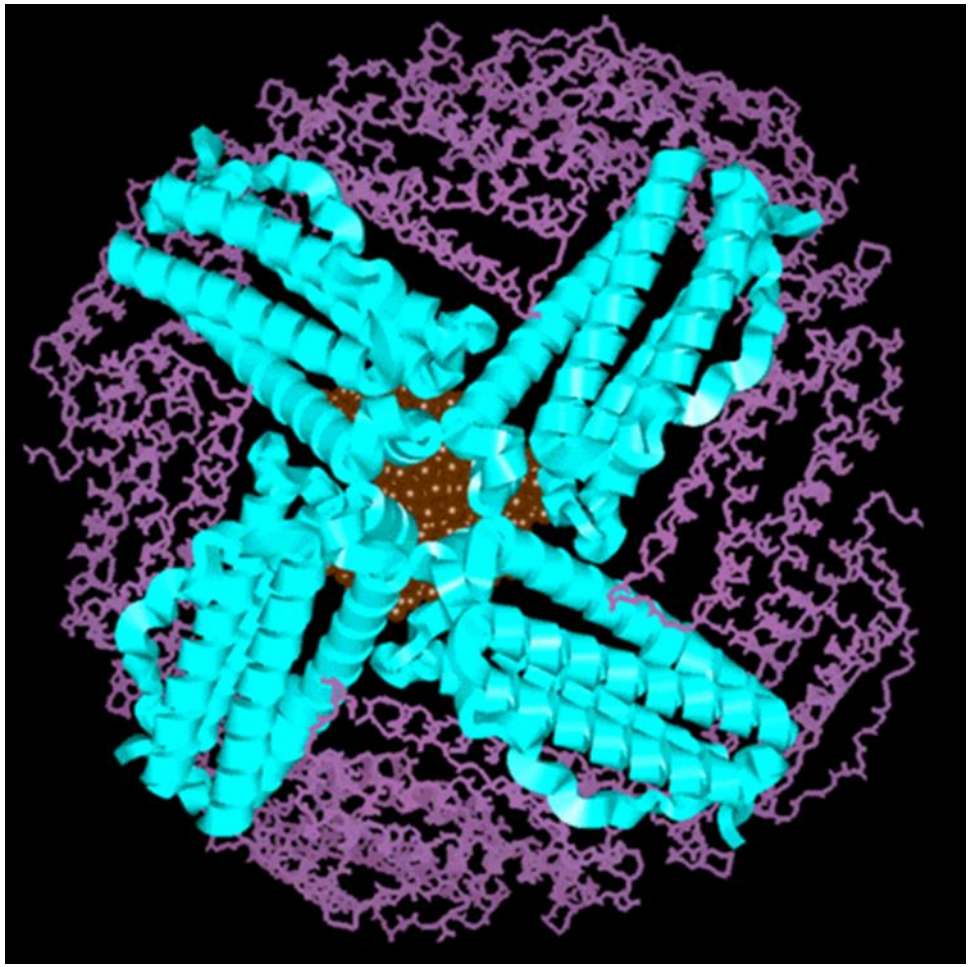
Iron storage

- Ferritin is a universal intracellular iron binding protein that stores iron in a soluble, mobilisable way, (in the liver, spleen, muscle tissue, and bone marrow) and is delivered throughout the body by transferrin (a protein in blood that binds to iron).
- Ferritin releases iron in a controlled fashion. The majority of iron is bound to ferritin. The protein is produced by almost all living organisms and keeps iron in a soluble and non-toxic form. In humans, it acts as a buffer against iron deficiency and iron overload.
- Haemosiderin is an iron storage complex located in the smooth endoplasmic reticulum that less readily releases iron for body needs.



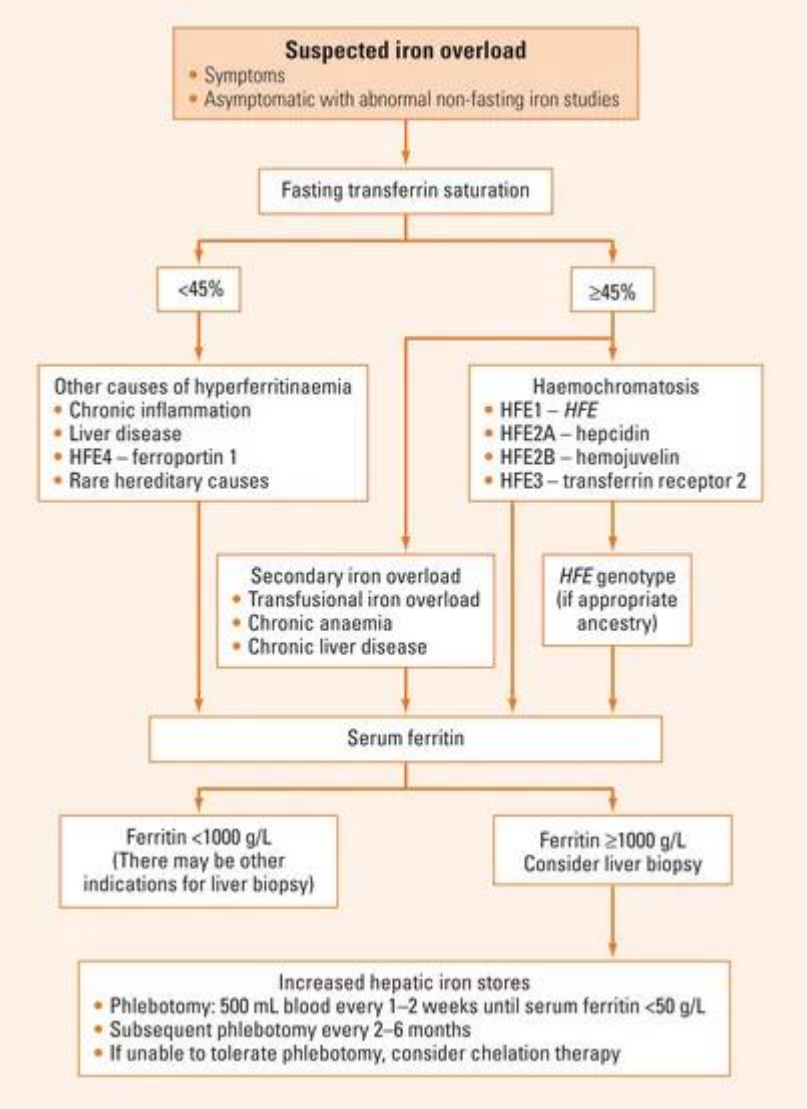
Iron storage

- Ferritin is found in most tissues, but small amounts are secreted into the serum where it functions as an iron carrier. Plasma ferritin is also an indirect marker of the total amount of iron stored in the body; hence, serum ferritin is used as a diagnostic test for iron-deficiency anaemia. Ferritin concentration together with that of haemosiderin reflects the body iron stores.
- Under steady state conditions, serum ferritin concentrations correlate well with total body iron stores. Thus, serum ferritin is the most convenient laboratory test to estimate iron stores.



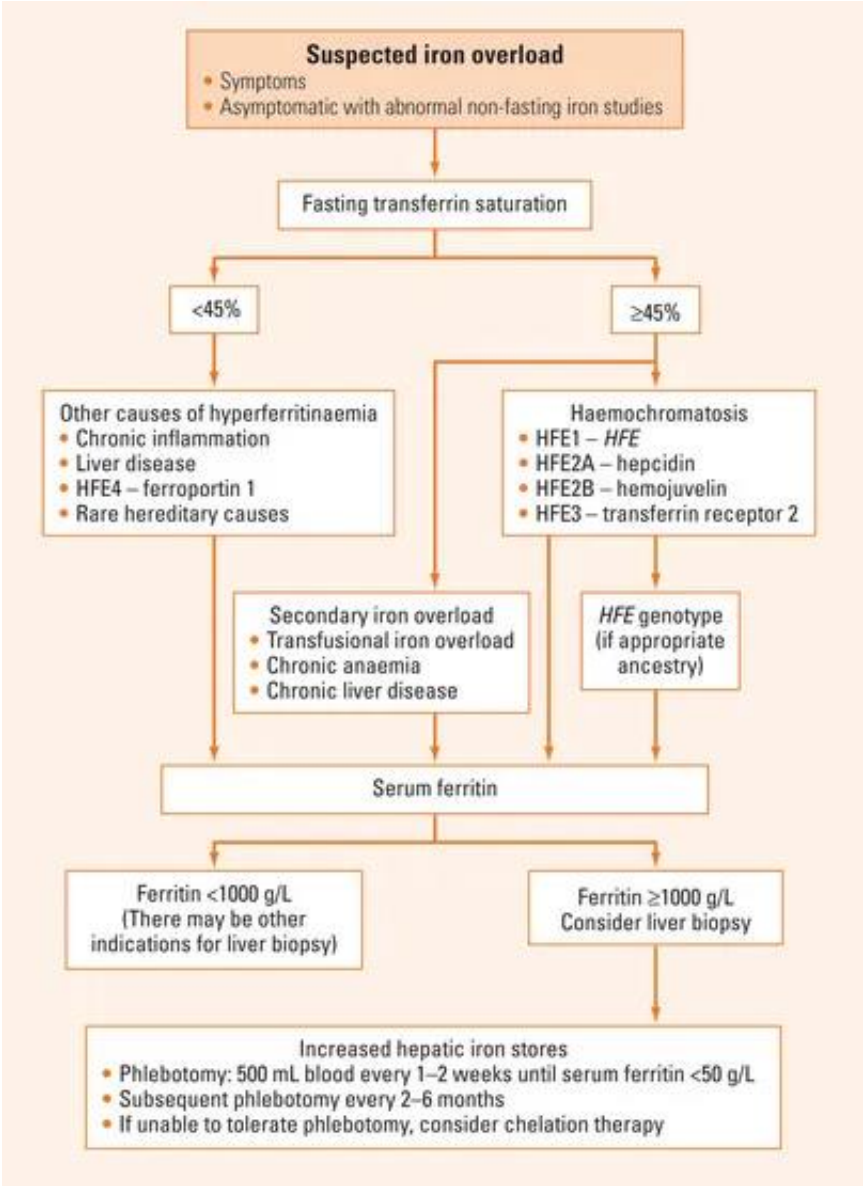
Excess ferritin

- Ferritin is an acute phase reactant and a marker of acute and chronic inflammation. It is elevated in a wide range of inflammatory conditions. Inflammation causes the body to store iron as ferritin. This is part of the body's defence mechanism.
- Anaemia develops in people suffering from diseases in which there is chronic activation of cell-mediated immunity, such as chronic infections, immune-mediated inflammatory disorders, or malignancy. It's characterised by the presence of low iron, but increased blood levels of ferritin.
- The elevated ferritin in these states reflects increased total body iron stores, but paradoxically, these stores are sequestered and not available for red blood cell production. This contributes to the development of anaemia.
- Ferritin is elevated in many types of cancer, primarily due to inflammation. However, some cancers can also be associated with low levels of ferritin, such as colon cancer.
- Studies have shown that ferritin is higher in people with Graves' disease, and that it can decrease back to normal when normal thyroid function is achieved by antithyroid drug therapy.



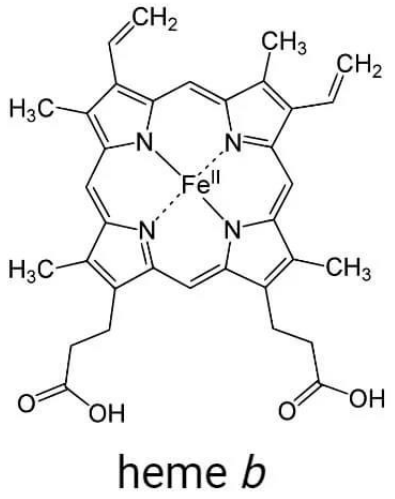
Excess ferritin

- Iron overload and elevated ferritin levels are common in sideroblastic anaemia, a disorder in which bone marrow fails to produce healthy red blood cells.
- Studies suggest that high ferritin and iron can contribute to abnormal heart electrical activity (arrhythmia) in a variety of medical conditions.
- Elevated ferritin has been associated with all components of metabolic syndrome individually. In addition, studies have shown that ferritin increases with the number of metabolic syndrome components a person has.
- In a study of 9.5k US adults, those with higher ferritin levels were more likely to also have diabetes.
- In a study of 524 type 2 diabetics, high ferritin was associated with higher fasting blood glucose, haemoglobin A1c (HbA1C), and CRP.
- In a study of 196 apparently healthy men and women, higher ferritin was linked with artery stiffness among women. Ferritin was also associated with clogged arteries in 506 people with fatty liver disease.
- Elevated ferritin and mildly increased iron stores are frequently observed in people with non-alcoholic fatty liver disease (NAFLD), where an increase in ferritin can reflect oxidative stress, inflammation, and liver damage.



Iron

- Iron in the form Fe2+ is found bound to proteins called haemoproteins. Haemoproteins are a large group of proteins that contain a haem group. This represents about 70% of the iron in the body.
- Iron exists mainly in erythrocytes (red blood cells) as a common haemoprotein called haemoglobin and contains about 60% of the body's iron (approximately 2 g of iron in men and 1.5 g in women), to a lesser extent in storage compounds (ferritin and haemosiderin) and in muscle cells as myoglobin.



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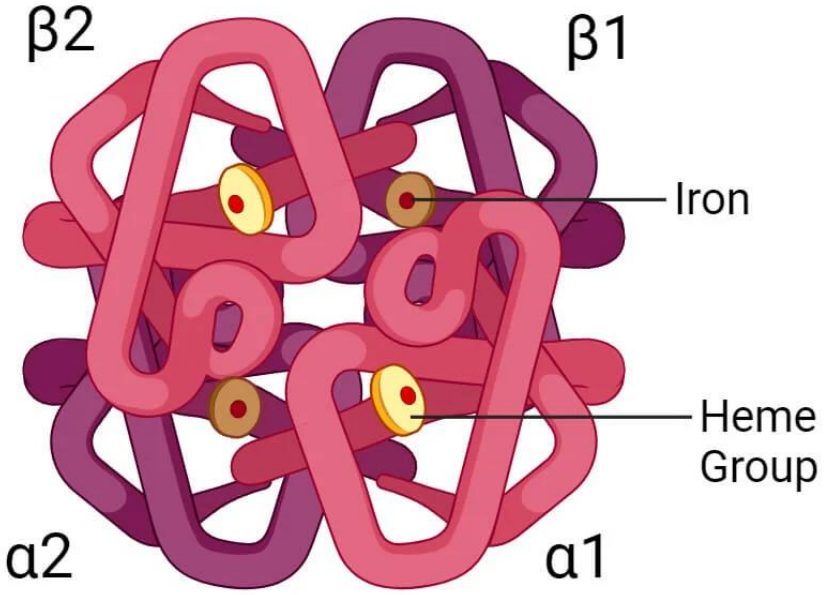
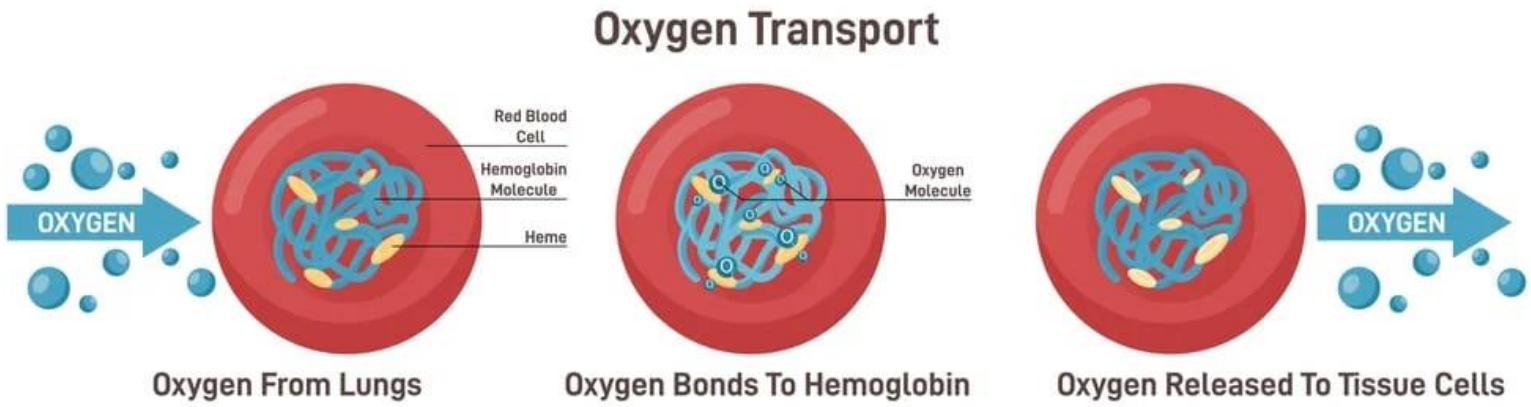
Hemoglobin



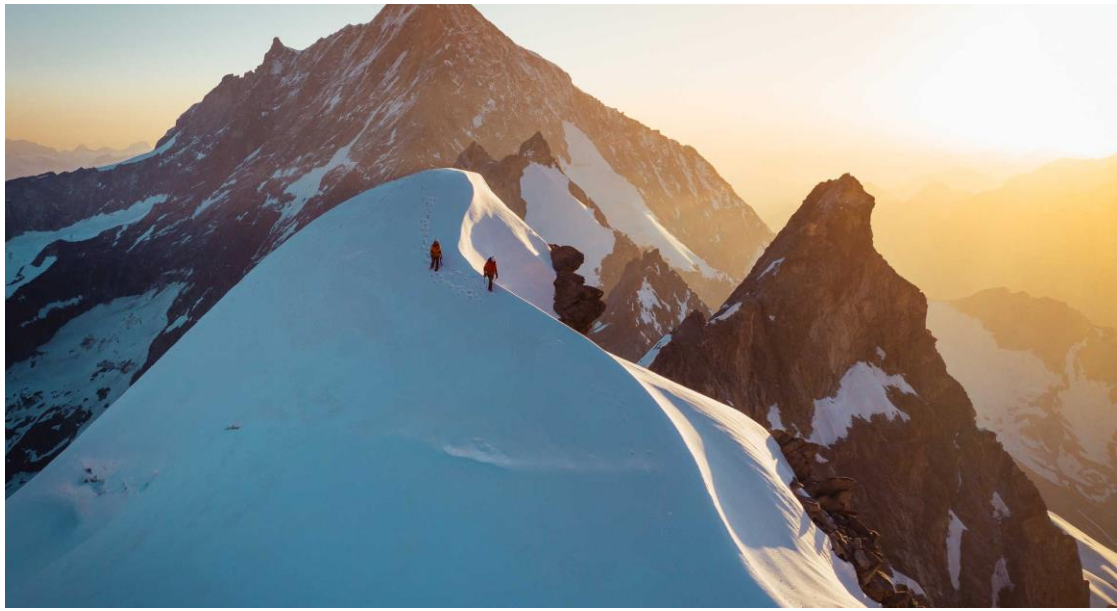
Iron

- Myoglobin supply oxygen to the muscles, in particular to heart and skeletal muscle. Myoglobin is very efficient at taking oxygen from blood, and it serves as an oxygen reservoir in muscle.
- Most iron in the body is used by the bone marrow tissue to make new haemoglobin and erythrocytes.
- The liver and spleen are regulatory and recycling sites on iron, respectively.
- In the lungs, haemoglobin binds to oxygen and transports it to the rest of the tissues in the body.



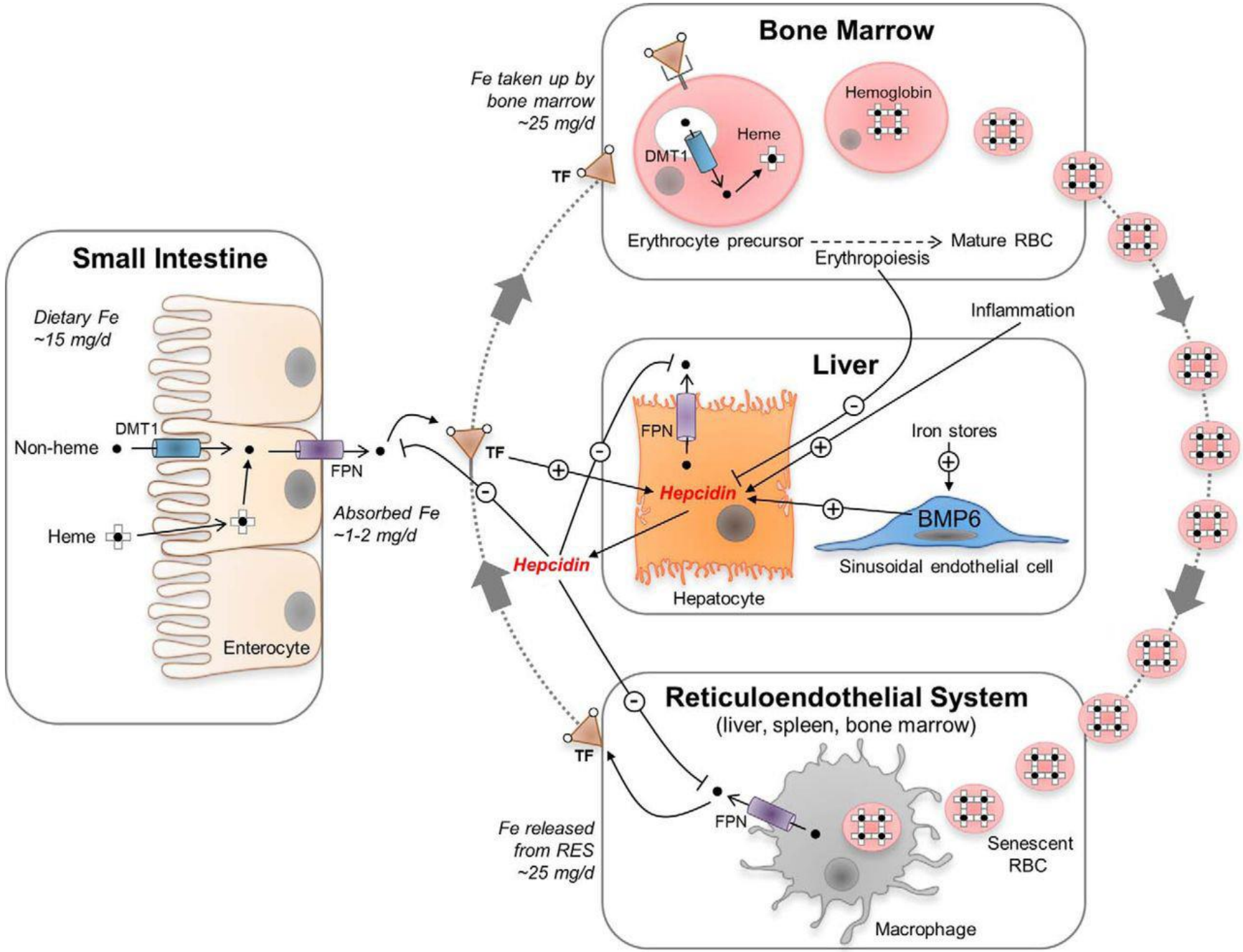
Iron

- How much haemoglobin is needed depends on multiple factors: for example, exposure to high altitude (lower oxygen conditions) and severe blood loss will increase haemoglobin production.
- Other haemoproteins include cytochrome proteins involved in electron transfer and oxidation-reduction reactions.
- Non-haem (non-heme) iron (Fe3+): in this form, is found in ferritin, transferrin, and other proteins.
- It is found in the bone marrow, liver, and spleen and can be found in iron sulfur cluster proteins such as respiratory complexes I-III and coenzyme Q10.



Iron-daily intake

- Apart from erythrocytes and muscle, iron is mainly found in the bone marrow, spleen and liver.
- The average daily dietary iron intake in developed countries is between 10 and 15 mg; under normal conditions, only between 5% and 10% of this quantity is absorbed, that is, 1–2 mg/day.

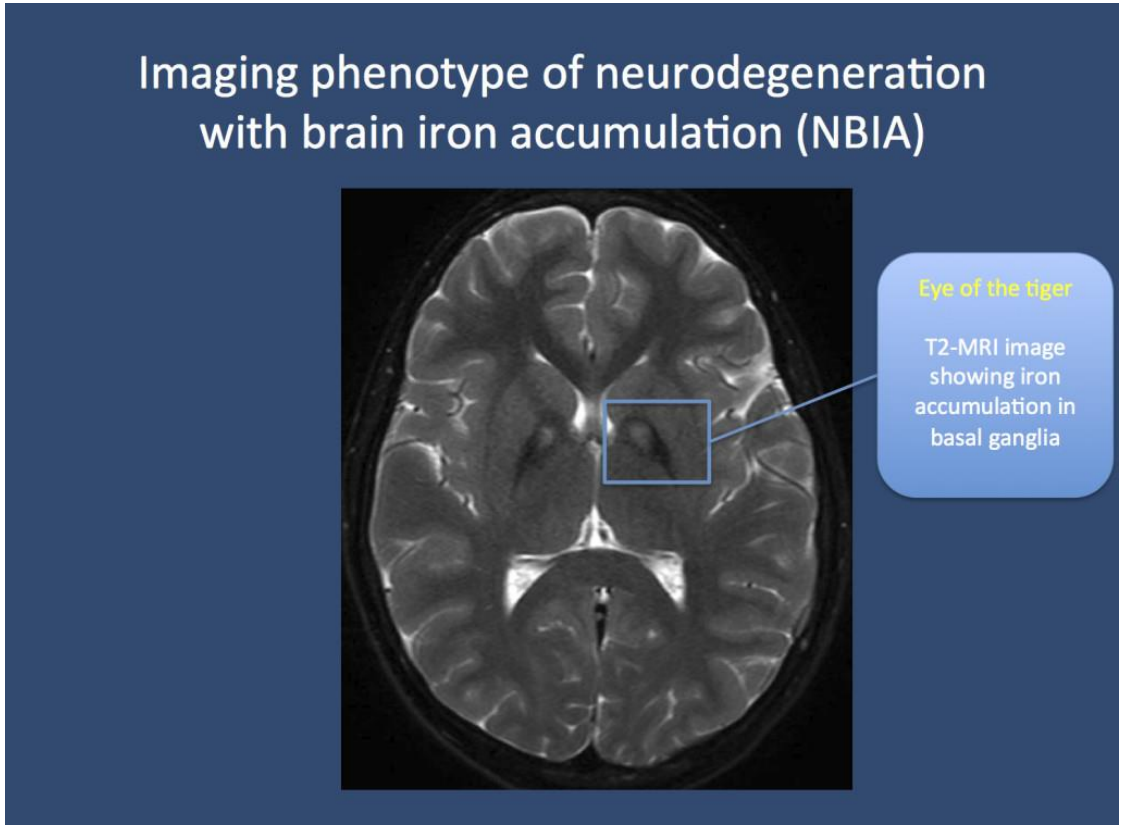


Iron and insulin resistance

- Disorders of iron metabolism are among the most common diseases of humans and encompass a broad spectrum of diseases with diverse clinical manifestations, ranging from anaemia to iron overload.
- Studies have shown that iron is involved in the aggravation of insulin resistance.
- Iron can modify hepatocytes' insulin sensitivity by interfering with insulin receptor and intracellular insulin signalling.

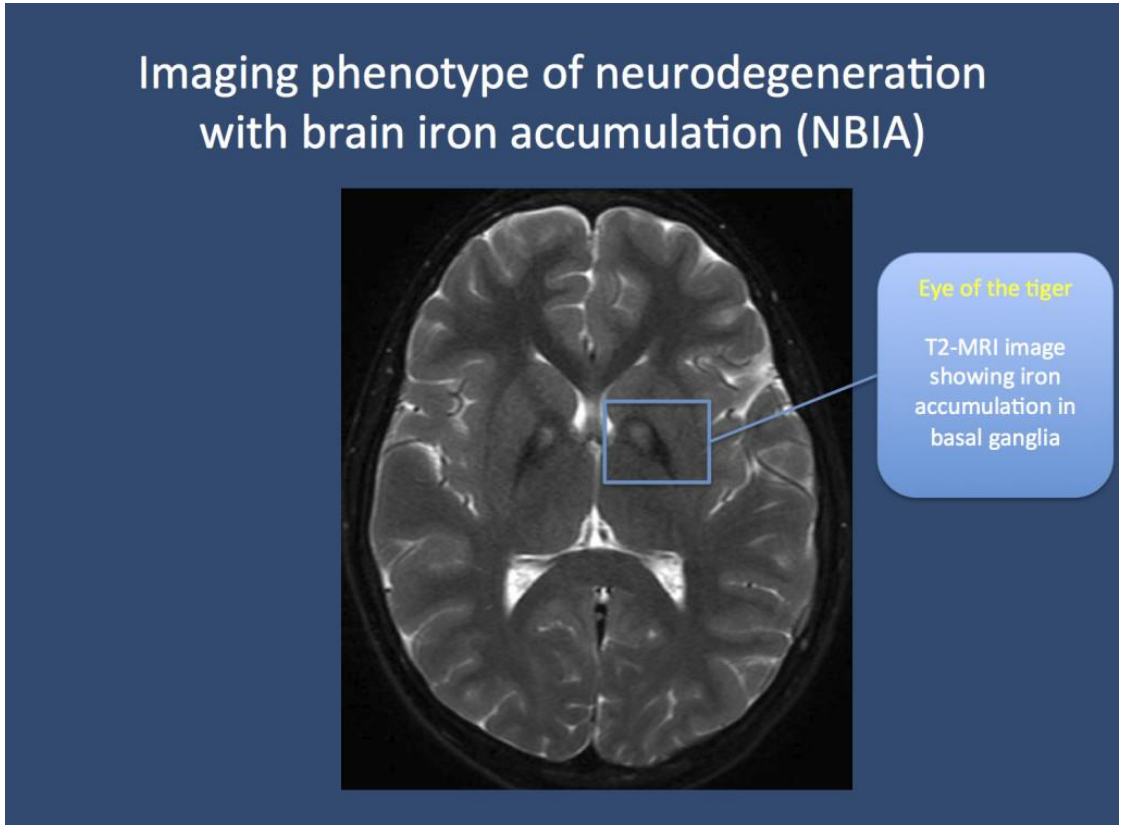
Iron and the brain

- The brain is a highly active tissue which consumes large amounts of oxygen. Maintaining good iron levels supports cognitive function including brain functions such as memory, concentration, learning and problem solving.
- Iron crosses the vascular endothelial cells of the blood–brain barrier, mainly bound to transferrin.
- Iron metabolism has been shown to play multiple roles in the central nervous system. In the CNS, iron in several proteins is involved in many important processes such as oxygen transportation, oxidative phosphorylation, iron is also vital for axon myelination, and the synthesis and metabolism of neurotransmitters such as dopamine and norepinephrine. Iron is critical for neuronal differentiation and proliferation
- Iron deficiency, especially during infancy and adolescence when brains are still developing, has been linked to decreased conscious mental activity and mental developmental problems



Iron and the brain

- Abnormal iron homoeostasis can induce cellular damage through hydroxyl radical production, which can cause the oxidation and modification of lipids, proteins, carbohydrates, and DNA.
- Iron deficiency and overload are associated with neurodegenerative diseases.
- During ageing, different iron complexes accumulate in brain regions associated with motor and cognitive impairment.
- Iron accumulation in the glia (supporting cells in the brain) can lead to inflammation and release of pro-inflammatory cytokines, which in turn can result in a cycle of continuous inflammation and neurodegeneration.
- In various neurodegenerative diseases, such as Alzheimer's disease and Parkinson's disease, changes in iron homoeostasis result in altered cellular iron distribution and accumulation.
- MRI can often identify these changes, thus providing a potential diagnostic biomarker of neurodegenerative diseases.



Iron-decreased absorption

Conditions that degrade the mucosa of the duodenum will decrease absorption of iron and include:

- Coeliac disease
- Tropical sprue
- Crohn’s disease
- Duodenal cancer
- Duodenal ulcers
- Familial adenomatous polyposis

Causes of low iron

Gastrointestinal disorder with increased iron losses	Cancer/polyp: colon, stomach, esophagus, small bowel
	Peptic ulcer, esophagitis
	NSAID use
	Inflammatory bowel disease: ulcerative colitis, Crohn's disease
	Intestinal parasites
	Vascular lesions: angiodysplasia, watermelon stomach
	Meckel's diverticulum
Gastrointestinal disorders that reduce iron absorption	Celiac disease
	Bacterial overgrowth
	Whipple's disease
	Lymphangiectasia
	Gastrectomy (partial and total) and gastric atrophy
	Gut resection or bypass
Urological and gynecological disorders	Menorrhagia
	Hematuria
	Chronic renal failure
Intravascular hemolysis	Prosthetic valves and cardiac myxomas
	Paroxysmal nocturnal hemoglobinuria
	Marathon runners
	Multiple blood donations
Deficient intake	Low socioeconomic class
	Vegetarian diets
	Dissociated diets
	Alcoholism
	Elderly patients
	High-risk ethnic groups
Medication that reduces gastric acid or iron affinity	Dietary factors
	Tannin
	Phytates in fiber
	Calcium in milk
	Tea
	Coffee
Increased requirements in various stages of life	Infants up to 3 years and adolescents
	Pregnant women
	Breastfeeding women
	Multiparous
	Post-partum

Abbreviation: NSAID, nonsteroidal anti-inflammatory drug.

Iron deficiency

ID is defined as a decrease in total iron levels (both in serum and deposits), regardless of clinical expression.

Iron deficiency occurs in stages.

- The mild form begins with a decrease in stored iron, usually either from a low-iron diet or from excessive bleeding.
- If this does not resolve, the next stage is a greater depletion of iron stores and a drop in red blood cells.
- Eventually this leads to iron-deficiency anaemia (IDA) where iron stores are used up and there is significant loss of total red blood cells.
- Typically, a doctor screens for anaemia by first checking a complete blood count (including haemoglobin, haematocrit, (a blood test that measures the percentage of red blood cells in your blood) and other factors that measure red blood cell volume and size).
- If this is below normal, ferritin and transferrin levels may be measured to determine if the type of anaemia is IDA (there are other forms of anaemia not caused specifically by an iron deficiency).

Iron-anaemia of chronic disease or IDA

Table 1. Interpretation of iron studies

Diagnosis	Haemo-globin	Mean corpuscular volume	Ferritin (µg/L)	Transferrin saturation	Iron
Iron deficien-cy without anaemia	Normal	Normal or low	<15–30	Low-normal or low	Low
IDA	Low	Low (or low-normal in early IDA)	<15–30 (adult) <10–12 (child)	Low	Low
ACD	Low	Normal or slightly low	Normal or high	Low	Low
IDA with ACD	Low	Low	Low or normal, but usually <60–100	Low	Low
Thalassae-mia minor	Low or normal	Low or normal	Normal or high	Normal	Normal
Iron overload	Normal	Normal	High	High	Normal or high

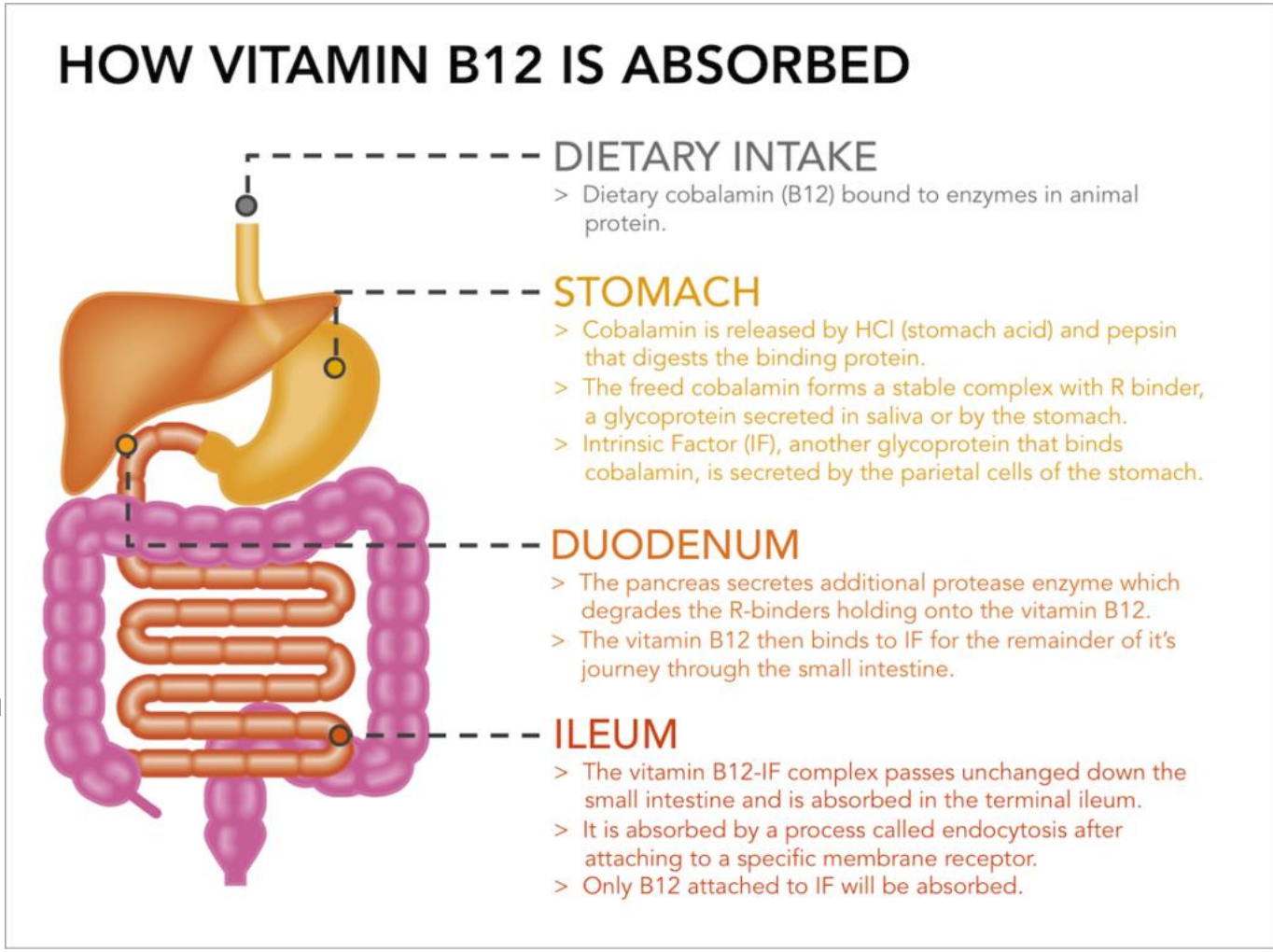
IDA, iron deficiency anaemia; ACD, anaemia of chronic disease

Other types of anaemia

- Diets lacking in vitamin B12 or can’t use or absorb Vitamin B12 (like pernicious anaemia).
- Diets lacking in folic acid, or body can’t use folic acid correctly (like folate-deficiency anaemia).
- Inherited blood disorders (like sickle cell anaemia or thalassemia).
- Conditions that cause red blood cells to break down too fast (like haemolytic anaemia).
- Chronic conditions causing the body to not have enough hormones to create red blood cells. These include hyperthyroidism, hypothyroidism, advanced kidney disease, lupus and other long-term diseases.
- Aplastic anaemia, damaged bone marrow so cannot make red blood cells.
- Blood loss related to other conditions such as ulcers, haemorrhoids or gastritis. (which can be caused by H.pylori)

B12

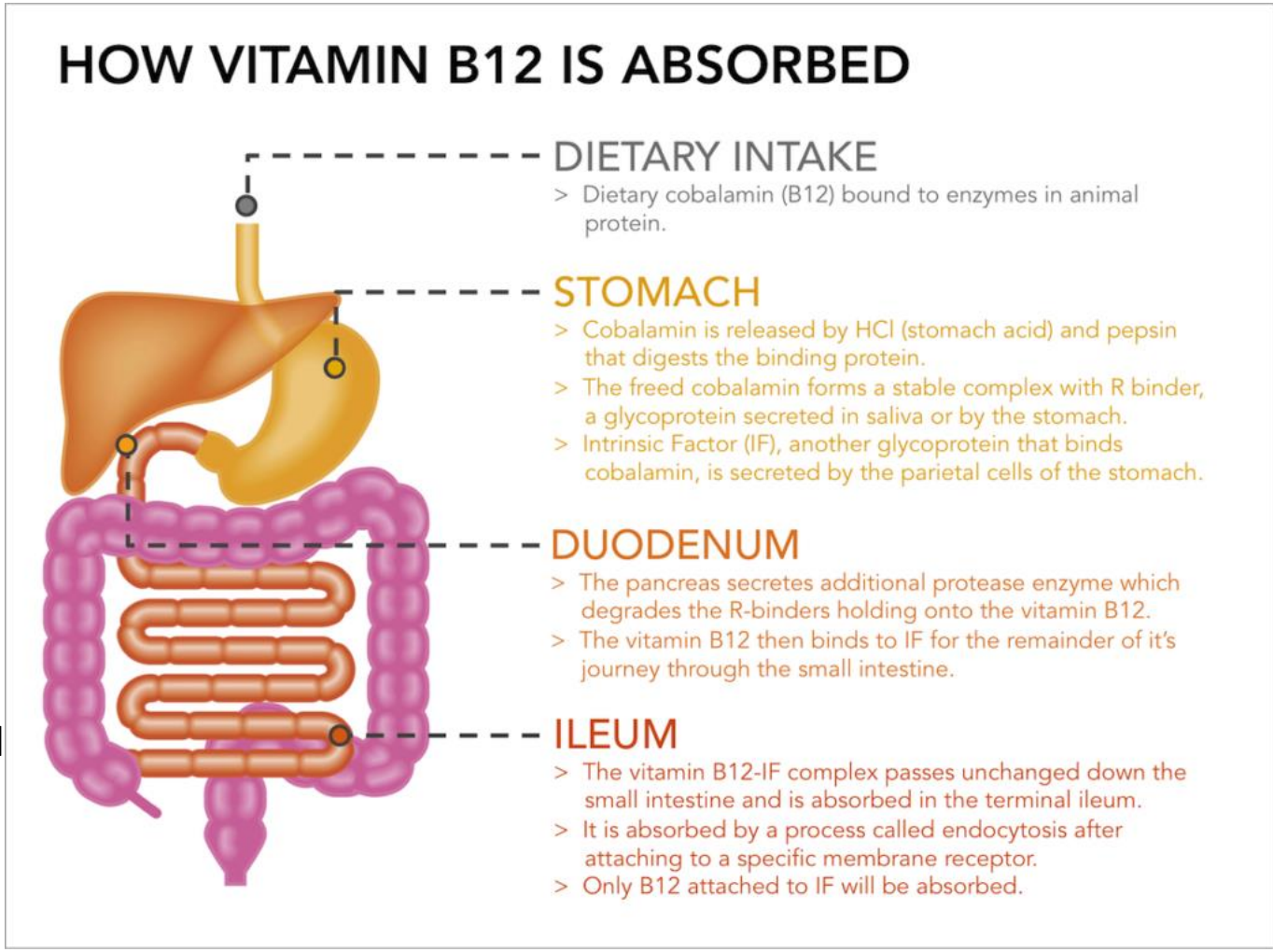
- B12 is required for the production of red blood cells, a deficiency in Vitamin B12 can lead to a deficiency in iron.
- Low stomach acid - without sufficient HCl and pepsin, the animal proteins that are bound to Vitamin B12 are unable to be digested.
- This means the B12 is not ‘free’ to bind with other glycoproteins and move through the GI tract for absorption.
- Anyone with Atrophic Gastritis or Hypochlorhydria as a result of conditions like H. pylori bacterium infection are at particular risk.
- As is anyone who has been prescribed proton pump inhibitors (PPIs) or acid suppressing medications.



B12

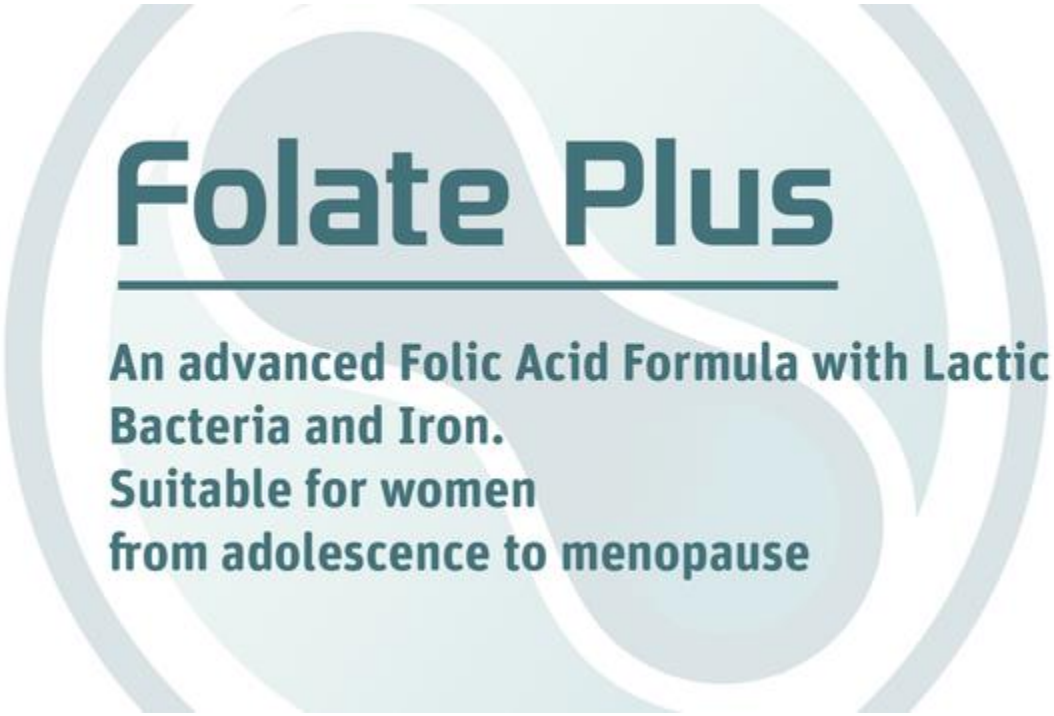
- Exocrine pancreatic insufficiency - without the production of sufficient pancreatic (digestive) enzymes, the body is unable to breakdown the Cobalamin-R complexes in the duodenum. As a result, the B12 cannot bind with Intrinsic Factor (IF) and make its journey through the small intestine to be absorbed.
- Bacterial dysbiosis and gut infections - high concentration of bacteria in the small intestine (e.g., SIBO) and certain parasites (e.g Giardia) can consume the Vitamin B12 before it is absorbed by the body.
- Surgical resection or disease of the distal ileum - because B12 is absorbed at the lower end of the small intestine, any surgical removal (e.g., weight loss surgery) or an inflammatory condition (e.g., Crohn's and Coeliac disease) that impairs the distal ileum will also impair absorption of Vitamin B12.

Individuals with gene mutations such as MTHFR or MTRR have trouble with the process of methylating B12 into its usable form.



Folate Plus


Bionutri
Folate Plus
An advanced Folic Acid Formula with Lactic Bacteria and Iron. Suitable for women from adolescence to menopause
Food Supplement
60 Capsules


Folate Plus
An advanced Folic Acid Formula with Lactic Bacteria and Iron.
Suitable for women
from adolescence to menopause

NAID

- Non-anaemic iron deficiency (NAID) is a common condition where iron stores are low but haemoglobin levels are normal.
- Non-anaemic absolute iron deficiency is common in older adults in England and associated with an increased mortality rate according to a 2022 study in the British Journal of Haematology.
- 10.9% of women and 6.35% of men are NAID candidates.

Causes

- Inadequate diet
- Increased requirements, such as during pregnancy and breastfeeding
- Impaired absorption, such as with coeliac disease or bariatric surgery
- Blood loss, such as from menstruation, blood donation, or gastrointestinal bleeding
- Drug-induced causes

PPI’s

- Taken together, PPIs directly affect iron metabolism by suppressing iron absorption through the inhibition of duodenal ferroportin via hepcidin upregulation.
- PPIs, as well as H2 blockers, increase the odds ratio of iron-deficient anaemia.

Iron deficiency

- Iron deficiency with or without anaemia is nearly always associated with diseases that trigger a negative balance between iron absorption and loss.
- Its management will be based on the treatment of underlying diseases, as well as on oral iron supplements, although these are limited by their tolerance and low potency, which on occasions may compel a change to intravenous administration.
- Because we do not have a physiological means for eliminating the excess of remaining iron, its intestinal absorption is low, similar to its physiological losses, and iron can increase only slightly, even in cases of deficiency. This accounts for the frequent development of iron deficiency when there are concomitant factors that increase its losses or requirements, or when its intake decreases.

Iron deficiency

- When the deficiency impairs erythropoiesis, it may result in a decrease in haemoglobin, with subsequent development of IDA.
- The diagnosis of anaemia is simple and objective: the WHO defines it as a decline in blood haemoglobin to a level less than 13 g/dL in men and 12 g/dL in women. However, confirming that ID is the mechanism responsible for this anaemia is not always easy.
- Sometimes, a simple blood cell count strongly suggests this. However, up to 40% of cases of “pure” IDA are normocytic. (underlying illness as the cause)
- The next step in assessing anaemia is to determine iron metabolism. In the absence of inflammation, serum ferritin reflects total iron deposits in the body. Thus, a low serum ferritin (30 ng/L) unequivocally means ID. Transferrin saturation is especially useful when the measurement of ferritin is equivocal; a percentage of transferrin less than 20% implies ID.
- Zinc protoporphyrin is another indicator of IDA and early iron depletion. When iron supply is diminished, zinc utilisation increases resulting in a high zinc protoporphyrin.

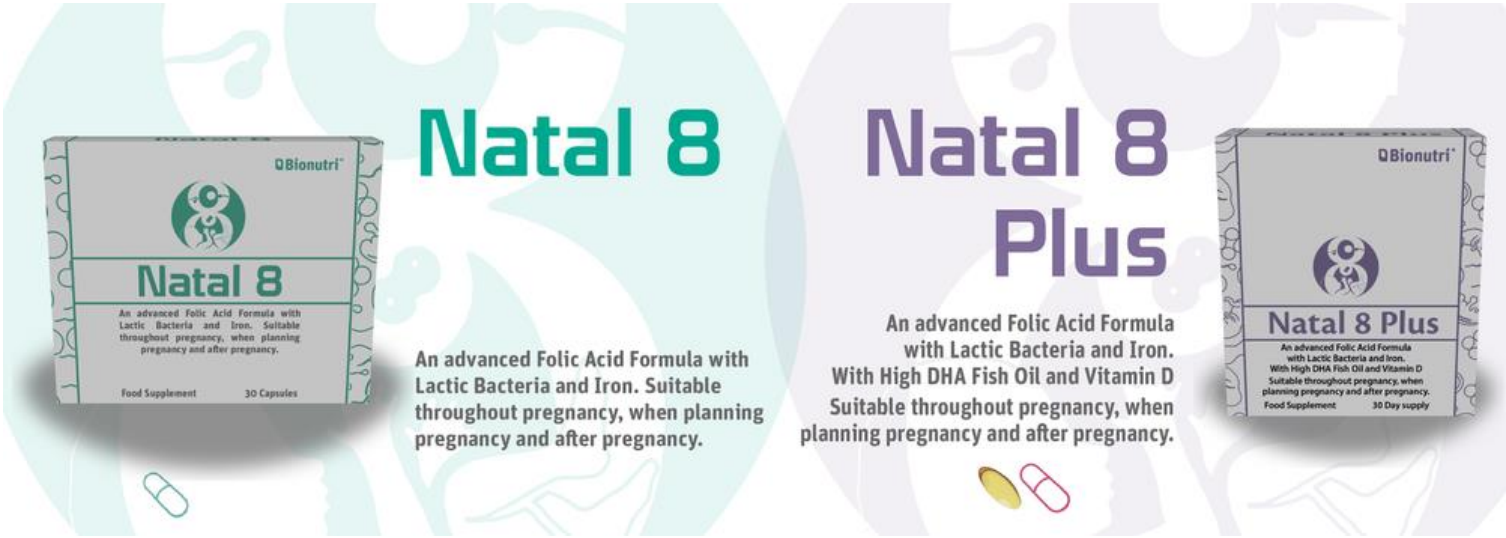
Iron deficiency anaemia (IDA)-causes

- Iron deficiency anaemia is the most common nutritional deficiency worldwide, causing extreme fatigue and lightheadedness.
- It affects all ages, with children, women who are pregnant or menstruating, and people receiving kidney dialysis among those at highest risk.
- Optimising iron status can be challenging. Currently, iron supplementation is a standard intervention for iron deficiency anaemia. Barriers to body iron repletion via oral supplementation include underlying systemic inflammation from chronic conditions such as obesity, dietary factors such as phytates and other symptoms including gastrointestinal distress.

Cause	Considerations
Dietary deficiency	In the UK, diet alone is unlikely to cause iron deficiency anaemia
Malabsorption of iron	Examples include coeliac disease, intestinal disorders, *Helicobacter pylori* colonisation in the gut
Increased blood loss	This is the most common pathology leading to iron deficiency anaemia. Examples include gastric ulcers, angiodysplasia, colon and gastric cancers, menstrual bleeding, surgery, haemorrhage
Increased iron requirement	In pregnancy, breastfeeding, children, infants
Drug induced	Can be caused by non-steroidal anti-inflammatory drugs, proton pump inhibitors and H2 receptor antagonists
Chronic conditions	Examples include chronic kidney disease, chronic heart failure, inflammatory bowel disease, lupus, cancer, rheumatoid arthritis
Genetic disorders	Increased hepcidin (TMPRSS6 gene mutation) may reduce iron absorption
Regular blood donation	

Groups at risk for IDA:

- Pregnant women—during pregnancy, a woman produces much greater amounts of red blood cells for the foetus, increasing the need for additional dietary or supplemental iron. IDA during pregnancy can lead to premature birth or low birth weight so iron is routinely included in prenatal vitamins.
- Menstruating women—women who experience heavy bleeding during menstruation (lasting longer than 7 days or soaking through tampons or pads once every hour) can develop IDA.
- Children—infants and children have high iron needs due to their rapid growth.
- Infants: Infants may get less iron when they are weaned from breast milk or formula to solid food. Iron from solid food is not as easily taken up by the body.
- People on blood thinners: These medications include drugs include aspirin, clopidogrel (Plavix®), warfarin (Coumadin®), heparin products, apixaban (Eliquis®), betrixaban (BevyxXa®), dabigatran (Pradaxa®), edoxaban (Savaysa®) and rivaroxaban (Xarelto®).



Groups at risk for IDA:

- Elderly—older ages are associated with a higher risk of poor nutrition and chronic inflammatory diseases that can lead to anaemia.
- Vegetarians—those who eat a diet without haem iron from meats, fish, and poultry may develop IDA if they do not include adequate non-haem iron foods in the diet. Because non-haem iron is not well-absorbed, either greater quantities of these foods my be required or careful attention is needed in how they are eaten to improve absorption (consuming with vitamin C-rich foods while avoiding eating with calcium-rich foods, calcium supplements, or tea).
- Endurance athletes—running can cause trace amounts of gastrointestinal bleeding and a condition called “foot-strike” haemolysis that breaks down red blood cells at a faster rate. Female endurance athletes who are also menstruating are at greatest risk for IDA.
- People with chronic kidney failure on dialysis—the kidneys make a hormone called erythropoietin (EPO) that signals the body to make red blood cells. Kidney failure reduces the production of EPO and therefore blood cells. In addition, there is some blood loss during haemodialysis

IDA signs

Signs of IDA:

- Fatigue, weakness
- Lightheadedness
- Confusion, loss of concentration
- Sensitivity to cold
- Shortness of breath
- Rapid heartbeat
- Pale skin
- Hair loss, brittle nails
- Pica: cravings for dirt, clay, ice, or other non-food items

Infants

- Most newborns have sufficient iron stored in their bodies for about the first 6 months of life depending on gestational age, maternal iron status, and timing of umbilical cord clamping. By age 6 months, however, infants require an external source of iron apart from breast milk. Breast milk contains little iron; therefore, parents of infants receiving only breast milk should talk to their infant's health care provider about whether their infant needs iron supplements before 6 months of age.
- If an infant is receiving only iron-fortified infant formula (during the time before complementary foods are given), then additional iron supplementation is not necessary.
- At about 6 months of age, an infant's iron needs can be met through the introduction of iron-rich foods, iron-fortified cereals, or iron supplement drops

IDA

Red blood cells live about 100 days, so the body is constantly trying to replace them. In adults, red blood cell production occurs in the bone marrow.

Doctors try to determine if a low red blood cell count is caused by increased blood loss of red blood cells or from decreased production of them in the bone marrow.

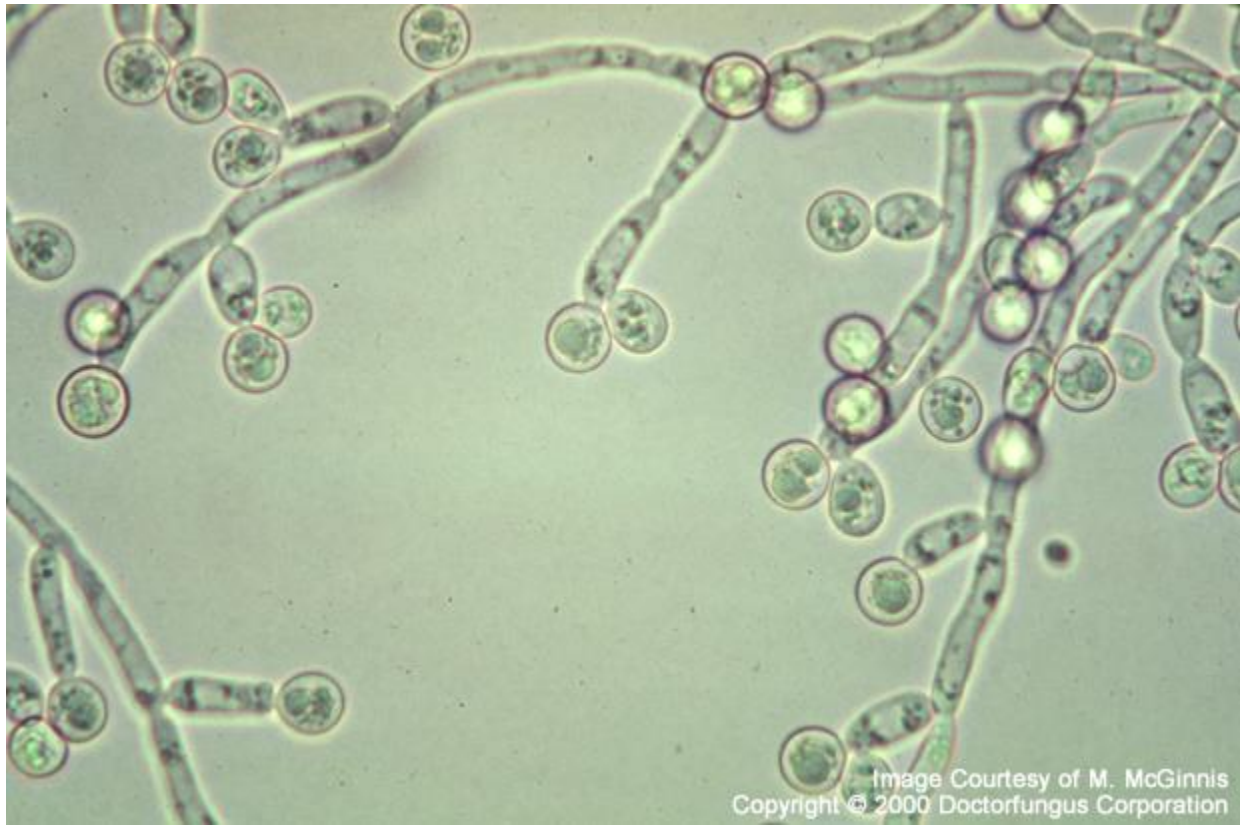
Knowing whether the number of white blood cells and/or platelets has changed also helps determine the cause of anaemia.

IDA

- If red blood cells are smaller than normal, this is called microcytic anaemia. The major causes of this type are iron deficiency (low-level iron) anaemia and thalassemia (inherited disorders of haemoglobin).
- If the red blood cell size is normal in size (but low in number), this is called normocytic anaemia, such as anaemia that accompanies chronic disease or anaemia related to kidney disease.
- If red blood cells are larger than normal, then it is called macrocytic anaemia. Major causes of this type are pernicious anaemia and anaemia related to alcoholism.

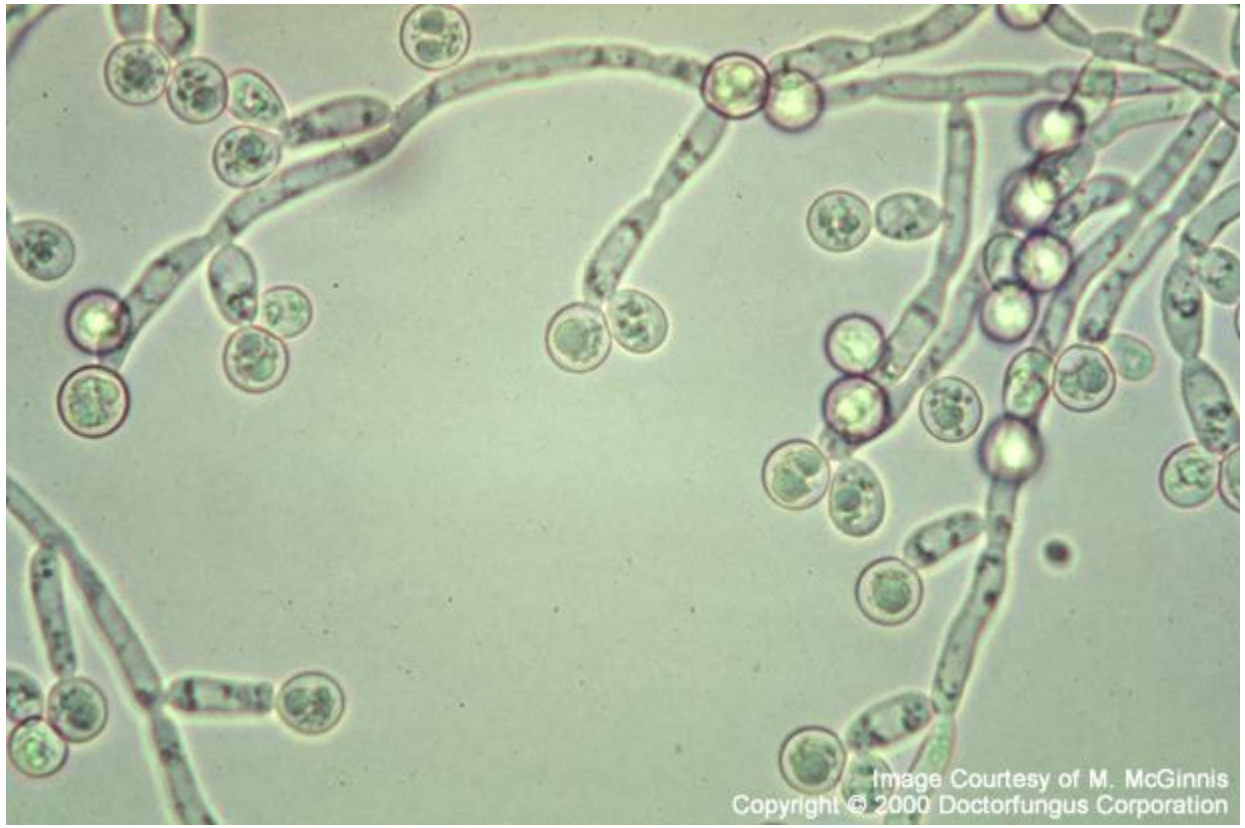
Iron and pathogens

- Iron acquisition during infection of a human host is a challenge that must be surmounted by every successful pathogenic microorganism.
- Iron is essential for bacterial and fungal physiological processes such as DNA replication, transcription, metabolism, and energy generation via respiration. Hence, pathogenic bacteria and fungi have developed sophisticated strategies to gain access to iron from host sources.



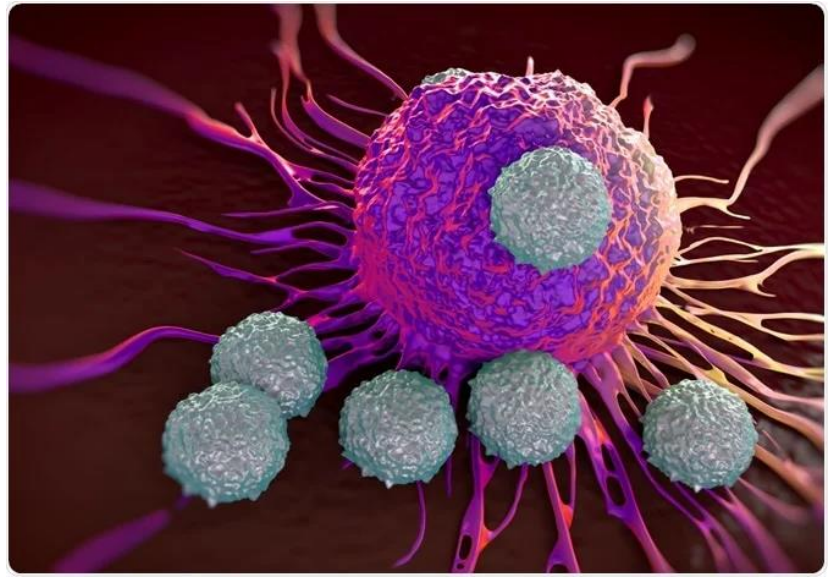
Iron and pathogens

- Siderophore (binds and transports iron in microorganisms) production and transport, iron acquisition from haem and host iron-containing proteins such as haemoglobin and transferrin, and reduction of ferric to ferrous iron with subsequent transport are all strategies found in bacterial and fungal pathogens of humans.
- Studies have been done on the mold Aspergillus fumigatus (a saprotroph that is also responsible for invasive pulmonary aspergillosis), the polymorphic fungus Candida albicans (the cause of skin or mucosal infections and invasive candidiasis), and the yeast Cryptococcus neoformans (the agent of cryptococcosis, a disease involving life-threatening meningoencephalitis).



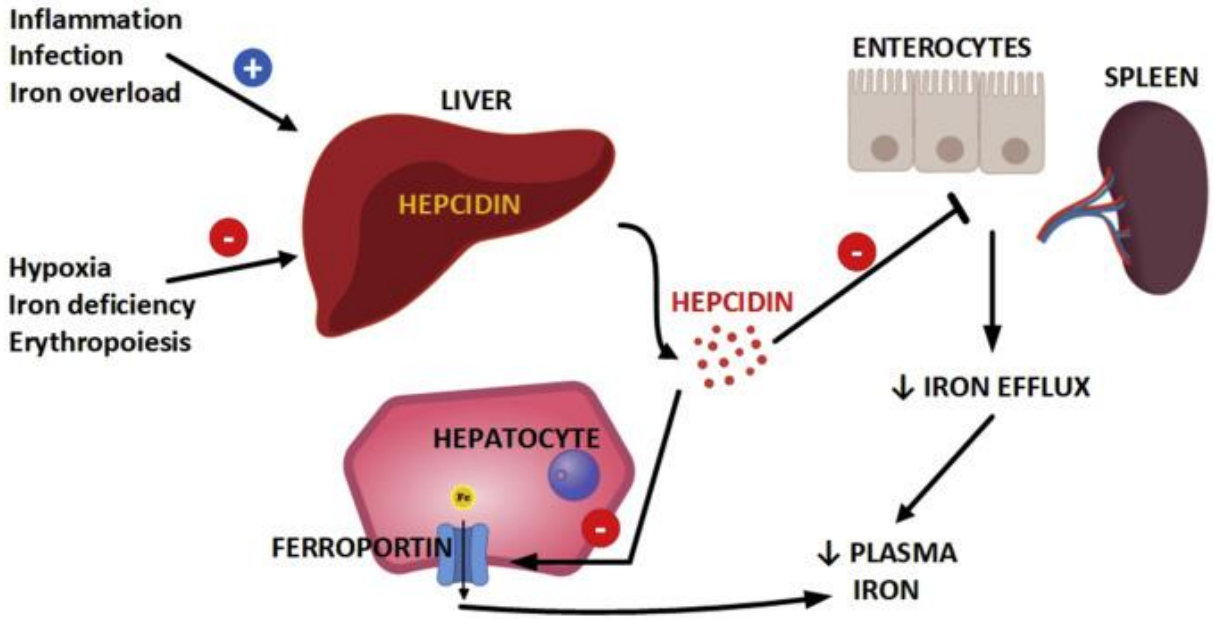
Iron and immune cells

- Iron can regulate both innate and adaptive immunity.
- Iron plays an important role in supporting the immune system and helping fight infections. It is important for cell division and growth, and it's necessary for differentiation and proliferation of multiple immune cells, such as the T lymphocytes.
- Iron is involved in the production and regulation of cytokines, the signalling molecules of the immune system, necessary to create the inflammatory response that helps to fight infections
- In research published in Med, the Drakesmith Group investigated how iron influences adaptive immune responses to infections and to vaccines, and how the iron regulating hormone hepcidin is involved in this process. The researchers found that low amounts of iron in the blood inhibits immune responses to vaccines, because immune cells T-lymphocytes need iron to support their metabolism. T-lymphocytes are crucial for destroying infected cells, for helping the antibody response to infections, and for remembering infections (immune memory).
- The team found that activated T-lymphocytes need large amounts of iron; and if iron is scarce, the mitochondria in T-lymphocytes generate less energy, making the T-cells less able to carry out their functions and fight infections.



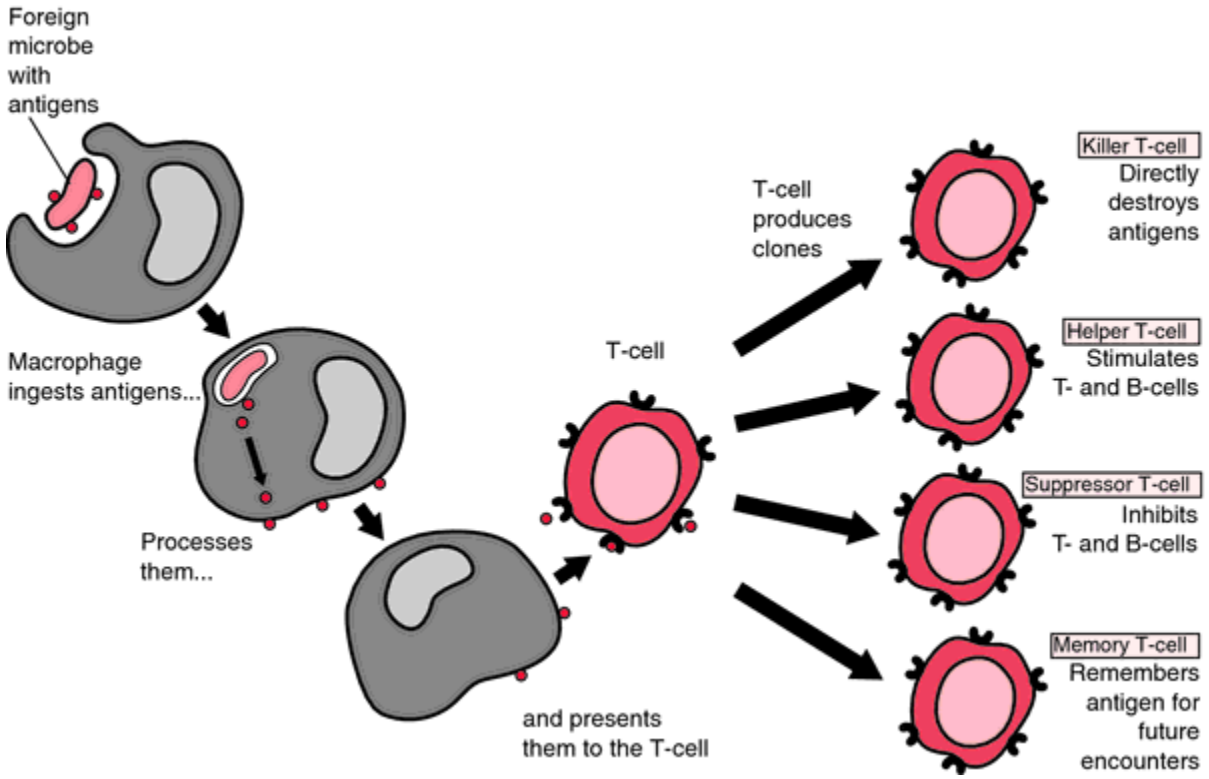
Iron and immune cells

- Hepcidin is the hormone that controls the amount of iron in the bloodstream. Mice with high hepcidin and low serum iron made poorer immune responses to vaccines, and were worse at forming immune memory, a crucial aspect of how the immune system remains protective over many years. Mice with high hepcidin were also worse at making an immune response to influenza virus infection, and their lungs were more damaged by the infection. This situation may be important in Covid-19, where high hepcidin and low iron also occur.
- People with a rare genetic mutation that results in high hepcidin, and low serum iron levels had fewer antibodies against some infectious pathogens, which meant that their immune systems were less able to fight off some infections.



Iron and immune cells

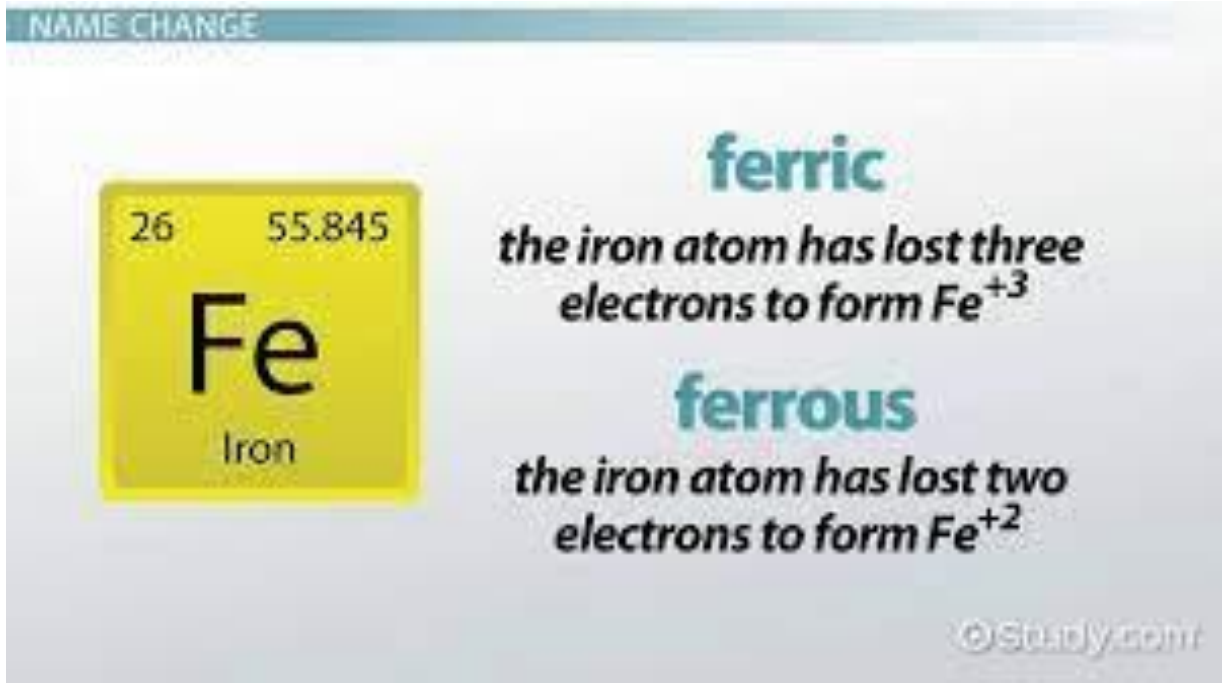
- Low blood iron (hypoferremia) caused by hepcidin is a common physiological response to infection – it acts to deny microbes access to the iron they need to grow and spread, potentially slowing the progress of infection.
- However, the new work from the Drakesmith group suggests there may be a price to pay for this response: the T-cells and B-cells that make up the adaptive immune response to infection are also denied access to iron. If the inhibition of adaptive immunity by hepcidin is severe enough, then while the short-term 'battle for iron' may be won by the host's fast hepcidin response, the 'war' might be lost because long-term immune protection is not achieved.



Forms of iron

Which form of iron is best absorbed ferrous or ferric?

- In general, ferrous iron, especially the more soluble compounds such as ferrous citrate or ferrous ascorbate, is more easily absorbed than the ferric compounds, which must be reduced from Fe3+ to Fe2+ before they can be absorbed. The absorption of most dietary iron depends heavily on the physical state of the iron atom.
- Ferrous gluconate is usually sold in liquid form, and some clinical studies have shown that it is better absorbed than ferrous sulfate tablets. However, ferrous gluconate contains less elemental iron than ferrous sulfate, so a greater dosage may be needed to correct a deficiency.



Iron forms

Example Ferrous sulphate (inorganic iron) – undesirable

Iron fumarate/citrate(organic iron) – desirable

The efficiency with which iron is absorbed depends to a large extent on the physico-chemical form of the iron

Supplemental Constituents-

Ligands such as ascorbic acid, malic acid, citric acid, fructose and amino acids form soluble monomeric complexes with iron thus preventing precipitation and polymerisation, therefore promoting its absorption.

- Chelating agents in the diet such as phosphates, polyphenols, oxalates, carbonates and phytates have an adverse effect on bioavailability.
- Competitive antagonism between similar cations for uptake into the mucosal cells has been identified.
- Dietary factors that inhibit gut secretions and intestinal transit time affect bio-availability of iron.
- Iron bio-availability is reduced – through laxatives, antacids and sedatives.

Dealing with the client

Preformed, organic mineral ligands

Advantages

- Require little or no acidification
- Higher bio-availability
- Bio-active
- Energy bio-efficiency sparing
- Cellular, tissue and enzymic incorporation

All above factors address the following criteria

- Correction of cellular deficiency
- Correction of enzymic insufficiency
- Repletion of serum
- Small amounts required
- Less stress to organism
- Smaller dosages = lower toxicity ratio

Dealing with the client

- Using individual pharmaceutical doses of a nutrient can upset the balance of other nutrients or cause other problems.
- The body is not used to isolates, may not absorb them, and may consider them toxic.
- The body prefers its vitamins and minerals bound to food -in their natural form
- So advisable to allow the body to absorb nutrients in their natural state with their cofactors i.e., with a variety of natural substances found in foods which enable natural absorption and biological advantage
- Bionutri use plants which contain organic sources of minerals and cofactors or use organic bonds such as ascorbates, citrates, gluconates and malates for individual minerals combined with co-factors.

Ferrolactin

- People who get little or no haem iron in their diet are at an increased risk of iron deficiency.
- Most dietary iron is in the non-haem form found in both animals and plants. Unfortunately, non-haem iron has a slightly different composition to haem iron.
- Non-haem iron is present mainly as ferric iron in food, it must be reduced to the ferrous form. Therefore, it's not as easily absorbed and usually needs an acidic component to help convert it to the haem form.
- Its absorption can be enhanced with vitamin C in part by acting as a weak chelator (sequestering iron) to help to solubilise it in the intestine. Vitamin C has also been shown to improve iron mobilisation but is decreased by inhibiting factors in the diet such as plant compounds like phytate.

Ferrolactin

Why Ferrolactin?

- Ferrolactin contains two highly bioavailable forms of iron, iron citrate and iron fumarate
- Ferrolactin combines the ferrous salts of iron, methylated forms of vitamin B12 and folate as well as vitamin C to enhance iron's absorption.
- Different forms of iron in supplements contain varying amounts of elemental iron. Ferrous iron is easily absorbed by the small intestine and is usually seen as the best approach to treating iron deficiency and anaemia. Ferrous fumarate is a good source providing 33% elemental iron by weight as compared to other forms such as sulphate or gluconate.
- Some people may experience gastric discomfort or constipation with less well absorbed forms of iron and some forms of iron including non-haem iron may be less well absorbed when taken with food. Ferrolactin negates these factors.

Ferrolactin

- Duodenal pH is important for the absorption of iron. Ascorbate and citrate increase iron uptake in part by acting as weak chelators to help to solubilise the metal in the duodenum. Iron is readily transferred from these compounds into the mucosal lining cells.
- Ascorbic acid will overcome the negative effect on iron absorption of inhibitors, which include phytate, polyphenols, and the calcium and proteins in milk products and will increase the absorption of both dietary and supplemental iron.
- Folic acid increases red blood cell development and Vitamin B12 supports growth and blood cell production. Studies indicate that combining iron with several B vitamins and vitamin C is superior to using these nutrients individually.

Ferrolactin

- Unlike many supplements Ferrolactin contains beneficial lactic acid forming bacteria which may help with low iron bioavailability from inhibiting factors in the diet, such as phytate and phenolic compounds.
- Increased non-haem iron absorption is due not only to an effect of lactic acid production, but also a specific effect of the lactic acid bacteria which additionally enhance digestion and tolerance within the digestive tract.
- Lactic acid-forming bacteria are thought to increase dietary iron bioavailability through several mechanisms including reducing intestinal pH, shifts in gut microbiota metabolism and metabolite formation.

Ferrolactin

Bionutri®

• Combining iron with bacteria helps to reduce gastric irritation and utilises lower doses of iron but with higher absorption rates. Lactobacillus plantarum was originally isolated from sourdough bread and found in kimchi, sauerkraut, yogurt, cheese, and cultured vegetables. A transient bacteria found in saliva and throughout the GI tract, it grows, functions and ferments in both aerobic and anaerobic environments and further enhances the absorption of iron.

• The transient lactic acid bacterium Lactococcus lactis is widely used in the fermentation of food especially cheese, yoghurt, sauerkraut and is found in the GI tract of humans, babies and in breast milk. L. lactis is one of the beneficial bacteria that produces folate.

The lactic acid bacteria in Ferrolactin are protected from the influence of iron while encapsulated so very stable.

Bionutri®

Nettle Plus

Nettle Plus

Nettle, Dandelion, Dong Quai & Hibiscus with Blueberry, Alpha Lipoic Acid & Vitaflavan.

30 and 90 Capsules

Aquasol-unique instant pure herb teas

- We source the best quality organic herbs around the world, fair trading with skilled farmers who maintain the complexity and full integrity of the herb.
- Superfine grade, smaller granules
- Whole herb is consumed-zero waste
- Liquids, hot and cold, food or yogurts

aquasol

- More bioactive and bioavailable after testing-higher than normal herbal powder
- Better than standardised herbs which may concentrate part of the herb making it more potent and not all of it so not concentrated materials without the wider part
- Aquasol overcomes this by through grinding has a much greater surface area, normally herbs may be 11-25 microns when ours are many times greater-250 microns

aquasol

- Elderflower
- Green Tea
- Turmeric Latte
- Hibiscus Flower
- White Ginseng Root
- Red Ginseng Coffee
- Ginger Root
- Gota Kola
- Camu Camu
- Ginkgo Biloba
- Artichoke Leaf
- Dandelion Root coffee
- Lemon Balm Leaf
- Echinacea Root
- Spearmint Leaf
- Ashwagandha
- Roast Chicory
- Nettle Root
- Passionflower
- Chamomile Flowers

aquasol


aquasol
Dandelion
Coffee
Filter Blend
Pure roasted Dandelion Roots

aquasol


aquasol
INSTANT
Dandelion
Coffee
100% Whole herb
Roast and Ground
Makes a delicious instant coffee alternative
Just add to boiling water or hot milk and stir


aquasol
INSTANT
Dandelion
Coffee
100% Whole herb
Roast and Ground
Makes a delicious instant coffee alternative
Just add to boiling water or hot milk and stir

Vegan/vegetarian recipe

- In a large bowl, combine cooked beans or lentils with diced fresh tomatoes, raw baby spinach, pumpkin seeds or cashews, and raisins or dried chopped apricots. Drizzle with a simple lemon vinaigrette made from 2 tablespoons lemon juice, ½ teaspoon Dijon mustard, 3 tablespoons olive oil, and 1 teaspoon of honey (optional).
- Use vitamin C rich foods

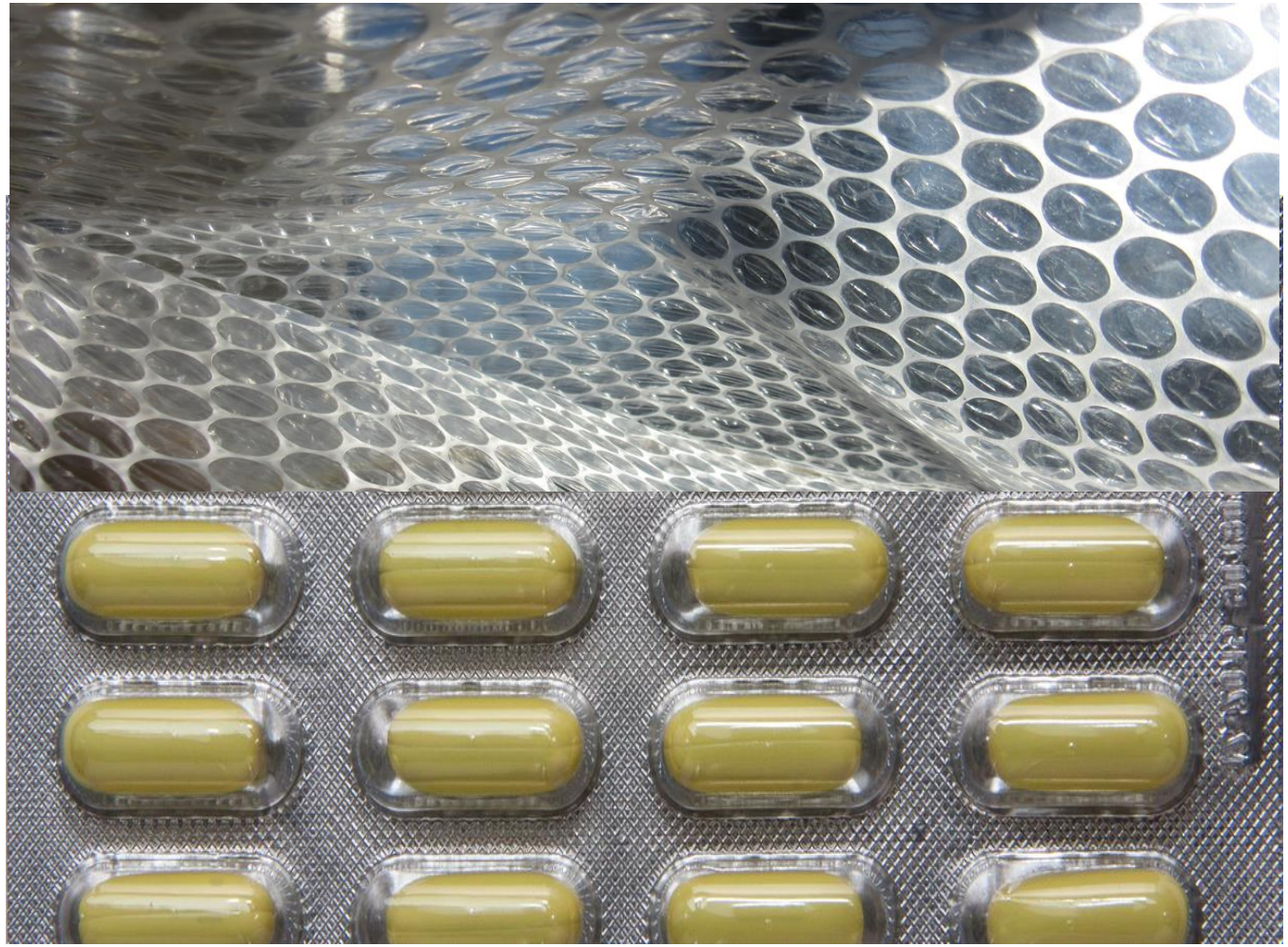
About Bionutri

- Products designed for specific straightforward solutions for daily supplementation
- Range is compact and comprehensive
- We draw on 25 years of experience in food supplement manufacture to create a system approach that simplifies your prescribing task
- Eases client management
- Improves compliance
- Cost effective

About Bionutri

- We take responsibility for much of our own procurement
- Of particular importance in dealing with botanicals and insuring the best constituent value of the end product

About Bionutri



Blister packing--our triplex foil sachets ensure the integrity of our products from the first to the last.
We have a specific policy in place to blister pack products containing volatile oils, probiotics, lipid nutrients or aromatic herbs

Practitioner Support

- Website for your clients to browse www.bionutri.co.uk and a password protected practitioner page where you have access to catalogue pages and webinar listings for online registration (for webinars contact adel@bionutri.co.uk).
- CPD opportunities to join the hundreds of healthcare professionals that visit our free weekly 11-12 Wednesday webinar. A wide range of topics covered plus interactive Q and A. Extensive back catalogue of recorded CPD webinars available. Sign up at www.bionutri.co.uk/practitioner-signup-form
- We are also on Facebook/Bionutri for practitioners/Instagram and LinkedIn (Bionutri)
- Professional Product catalogue
- Technical Support by Zoom/phone or email-Sue McGarrigle ND (suem@bionutri.co.uk), Edward Joy Herbalist (ed@bionutri.co.uk), Rosie Rayner ND rosie@bionutri.co.uk
- Product training-one to one or small groups by telephone or Zoom/Teams.
- Kinesiology samples
- Samples for sensitive clients

Product sources

Practitioner/Patient

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The Natural Dispensary

Ireland-Maria Cadogan at NT Supplies-
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