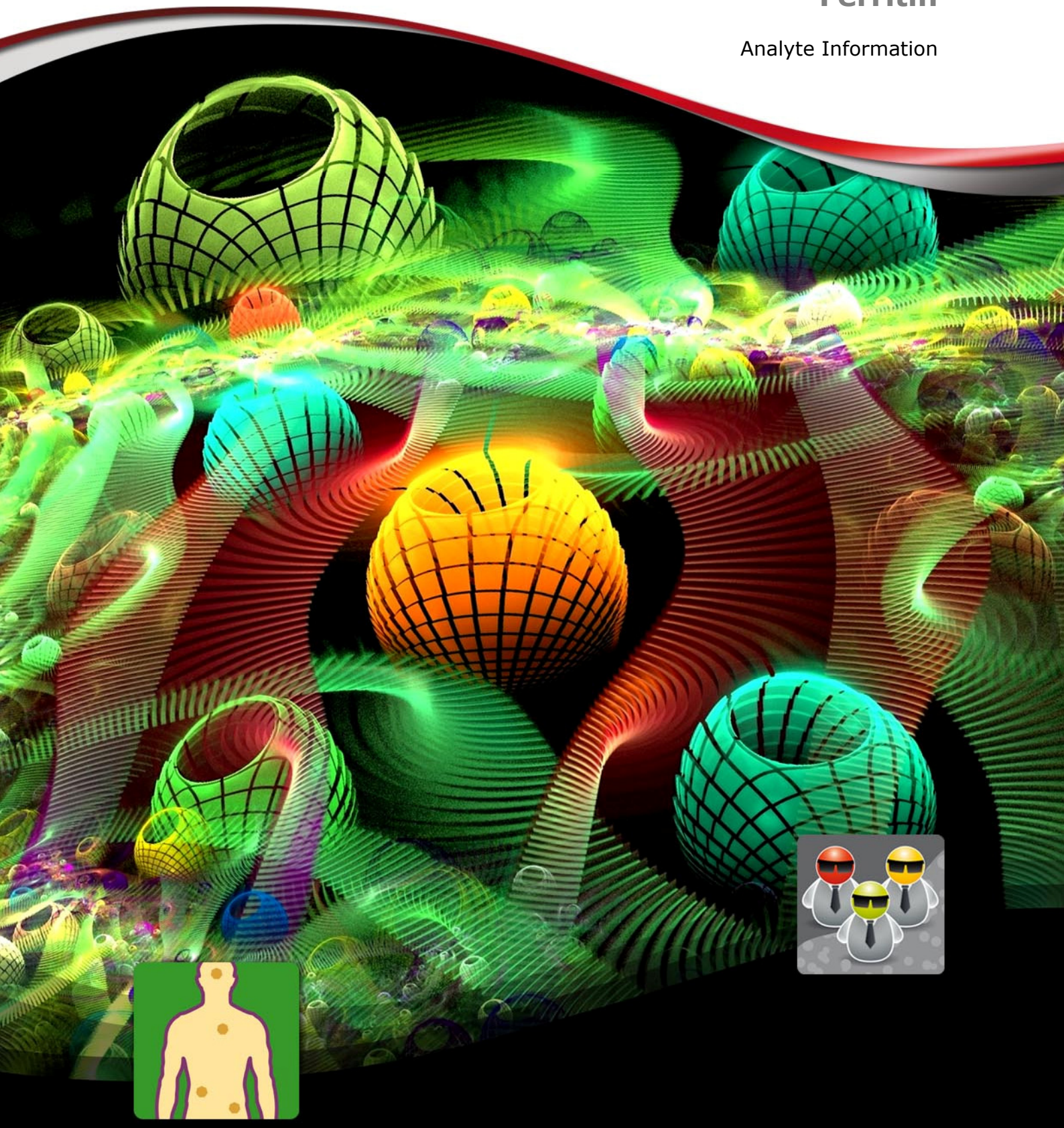
Specialty

Ferritin

Analyte Information



Ferritin

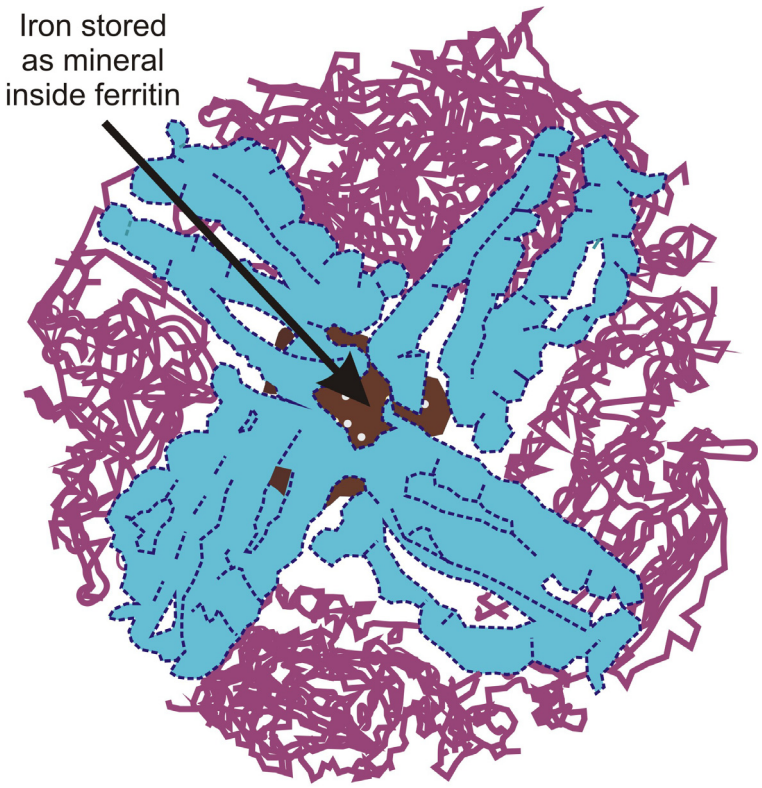
Introduction

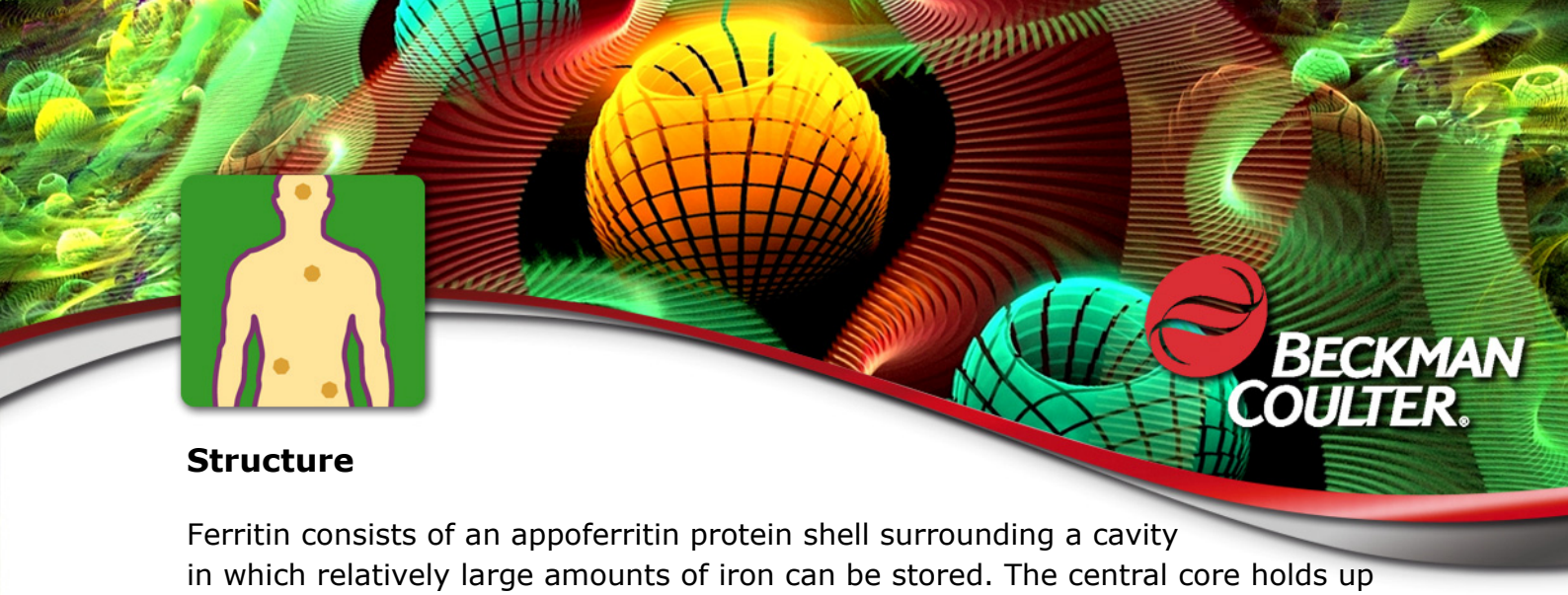
Ferritin is an intracellular iron-binding protein that stores iron and releases it in a controlled fashion. The protein is produced by almost all living organisms, including bacteria and algae. In humans, it acts as a buffer against iron deficiency and iron overload[1].

Most of the iron stored in the body is bound to ferritin. Ferritin is found in almost all tissues of the body, but especially in hepatocytes in the liver, reticuloendothelial cells in the spleen, skeletal tissue, muscles and bone marrow. The amount of ferritin in the blood correlates well with total iron content in the body.

Ferritin (Fig.1) has a molecular weight of 450 kDa.

Fig.1: Ferritin[1]





Structure

Ferritin consists of an appoferritin protein shell surrounding a cavity in which relatively large amounts of iron can be stored. The central core holds up to 4500 iron ions in the form of ferric hydroxyphosphate.

The appoferritin shell is composed of 24 subunits, which are either light (L) or heavy (H) ferritin chains. The relative proportion of light and heavy chains differs from tissue to tissue. L-rich ferritin is found in the spleen, liver and placenta. H-rich ferritin is found in the heart and in red blood cells.

Physiological Function

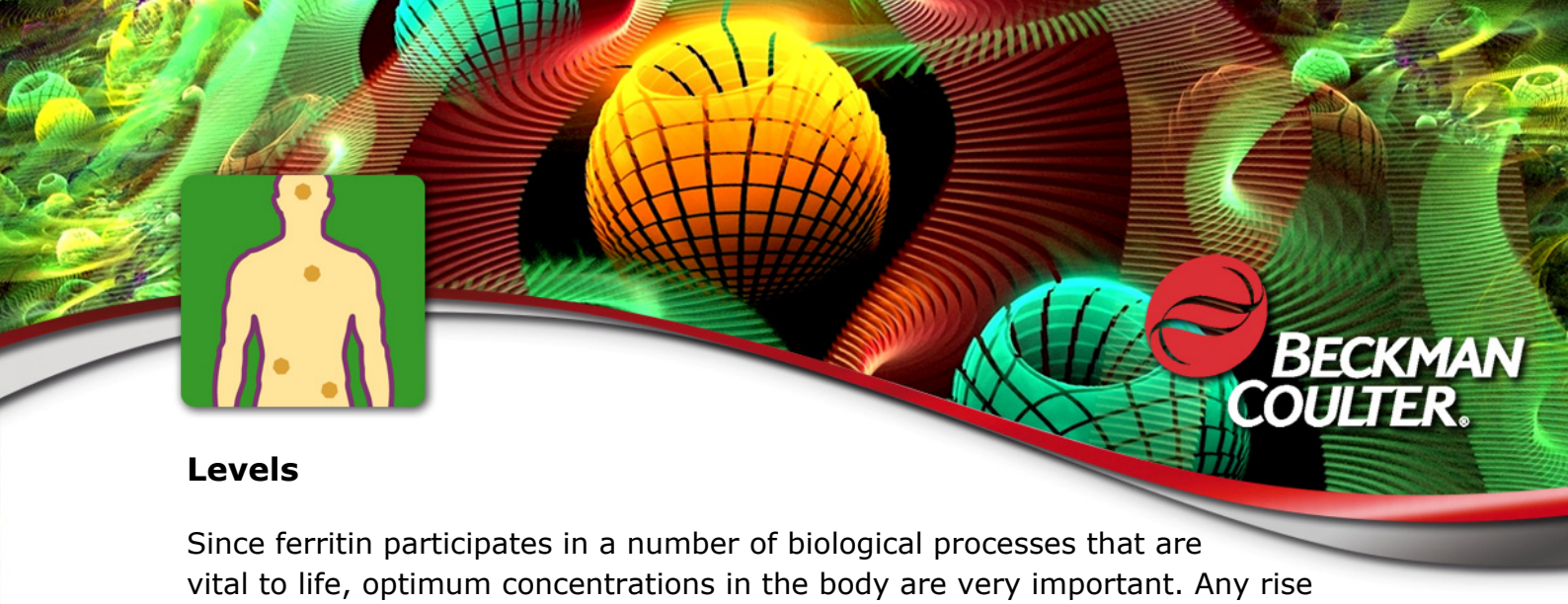
Ferritin is the primary protein responsible for iron storage. In the physiology of iron metabolism, ferritin plays the important role of maintaining iron in a soluble, nontoxic and biologically useful form. It isolates and stores vast quantities of iron and acts as a buffer against normal physiological variation in the iron requirements of tissues[2].

The presence of iron itself is a major trigger for the production of ferritin[3] from apoferritin. When needed, iron molecules are released from the apoferritin shell and bind to transferrin, the circulating plasma protein that transports iron to erythropoietic cells.

Iron plays a crucial role in many metabolic processes. The average adult human body contains between 3 – 5 g of iron, two-thirds of which is present in the oxygen-carrying molecule hemoglobin.

The release of iron from ferritin is probably nonenzymatic and may involve reduction by reduced flavin mononucleotide or other reducing substances. The resultant Fe^{2+} leaves the core crystal and diffuses out through a pore in the ferritin shell.

The complex consisting of aggregated and partially deproteinized ferritin is called hemosiderin. In contrast to ferritin, hemosiderin is insoluble in aqueous solutions. Iron is only slowly released from hemosiderin, possibly because it occurs in relatively large aggregates and therefore has a much smaller surface ratio.



Levels

Since ferritin participates in a number of biological processes that are vital to life, optimum concentrations in the body are very important. Any rise or fall in ferritin level may result in numerous health issues.

There is a good correlation between the amount of serum ferritin and the stock of iron in the body.

Significant differences between men and women in ferritin concentrations are consistent with differences in iron storage. Values of ferritin rise with age (Fig.2). In pre-menopausal women, ferritin levels may be influenced by the lack of iron cased by the menstrual bleeding. Therefore, mean concentrations are similar in older women and men.

Serum ferritin concentrations in children are generally lower than in adults.

In patients with an iron deficiency, serum ferritin concentrations are less than 8 – 12 ng/mL. A reduction in the level of reticuloendothelial stores is the most common cause of low serum ferritin concentration.

An iron-depleted state, with a decreased serum ferritin value, is quite common in menstruating or reproductively active females and in children.

A high serum ferritin value is seen in instances of hemochromatosis and other iron-overload states, as well as in acute hepatitis, Gaucher's disease[4] (in which fatty substances accumulate in certain organs, e.g., liver, spleen, kidneys, lung, brain), malignancies and chronic inflammatory disorders.

Ferritin is an acute-phase reactant and thus may be elevated in people with inflammation, liver disease, chronic infection, autoimmune disorders and some types of cancer. With active inflammation, serum levels of ferritin can rise sharply without any corresponding change in total iron stores.

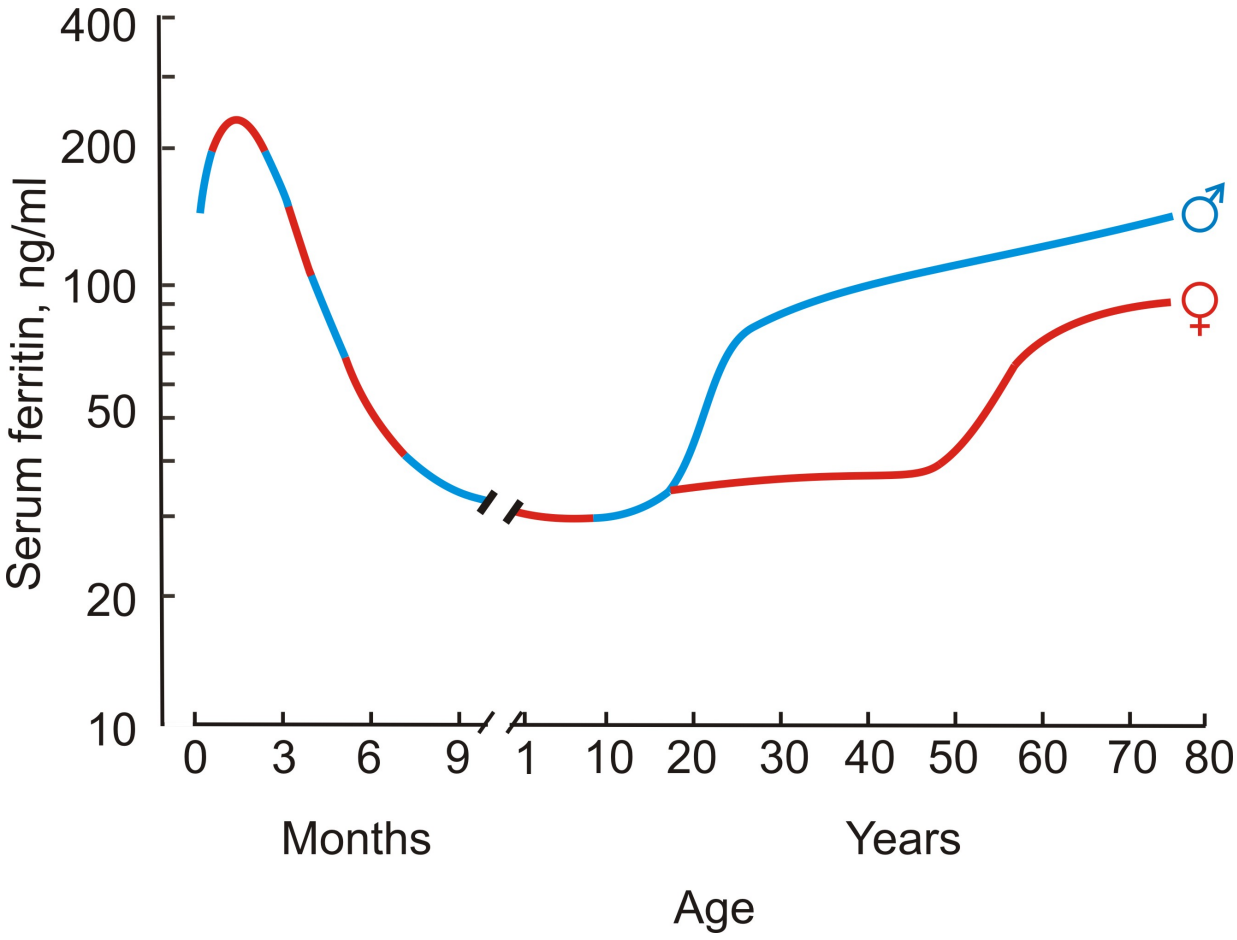
A normal serum ferritin value cannot be used to exclude iron deficiency if hepatic or malignant conditions are present.

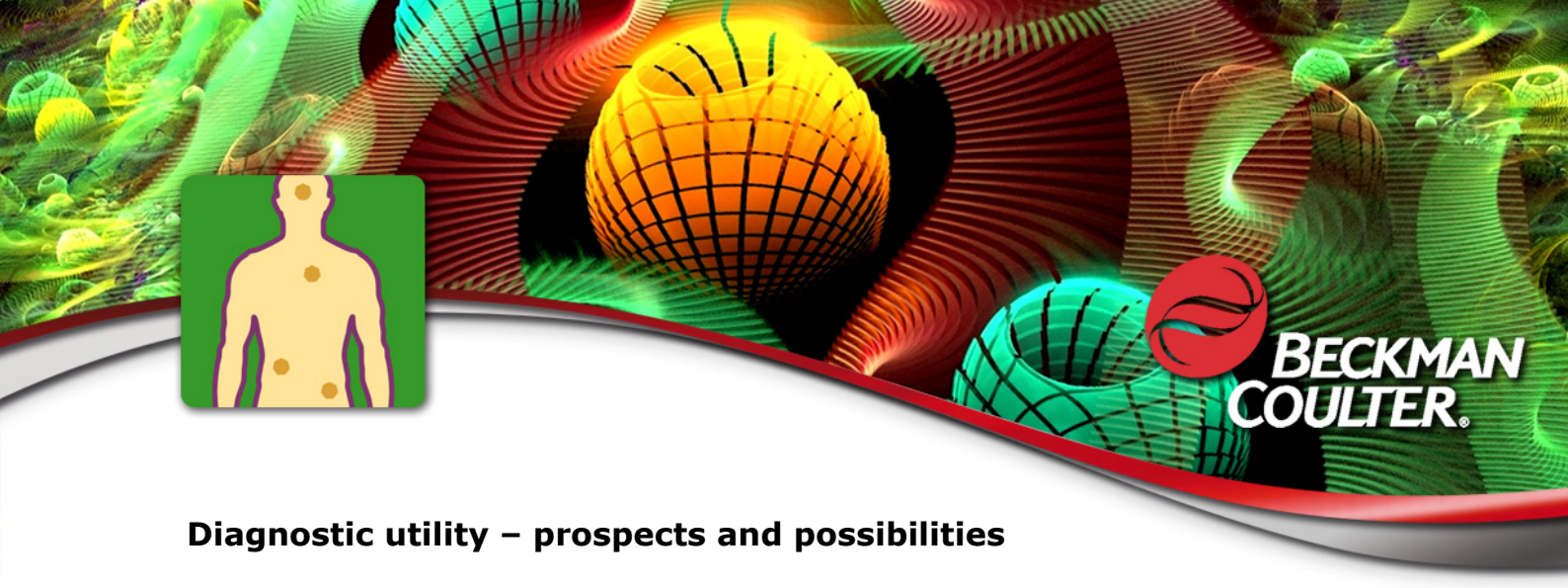
Typical ferritin levels[5] in children and in adult males and females are given in Table 1. For each assay, the relevant reference values are shown in the appropriate Instructions for Use (IFU).

Table 1: Typical ferritin levels

Specimen (serum)	**Reference interval** (ng/mL)
Newborn	25 – 200
1 month:	200 – 600
2 – 5 months:	50 – 200
0.5 – 15 years	7 – 140
Adult	
male:	20 – 250
female:	10 – 120

Fig.2: Changes in serum ferritin concentrations in healthy normal subjects[2]



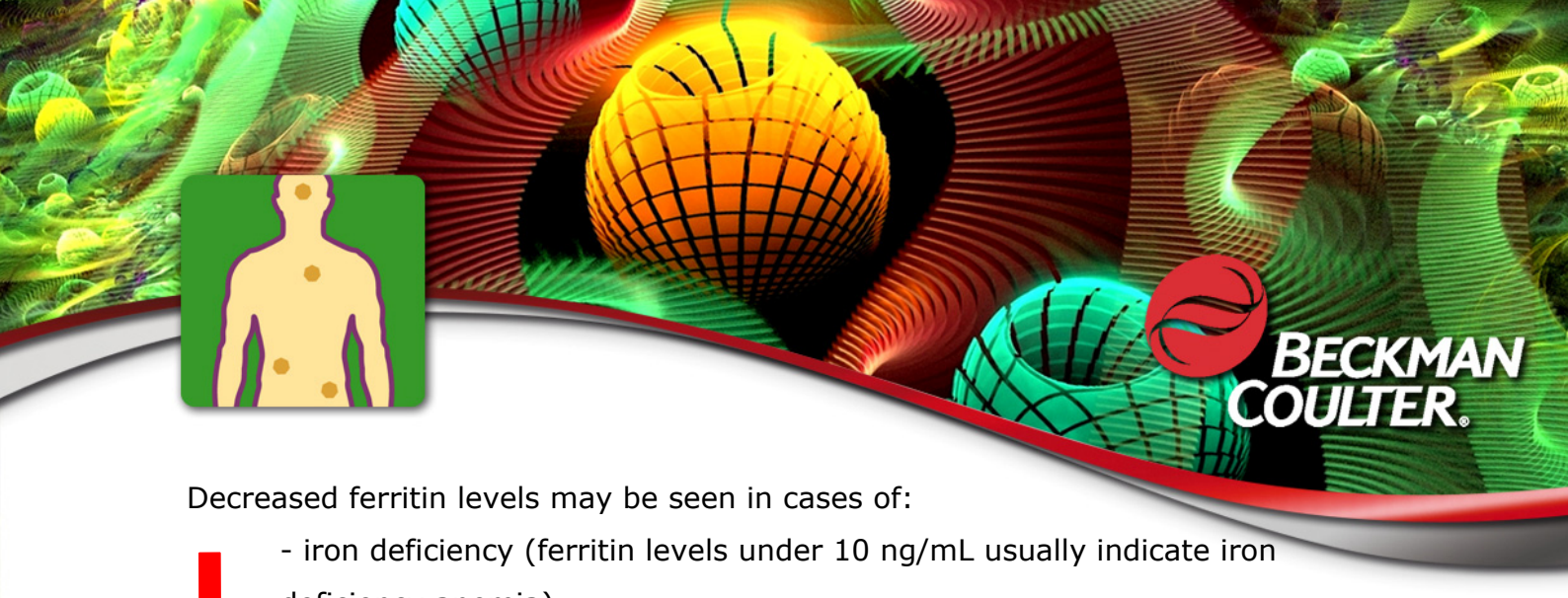


Diagnostic utility – prospects and possibilities

Ferritin is present in the blood in very low concentrations.
Although it is an acute-phase protein, under normal conditions it roughly reflects total iron content in the body.

Elevated ferritin levels may be seen in cases of:

- hemochromatosis (primary/hereditary hemochromatosis)
- fasting or inanition (anorexia)
- thalassemia
- sideroblastic anemia
- leukemia
- Hodgkin's disease
- neoplasia
- malignant diseases (breast, pancreatic, uterine and gastric carcinoma)
- patients receiving frequent blood transfusion (secondary hemochromatosis)
- patients with chronic renal failure and hemodialysis (iron overload)
- inflammatory disease (e.g., pulmonary infections, osteomyelitis, chronic urinary tract infections, rheumatoid arthritis)
- certain acute and chronic hepatocellular diseases (e.g., alcoholic and inflammatory liver disease)
- Gaucher's disease



Decreased ferritin levels may be seen in cases of:

- iron deficiency (ferritin levels under 10 ng/mL usually indicate iron deficiency anemia)
- patients with chronic disease such as rheumatoid arthritis, who may have hypochromic microcytic anemia
- pregnancy
- patients with nephrotoxic or malabsorption syndromes
- patients undergoing hemodialysis (loss of iron)

Elevated levels due to inflammatory conditions may mask diagnostically low results.

Diagnostic utility – Practical applications

Examination of iron stores in the body – iron overload

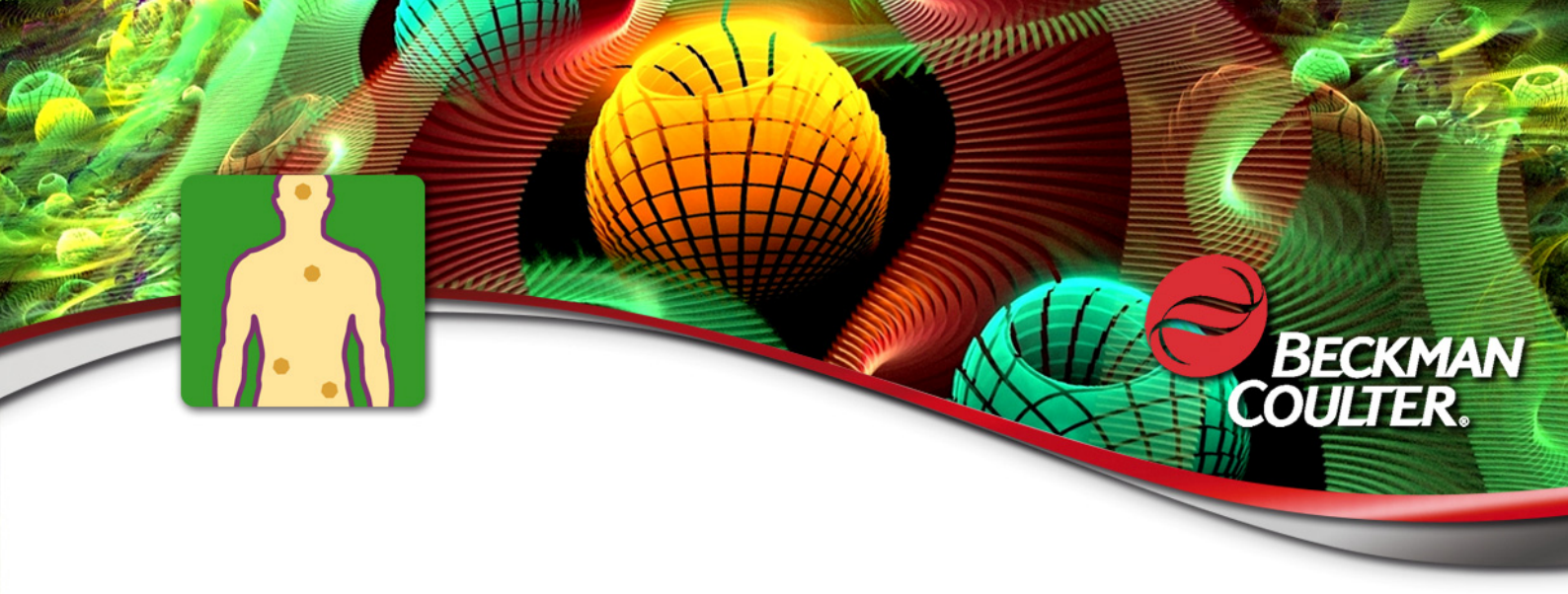
A ferritin level test may be ordered when iron overload is suspected. Symptoms of iron overload will vary from person to person and tend to worsen over time. They are due to the accumulation of iron in the blood and in tissues. To confirm the presence of iron overload, other tests (e.g., iron level determination, total iron binding capacity [TIBC], genetic tests for hereditary hemochromatosis) may be ordered as well.

In patients with hereditary/primary hemochromatosis, the rate of intestinal iron absorption is accelerated. Iron is deposited in various tissues.

Secondary hemochromatosis is caused by excessive blood transfusions in which iron accumulates in the organs.

An increase in iron deposits has been observed in patients with beta- thalassemia who have undergone splenectomy.

Determination of ferritin is very useful in all the above-mentioned conditions.



Examination of iron stores in the body – iron deficiency

Plasma ferritin concentrations decline very early in the development of iron deficiency, long before changes are observed in blood hemoglobin concentration, red blood cell size or serum iron concentration. Thus, measurement of serum ferritin levels can serve as a very sensitive indicator of iron deficiency in cases that are not complicated by another concurrent disease.

The ferritin test may be indicated, along with other iron tests, when a routine complete blood count (CBC) shows that a person's hemoglobin and hematocrit levels are low and that their red blood cells are smaller (microcytic) and paler (hypochromic) than normal. This may suggest iron deficiency anemia even if other clinical symptoms have not yet developed.

Early-stage iron deficiency does not usually provoke any physical effects at all. If a person is otherwise healthy, symptoms will seldom appear before blood hemoglobin drops below a certain level (10 g/dL).

As iron stores continue to be depleted, patients may experience shortness of breath, ringing in the ears (tinnitus), drowsiness and irritability. If the anemia progresses in severity, chest pain, headaches, leg pains, shock and even heart failure may occur. Children may develop learning (cognitive) disabilities. In addition to the general symptoms of anemia, there are certain symptoms that are characteristic of iron deficiency; these include pica (cravings for specific substances, such as licorice, chalk, dirt or clay), a burning sensation in the tongue or a smooth tongue, sores at the corners of the mouth and spoon-shaped finger- and toenails.

Ferritin levels are often evaluated in conjunction with other iron tests. A summary of the changes in iron tests seen in various diseases affecting iron status is shown in Table 2.

Table 2: Summary of iron tests in various diseases

Disease	Ferritin	Iron	TIBC/ transferrin	UIBC	% transferrin saturation
Iron deficiency	↓	↓	↑	↑	↓
Hemochromatosis	↑	↑	↓	↓	↑
Chronic illness	**Normal/↑**	↓	↓	Normal/↓	↓
Hemolytic anemia	↑	↑	Normal/↓	Normal/↓	↑
Sideroblastic anemia	↑	Normal/↑	Normal/↓	Normal/↓	↑
Iron poisoning	**Normal**	↑	↓	↓	↑

TIBC: Total iron-binding capacity

UIBC: Unsaturated iron-binding capacity

References

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