



IRON

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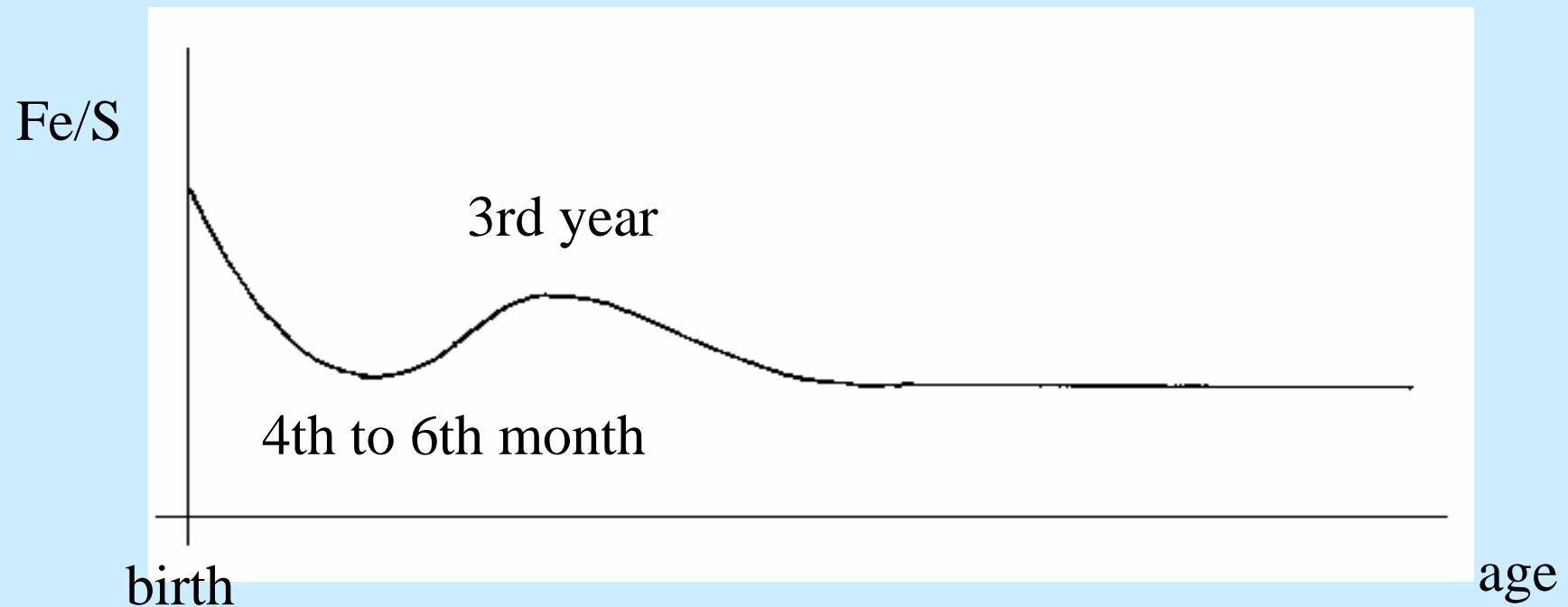
Fe²⁺, Fe³⁺

- **The total iron content of the adult body:
about 4 g in males
2.5 g in females**
- **Daily intake 10 - 30 mg, absorption about 10%**
- **Daily loss about 1 mg**

SERUM IRON CONCENTRATION

newborns	9 - 36 $\mu\text{mol/l}$	• adult men 12 - 27 $\mu\text{mol/l}$
sucklings	4 - 28 $\mu\text{mol/l}$	• women 10 - 24 $\mu\text{mol/l}$
children	9 - 22 $\mu\text{mol/l}$	• 560 - 1500 $\mu\text{g/l}$

SERUM IRON CONCENTRATION DURING LIFE



circadian variation with maximal values in the morning

IRON ABSORPTION

- **duodenum, jejunum**
- ferric (Fe^{3+}) ions must be converted to ferrous (Fe^{2+}) - presence of gastric **HCl is needed**
- ascorbic acid, alcohol and other **reducing substances**, HCl, intrinsic factor - **facilitate absorption**
- phosphates, phytic acid, oxalates, Co, Mn, Ni, Zn, chelates - **decrease absorption**
- **regulated by the capacity of ferritin of the enterocytes** (the amount sequestered within the cells depends on the body stores of iron)

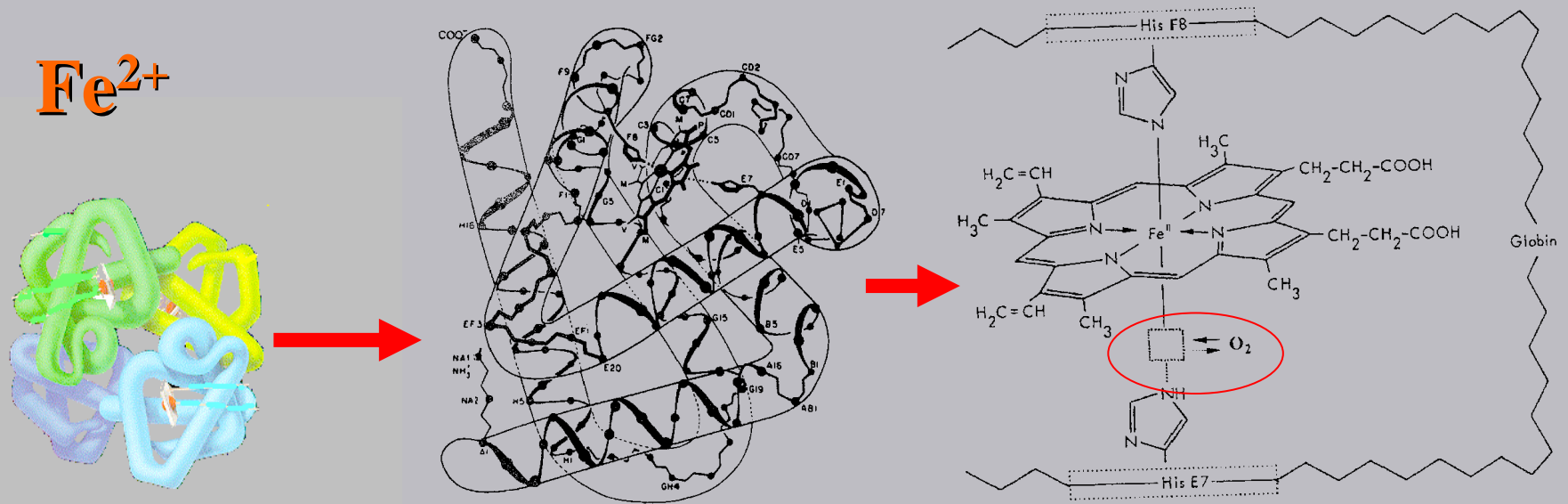
IRON LOSS

- **faeces (0.6 mg/d): non-absorbed (90%), bile, and shed mucosal iron**
- **skin desquamation (0.1 mg/d)**
- **perspiration (0.1 mg/d)**
- **urine (0.1 mg/d)**
- **menstruation (0.4 mg/d)**

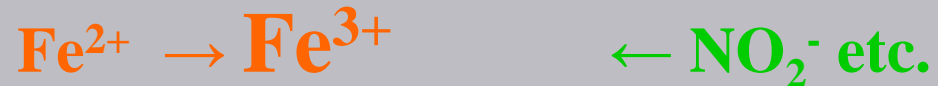
IRON IN ORGANISM

- **Functional:** haemoglobin (65-70%), myoglobin (10%), cytochromes, FeS-proteins, enzymes
- **Transport:** transferrin (0.15%)
- **Storage proteins (20%):** ferritin
haemosiderin

HAEMOGLOBIN



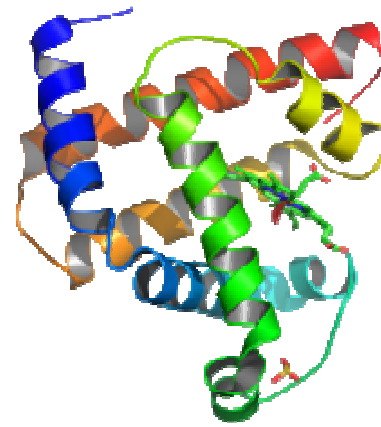
METHAEMOGLOBIN



HbM (HisF8 \rightarrow Tyr), deficiency of methaemoglobinreductase or G6PD

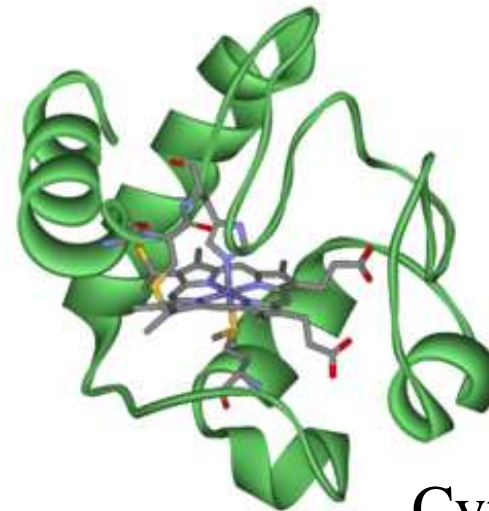
MYOGLOBIN

- Fe^{2+}
- 1 heme and 1 globin chain
- \uparrow affinity for O_2 than Hb



CYTOCHROMES

- heme metalloproteins of respiratory chain
- $\text{Fe}^{3+} \leftrightarrow \text{Fe}^{2+}$



Cyt c

DIAGNOSTIC TESTS OF IRON STATUS

- **HAEMATOLOGICAL**
 - **haemoglobin**
 - **red cell indices**
 - **examinations of bone marrow**
- **BIOCHEMICAL**

BIOCHEMICAL TESTS OF IRON STATUS

- **SERUM IRON**
- **TRANSFERRIN**
- **TRANSFERRIN RECEPTORS**
- **FERRITIN**

SERUM IRON

- **normal values (adults) in males 12 - 27 $\mu\text{mol/l}$
in females 10 - 24 $\mu\text{mol/l}$**
- **is of little value in the investigation of iron metabolism (a fall is a late feature of iron deficiency)**
- **\downarrow : iron deficiency, infection, chronic inflammation, malignancies, blood loss**
- **\uparrow : haemolytic anemia, iron poisoning, hepatitis, iron overload**

TRANSFERRIN

- **transport protein for Fe^{3+} , β_1 -globulin from liver**
- **normal serum concentration 2-4 g/l = 23 – 45 $\mu\text{mol/l}$**
- **\downarrow : atransferrinemia (hereditary dis.), hypotransferrinemia (exsudative enteropathy, nefrotic sy), protein malnutrition, chronic liver disease, inflammation (negative acute phase protein), anemia**
- **\uparrow : Fe/S \uparrow : acute hepatitis, cirrhosis, hemolytic anemia
Fe/S \downarrow : iron deficiency, pregnancy**

TRANSFERRIN

- normally only 30 - 40% of the iron binding sites of transferrin (**total iron-binding capacity – TIBC**) are occupied by Fe^{3+} = **transferrin saturation**, the rest is serum **unsaturated iron binding capacity (UIBC)**
- total iron binding capacity (TIBC) is the maximal iron concentration, that serum (principally transferrin) can bind

Normal values and calculations

- **TIBC ($\mu\text{mol/l}$) = transferin/S ($\mu\text{mol/l}$) x 2**
= 46 - 90 $\mu\text{mol/l}$
- **TIBC (mg/l) = transferin/S (g/l) x 2 x $\frac{56}{79\ 570}$**
= 2.8 – 5.6 mg/l
- **saturation [%] = $\frac{\text{Fe/S } [\mu\text{mol/l}]}{\text{transferin/S } [\text{g/l}]} \times 4,41$**
= 15 – 45%

- **TIBC**

- ↓: **hemolytic anemia, hemochromatosis, cirrhosis**
- ↑: **iron deficiency**

- **Saturation**

- ↓: **iron deficiency**
- ↑: **iron abundance**

TRANSFERRIN RECEPTORS

sTfR

- **estimation of amount released into circulation is the most sensitive indicator of cell iron deficiency**
- **↑: iron deficiency**
- **↓: IC abundance of iron**
- **sTfR /S = 0.85 – 2.29 mg/l**

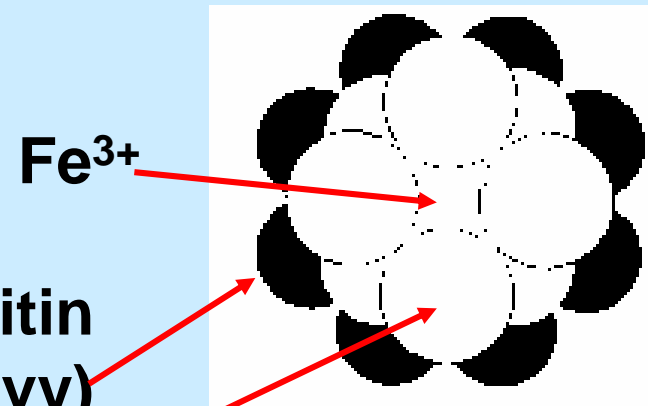
Receptor index

- **sTfR / log ferritin**
- **differentiation of iron deficiency ↑**
- **deficiency in malignancies and chronic inflammations ↓**

FERRITIN

- **Fe³⁺ storage protein found in nearly all cells of the body.**
- **In the liver and in the macrophage system, it provides a reserve of iron readily available for formation of haemoglobin and other iron-containing proteins.**
- **tissue specific isoferritins**

protein capsule – apoferritin
24 subunits, type H (heavy)
L (light)



FERRITIN

- **normal serum concentration in males 50 - 710 pmol/l**
- **females 20 - 640 pmol/l**
- **the value indicates the tissue stores of iron**
- **↓: iron deficiency**
- **↑: iron overload, malignancies (non-specific tumor marker), chronic inflammation (acute phase protein)**

Iron in organism

- **! negative consequence – prooxidative effect:**
- **Fenton reaction:**
- $\text{H}_2\text{O}_2 + \text{Fe}^{2+} \rightarrow \text{OH}^- + \cdot\text{OH} + \text{Fe}^{3+}$
- $\text{Fe}^{3+} + \text{O}_2^{\cdot-} \rightarrow \text{Fe}^{2+} + \text{O}_2$

Iron deficiency

- one of the most prevalent disorders of humans, particularly children, young women, and elderly
- **hypochromic mikrocytic anemia**
- due to dietary iron deficiency, chronic blood loss, malignancy or increased requirement of iron in pregnancy, breastfeeding, children or blood donors

Hypochromic mikrocytic anemia

- **Haematological and biochemical findings:**
- **↓ ery, ↓ Hb, ↓ MCV, ↓ MCH, ↓ MCHC**
- **↓ Fe/S**
- **↓ ferritin** – early and sensitive indicator
- **↑ transferrin**
- **↑ TIBC** – late indicator, **↓ transferrin saturation**
- **↑ sTfR** – the most sensitive indicator

Iron overload

- **Haemochromatosis**
- **hereditary** disorder, an inborn error of regulation of iron absorption
- **clinical features:** hepatic cirrhosis, cardiomyopathy, diabetes mellitus, hyperpigmentation and arthritis

- **Hemosiderosis**
- **non-hereditary** disorder; term used to imply iron overload