MEDICAL EDUCATION RESOURCE

Iron Absorption, Transport, Storage and Excretion

Introduction (Iron)

- **Definition of iron in physiology**
  - **Iron = an essential trace mineral** required mainly for **oxygen transport** and **cellular oxidation reactions** (because it forms part of haemoglobin/myoglobin and several oxidase enzymes).
- **Total body iron content**
  - **RBC iron (in Hb) ? ~3 g** (total quantity present in all red cells).
  - **Rest of the body ? ~1–3 g** (tissue iron pool).
  - Whole blood contains **~45–50 mg iron/100 mL**.
- **Distribution in body**
  - **Haemoglobin (major share in blood)**
    - Hb contains **~92–98% of total blood iron**.
  - **Myoglobin**
    - Iron is present as iron-porphyrin in **myoglobin** (muscle oxygen store).
  - **Enzymes**
    - Iron-containing enzymes include **catalase, cytochrome, peroxidase** (tissue oxidation).
  - **Storage form**
    - Stored mainly as **ferritin** (water-soluble) and **haemosiderin** (granular, insoluble).

        - Storage sites: **reticuloendothelial system—especially liver, spleen, bone marrow**.

    - **Transport/other forms**

        - Iron also exists in functional pools like **transferrin, ferritin, haemosiderin**.

- **Importance in oxygen transport**

    - **Hb formation is the primary function of iron.**

    - **Oxygen carriage: 1 g Hb carries ~1.34 mL O?** when fully saturated.

    - **Myoglobin supplies O? to muscle** and acts as an **oxygen store**.

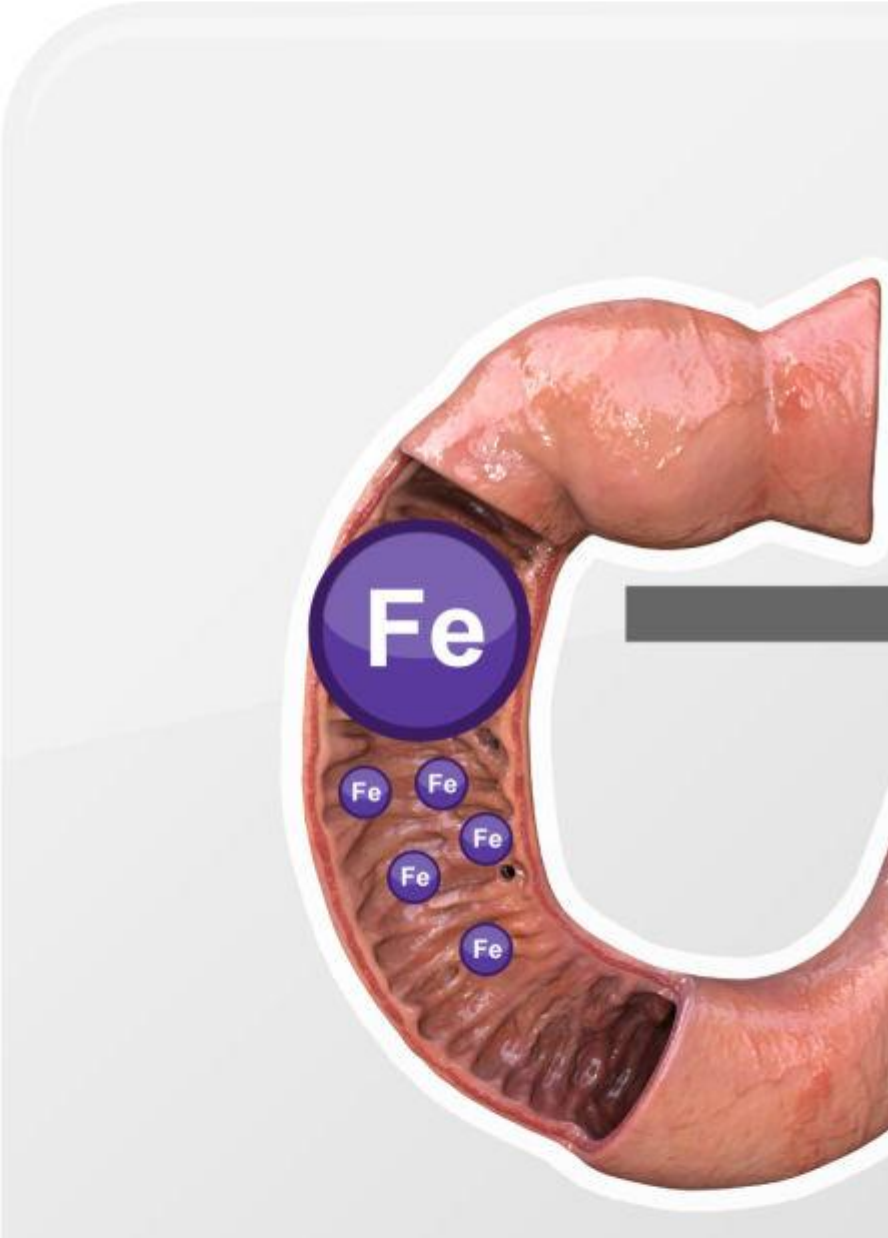
- **Clinical relevance**

    - Body iron is controlled mainly by **regulation of absorption (not excretion)**; excretion is only in traces (urine/bile/faeces).

    - **Iron loss states:** pregnancy, labour, menstrual blood loss ? can predispose to iron deficiency.

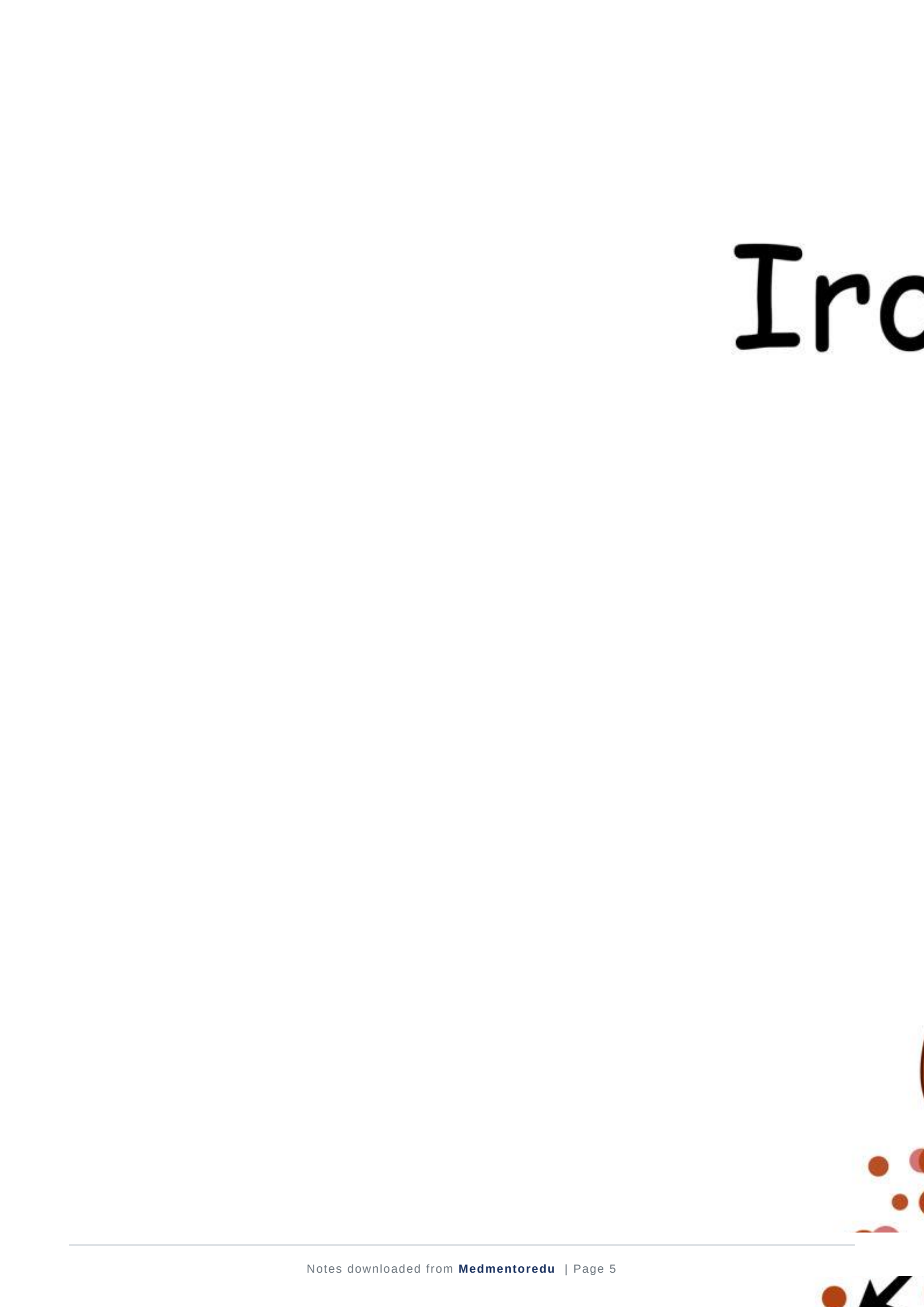
    - If **iron loss exceeds absorption ? Hb falls ? anaemia develops**.

Absorption and Transport (Iron)


Fe
Fe
Fe
Fe
Fe
Fe

https://www.researchgate.net/publication/347798474/figure/fig1/AS%3A1143128121196366 8%401702509136133/Absorption-of-haem-anc

Ir



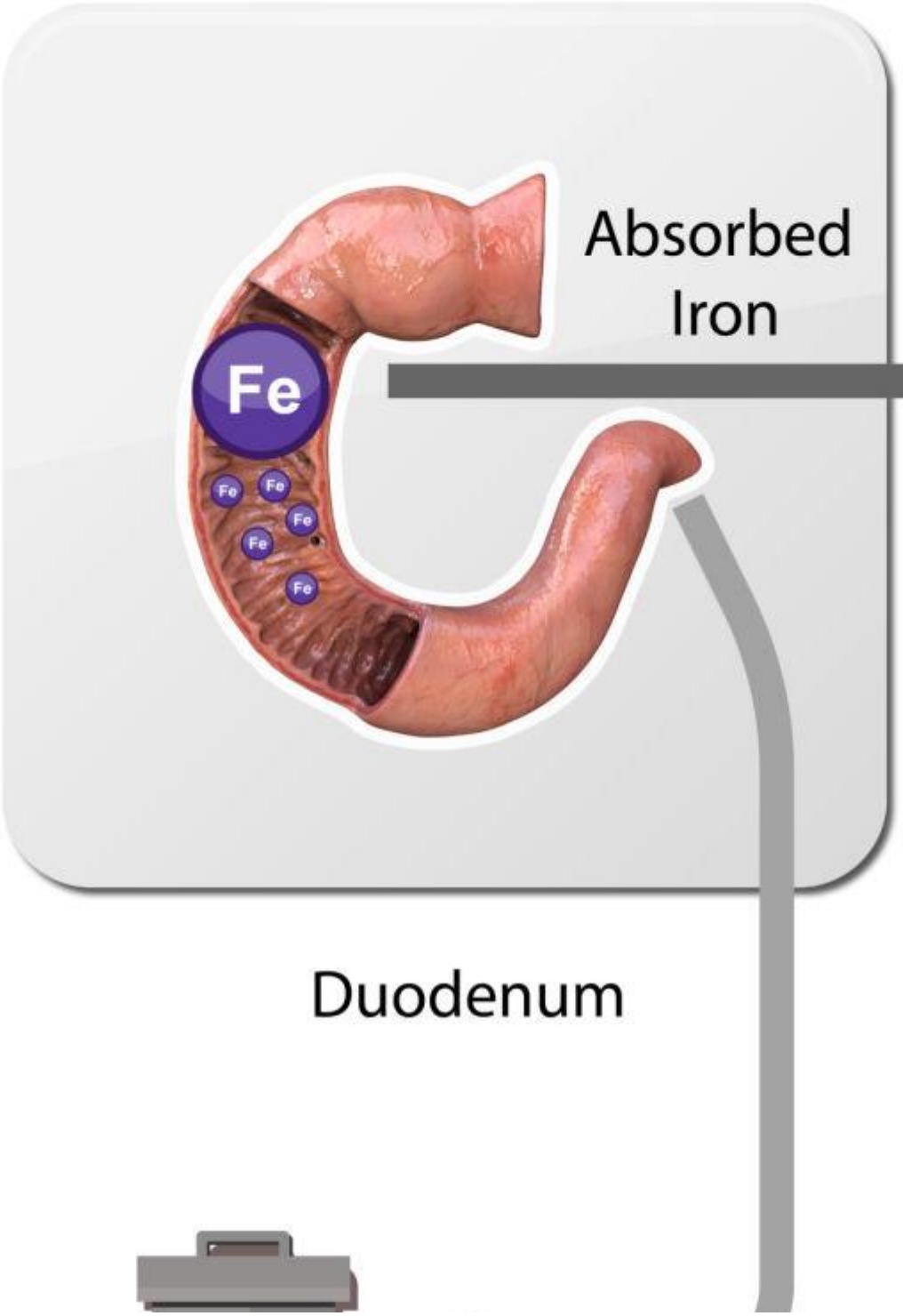
- **Site of absorption**
  - Mainly in the **duodenum and upper jejunum**.
  - Enterocytes of proximal small intestine are specially adapted for iron uptake.
- **Forms of dietary iron**
  - **Heme iron**
    - Present in **animal sources** (meat, liver, fish).
    - Absorbed intact via heme carrier protein.
    - **Better absorbed** (less affected by dietary factors).
  - **Non-heme iron**
    - Present in **plant sources** (green leafy vegetables, cereals, pulses).
    - Usually in **ferric (Fe^{3}?) form**.
    - Must be reduced to **ferrous (Fe^{2}?)** form for absorption.
    - Absorption is **less efficient and more variable**.
- **Factors affecting absorption**
  - Increased by:
    - Iron deficiency state
    - Increased erythropoiesis
    - Pregnancy

        - Vitamin C
    - Decreased by:
        - Phytates (cereals)
        - Oxalates
        - Tannins (tea)
        - Excess calcium
- **Role of gastric acid**
    - Converts **ferric (Fe^{3}?) ? ferrous (Fe^{2}?)** form.
    - Maintains iron in soluble form.
    - Achlorhydria ? ? iron absorption.
- **Role of vitamin C**
    - Reduces **Fe^{3}? ? Fe^{2}?**.
    - Forms soluble complexes with iron.
    - Enhances non-heme iron absorption.
- **Regulation by body iron stores**
    - Low iron stores ? ? absorption.
    - High iron stores ? ? absorption.
    - Regulation occurs mainly at the level of **intestinal mucosa**.
- **Hepcidin regulation (concept)**

- **Hepcidin = hormone produced by liver**.
- High hepcidin:
  - Blocks **ferroportin** (iron exporter) in enterocytes and macrophages.
  - ? iron release into plasma.
- Low hepcidin:
  - ? ferroportin activity.
  - ? iron absorption and release.
- Acts as the **master regulator of iron metabolism**.

- **Transport in plasma**
  - Iron transported in plasma bound to **transferrin**.
  - Each transferrin molecule binds **two Fe^{3}? ions**.
  - Transferrin delivers iron mainly to:
    - Bone marrow (for Hb synthesis)
    - Liver (for storage)
    - Other tissues (for enzymes)

Absorption of Iron


Absorbed
Iron
Fe
Fe
Fe
Fe
Fe
Fe
Duodenum

https://www.researchgate.net/publication/50851364/figure/fig2/AS%3A340577104220165%401458211317808/Enterocyte-iron-absorption-

https://www.researchgate.net/publication/273311041/figure/fig1/AS%3A272541923147783%401441990466474/Regulation-of-iron-export-

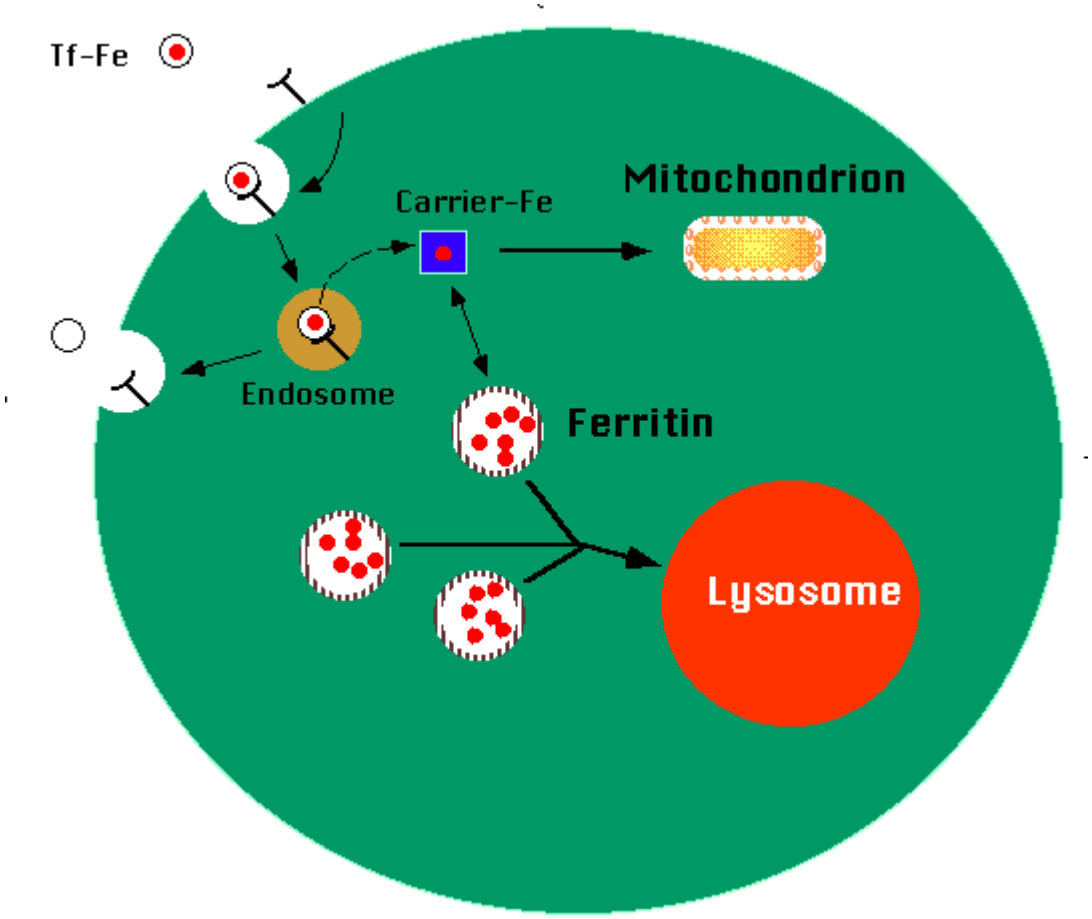
4

- **Reduction of ferric ($Fe^{3?}$) to ferrous ($Fe^{2?}$) form**
    - Dietary non-heme iron is mainly in **ferric ($Fe^{3?}$)** form.
    - At the brush border of enterocytes, $Fe^{3?}$ is reduced to **ferrous ($Fe^{2?}$)** form.
    - This reduction is essential because only $Fe^{2?}$ can be transported into the cell.
- **Transport across enterocyte membrane**
    - $Fe^{2?}$ crosses the **apical membrane of enterocyte**.
    - Occurs mainly in the **duodenum**.
- **Role of divalent metal transporter (DMT1 concept)**
    - **DMT1 (Divalent Metal Transporter-1)** transports $Fe^{2?}$ into enterocyte.
    - It is a **proton-coupled transporter**.
    - Also transports other divalent metals (e.g., $Mn^{2?}$).
- **Storage as ferritin in enterocytes**
    - Inside enterocyte, iron may:
        - Bind to **ferritin** for temporary storage.
    - If not required by body ? stored iron is lost when enterocytes are shed.
    - This is called the **mucosal block theory** (physiological control mechanism).

- **Transfer to plasma via ferroportin**
    - If body requires iron:
        - $Fe^{2?}$ exits enterocyte through **ferroportin** (basolateral membrane iron exporter).
    - Ferroportin is the **only known iron export protein**.
- **Oxidation to ferric form**
    - During transfer to plasma:
        - $Fe^{2?}$ is oxidized back to **$Fe^{3?}$**.
    - This step is necessary for binding to transferrin.
- **Regulation mechanism**
    - Controlled mainly by **body iron stores and hepcidin**.
    - High hepcidin:
        - Degrades ferroportin.
        - ? iron absorption.
    - Low hepcidin:
        - ? ferroportin activity.
        - ? iron absorption.
    - Thus, regulation occurs at the level of **intestinal absorption, not excretion**.
- **Clinical relevance**
    - Achlorhydria ? ? $Fe^{3?}$ reduction ? ? absorption.

- Chronic blood loss ? ? iron absorption (compensatory).
- Inflammation ? ? hepcidin ? anemia of chronic disease.
- Excess absorption ? risk of iron overload states.

Iron in Blood



https://med.libretexts.org/%40api/deki/files/69708/figure17.8.jpg?height=525&revision=1&size=bestfit&width=714

4

- **Transport protein – Transferrin**
    - Iron circulates in plasma bound to **transferrin** (a ?-globulin).
    - Synthesized in the **liver**.

- Each transferrin molecule binds **two ferric ($Fe^{3?}$) ions**.
- Prevents free iron toxicity and delivers iron to tissues (especially bone marrow).

- **Iron-binding capacity**
  - Refers to the ability of transferrin to bind iron.
  - Depends on the amount of transferrin available in plasma.

- **Serum iron**
  - Represents the amount of iron bound to transferrin in plasma.
  - Normal value:
    - **Males:** ~60–170 µg/dL
    - **Females:** ~50–150 µg/dL
  - Shows diurnal variation (higher in morning).

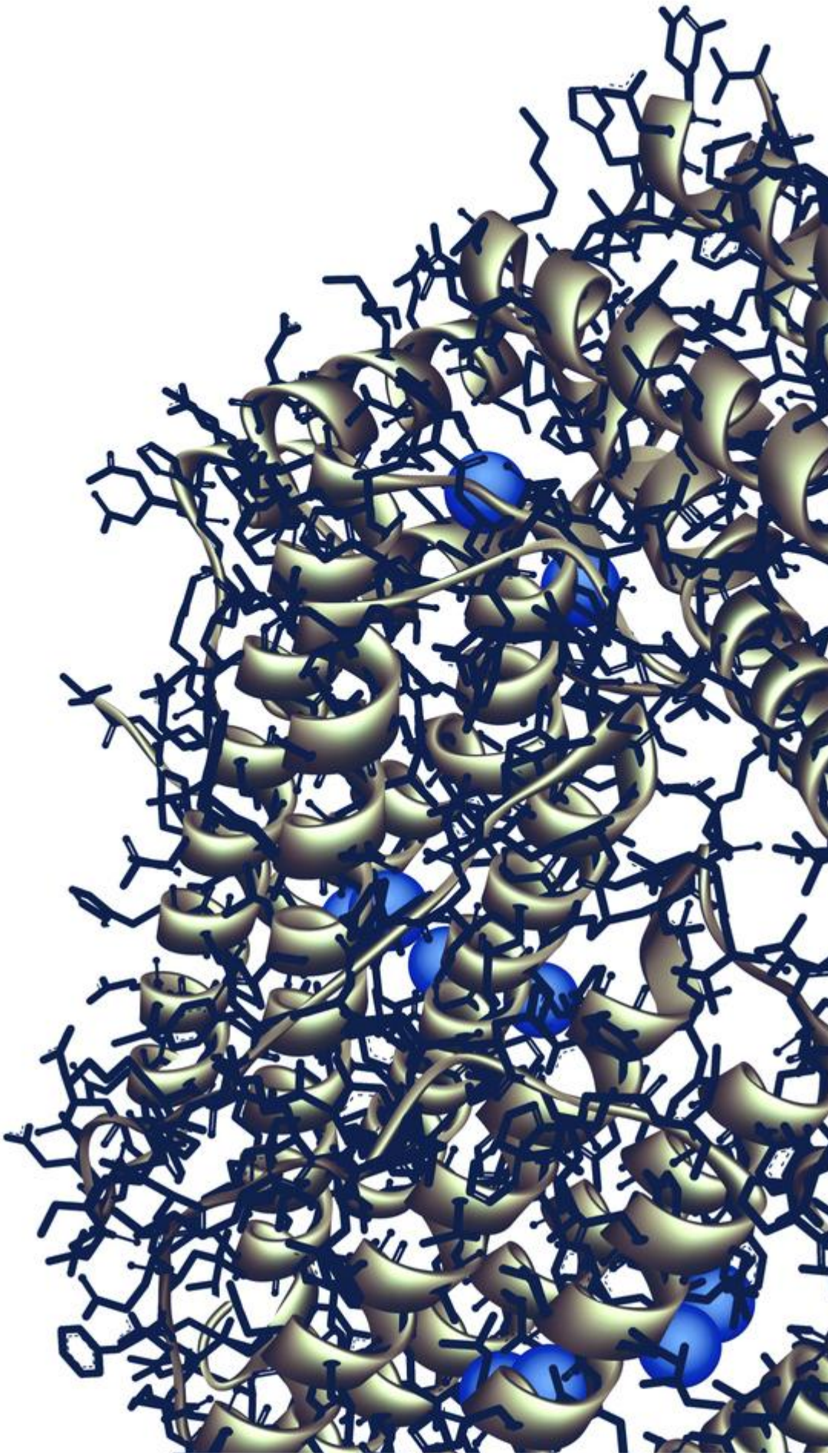
- **Total Iron-Binding Capacity (TIBC)**
  - Measures the **maximum amount of iron that transferrin can bind**.
  - Indirect measure of transferrin level.
  - Normal value: **250–400 µg/dL**.

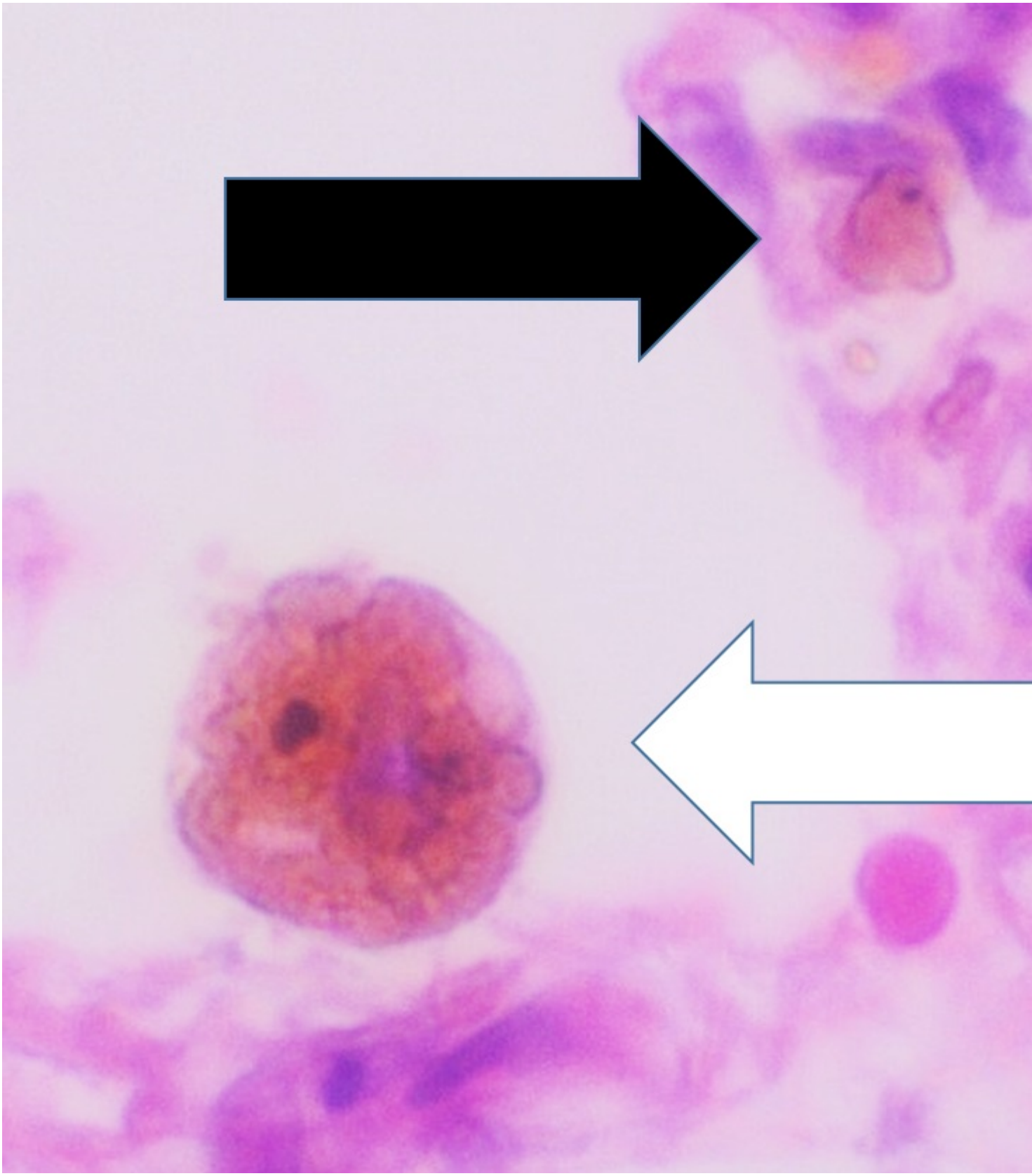
- **Transferrin saturation**
  - Percentage of transferrin binding sites occupied by iron.
  - Formula:
    - **Transferrin saturation (%) = (Serum iron / TIBC) × 100**

    - Normal value: **20–45%**.

- **Normal values (summary)**
    - Serum iron: **~60–170 µg/dL**
    - TIBC: **~250–400 µg/dL**
    - Transferrin saturation: **20–45%**
- **Clinical significance**
    - **Iron deficiency anemia**
        - ? Serum iron
        - ? TIBC
        - ? Transferrin saturation
    - **Anemia of chronic disease**
        - ? Serum iron
        - ? or normal TIBC
        - ? Transferrin saturation
    - **Iron overload (e.g., hemochromatosis)**
        - ? Serum iron
        - ? TIBC
        - ? Transferrin saturation

Storage of Iron





Iro

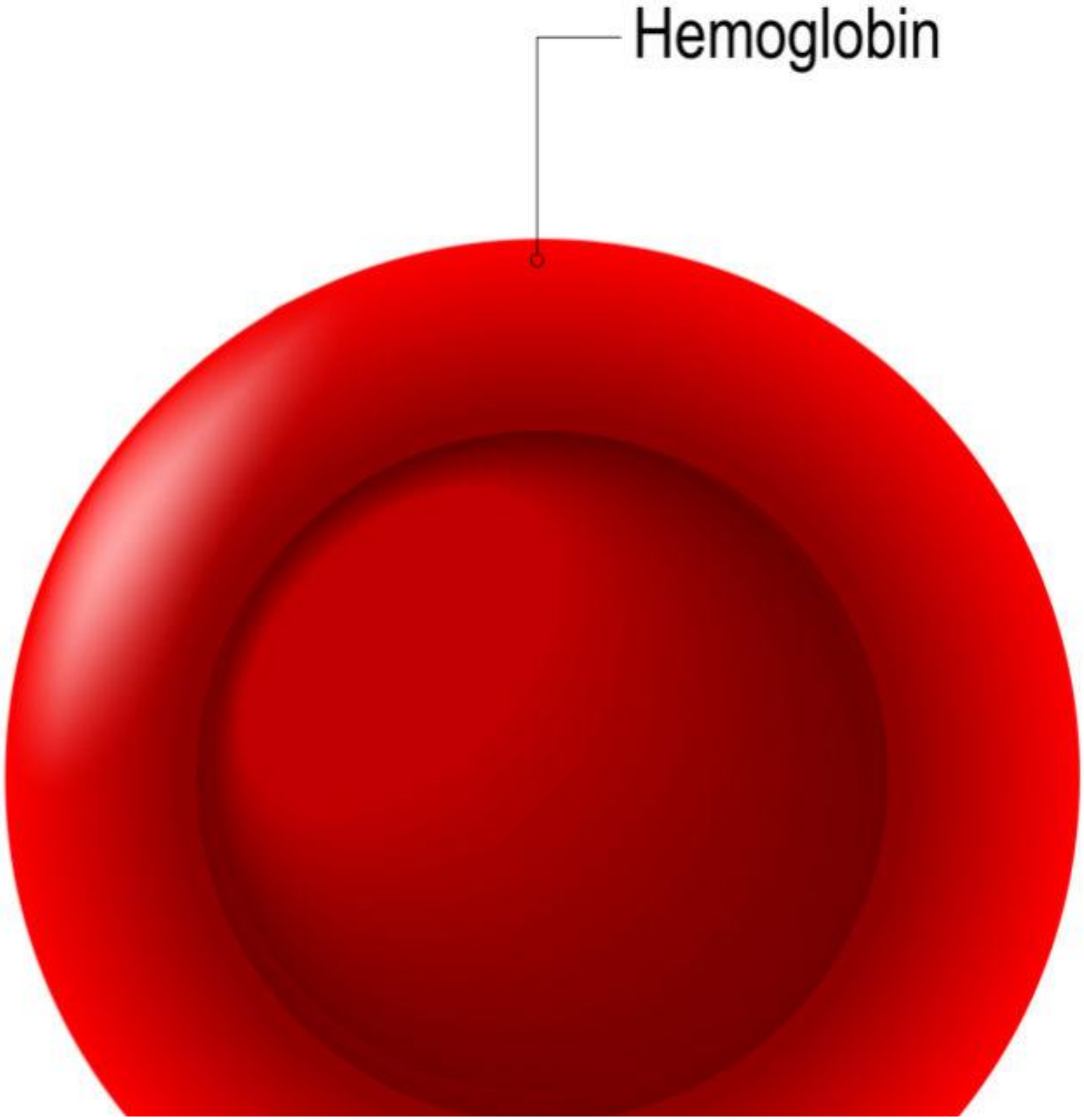
- **Ferritin**
  - Main **storage form of iron**.
  - Water-soluble protein complex.
  - Stores iron in **ferric (Fe^{3}?) form**.
  - Present in cytoplasm of cells.
  - Serum ferritin reflects **body iron stores**.
- **Hemosiderin**
  - Insoluble, granular storage form.
  - Formed when iron stores are **excessive**.
  - Seen as coarse golden-brown granules on microscopy.
  - Less readily available for mobilization than ferritin.
- **Sites of storage**
  - **Liver**
    - Major storage organ.
    - Iron stored in hepatocytes and Kupffer cells.
  - **Spleen**
    - Stores iron from breakdown of old RBCs.
  - **Bone marrow**

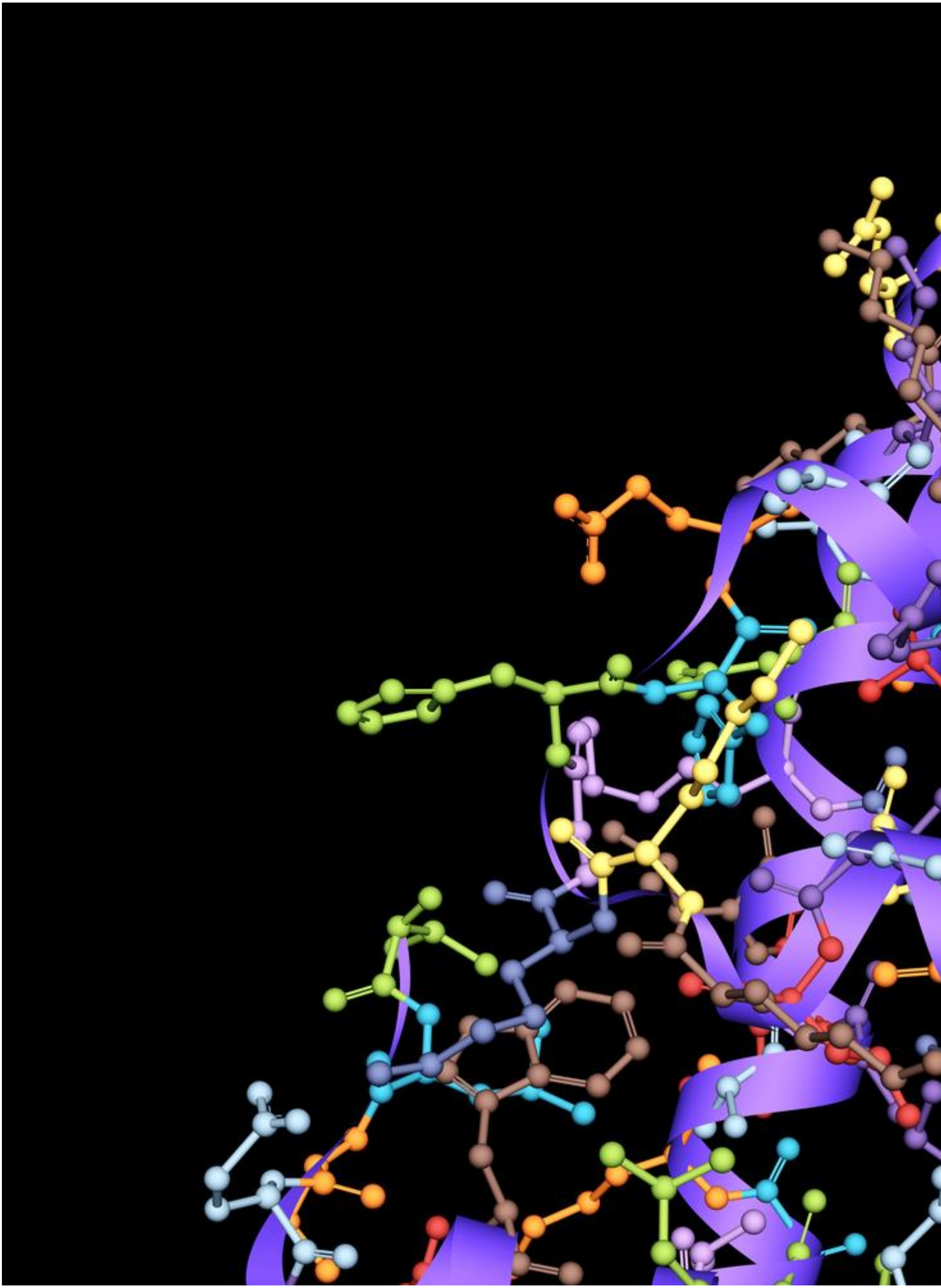
        - Iron available for hemoglobin synthesis.

- **Regulation of storage**
    - Controlled mainly by **body iron requirements and hepcidin**.
    - High iron levels ? increased storage.
    - Low iron levels ? decreased storage.
    - Balance maintained between absorption, utilization, and storage.
- **Mobilization of stored iron**
    - Iron released from ferritin when needed.
    - Exported via **ferroportin**.
    - Binds to **transferrin** in plasma for transport to bone marrow.
    - Enhanced during anemia and increased erythropoiesis.
- **Clinical importance**
    - **Serum ferritin** = best indicator of total body iron stores.
    - ? Ferritin ? iron deficiency.
    - ? Ferritin ? iron overload, inflammation, liver disease.
    - Excess deposition ? hemosiderosis, hemochromatosis.

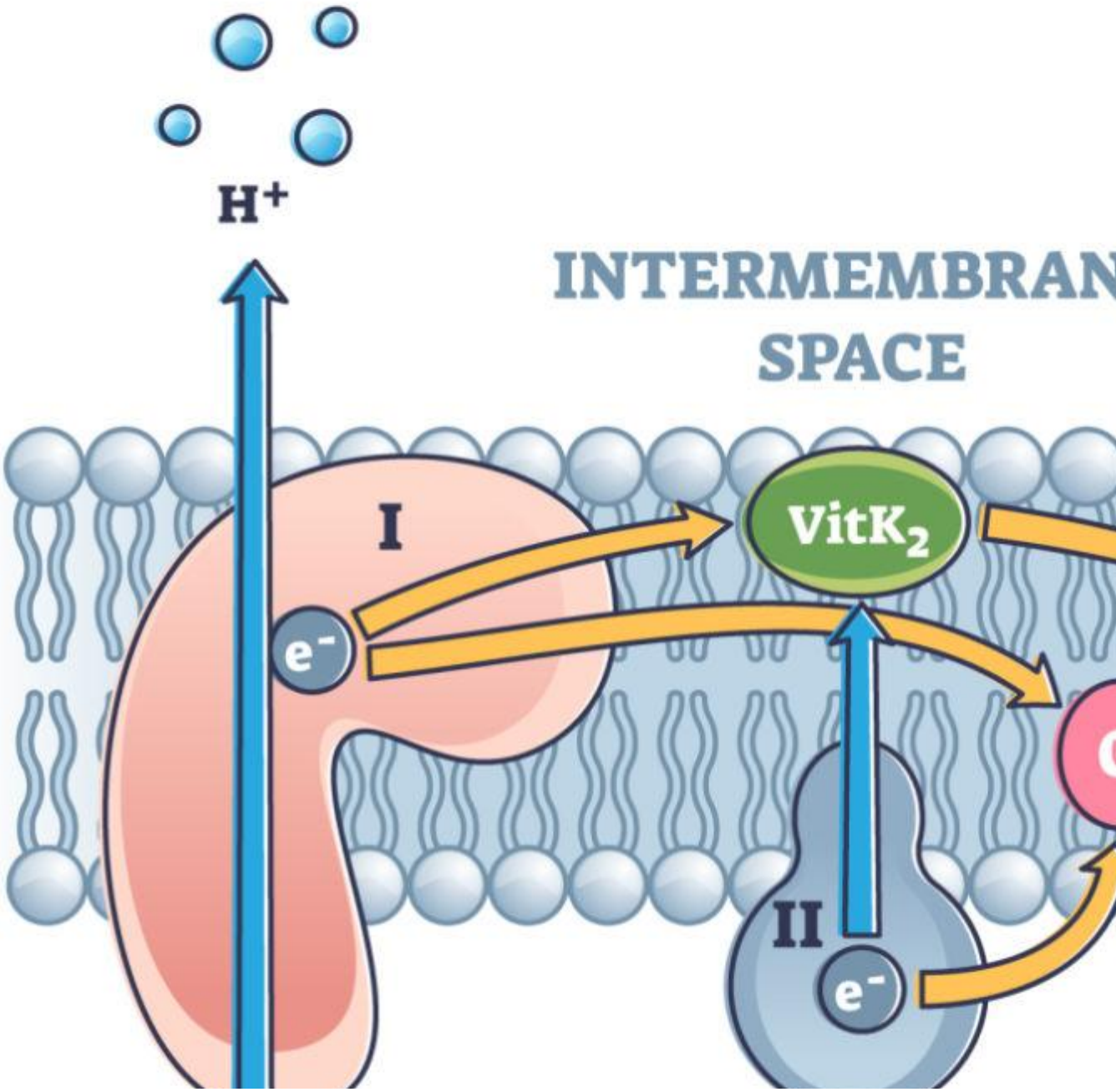
Functions of Iron

Stru





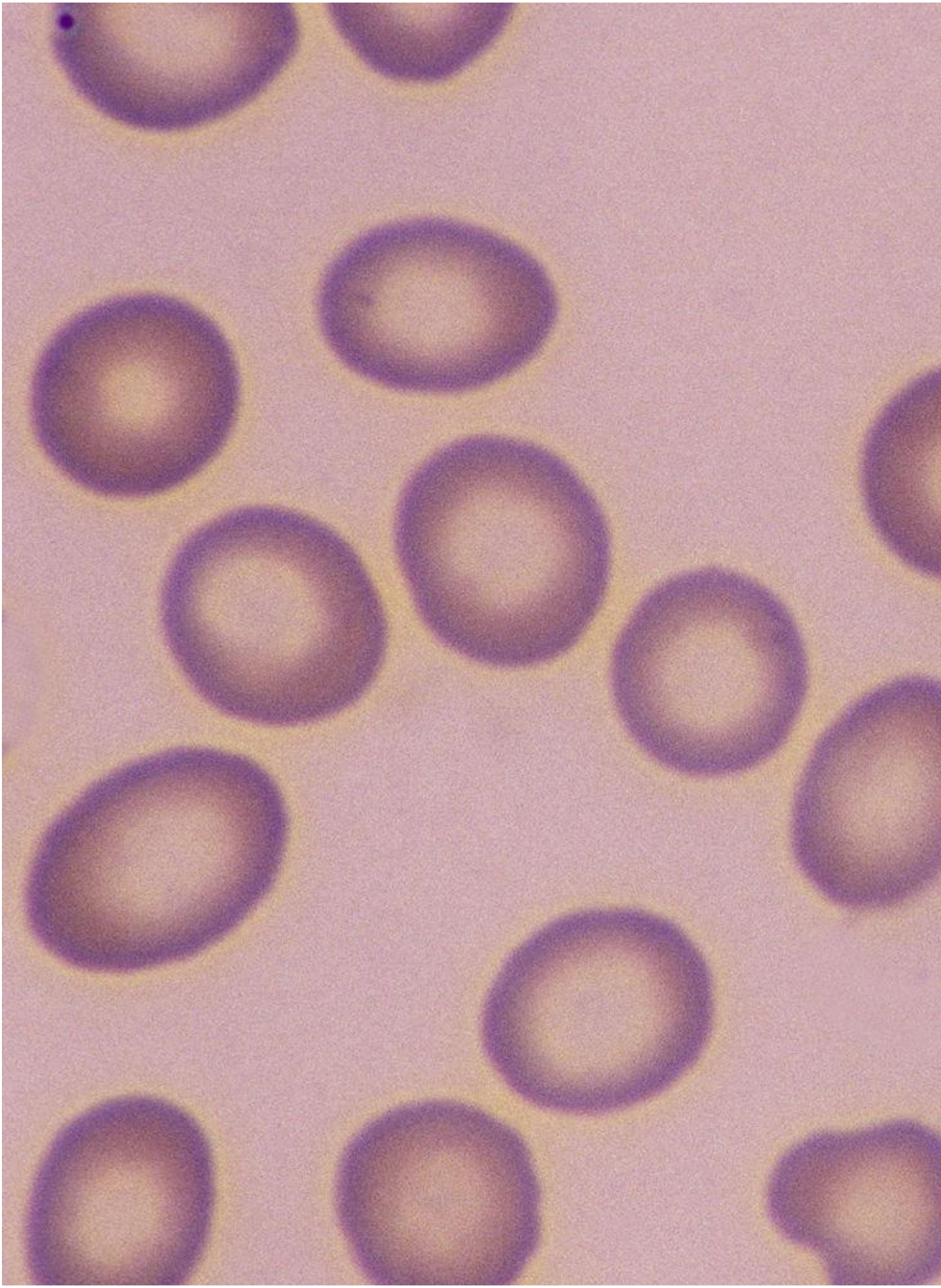
ELECTRO

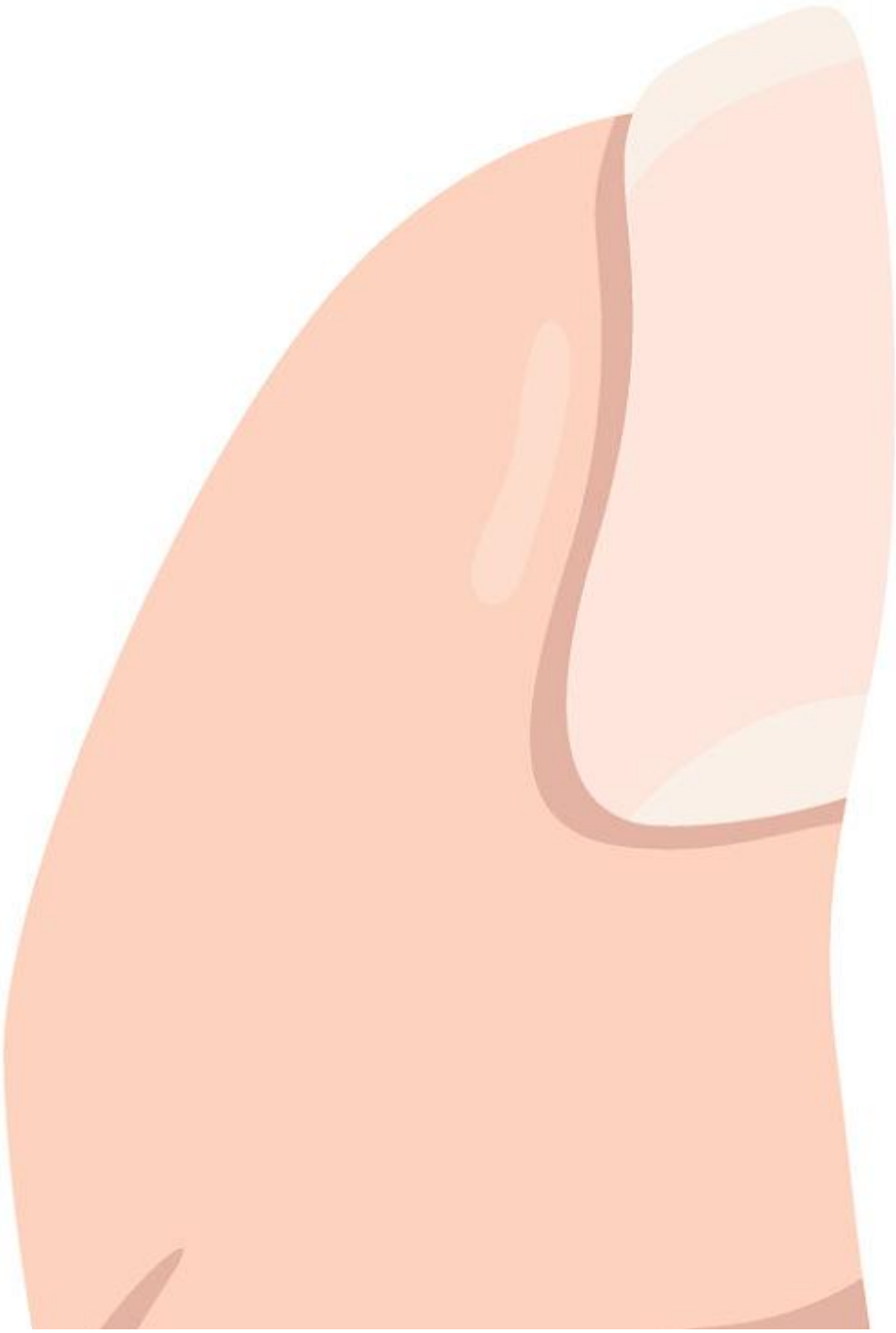


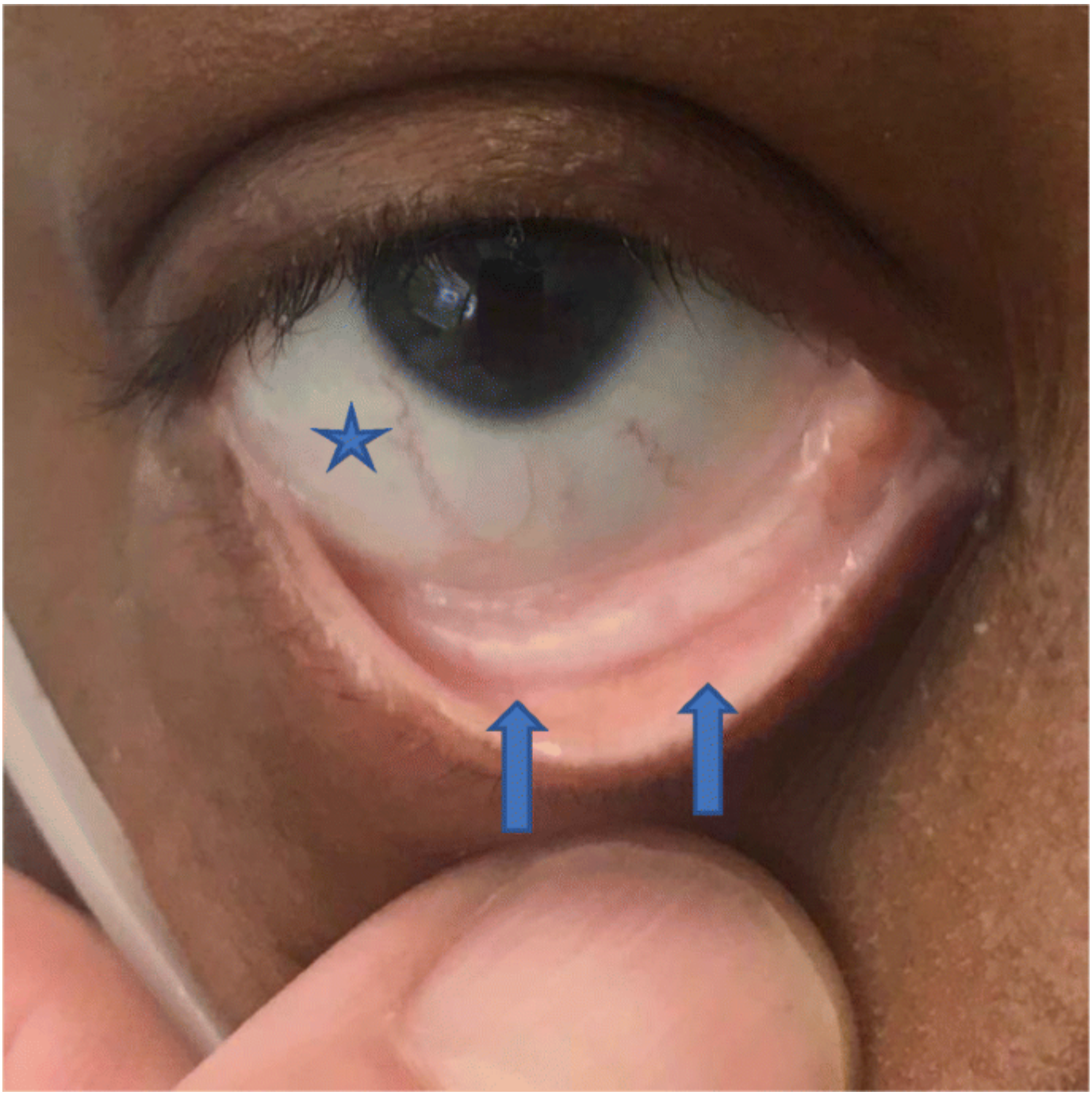
- **Hemoglobin synthesis**
  - Essential component of **heme** molecule.
  - Required for formation of **hemoglobin (Hb)** in RBCs.
  - Each Hb molecule contains **four heme groups**, each with one iron atom.
  - Enables **reversible binding of oxygen**.
  - Without iron ? defective Hb synthesis ? microcytic hypochromic anemia.
- **Myoglobin formation**
  - Present in **skeletal and cardiac muscle**.
  - Acts as **oxygen reservoir**.
  - Facilitates diffusion of oxygen within muscle cells.
  - Important during intense muscular activity.
- **Enzyme function**
  - Component of several **iron-containing enzymes**, such as:
    - Catalase
    - Peroxidase
    - Cytochromes
  - Participates in oxidation–reduction reactions.
  - Essential for detoxification of hydrogen peroxide.

- **Role in electron transport chain**
    - Iron is part of **cytochromes** and **iron–sulfur (Fe–S) proteins**.
    - Facilitates electron transfer in mitochondria.
    - Critical for **ATP production**.
    - Without iron, oxidative phosphorylation is impaired.
- **Role in oxidative metabolism**
    - Required for cellular respiration.
    - Participates in redox reactions.
    - Supports efficient utilization of oxygen in tissues.
- **Importance in cell growth and division**
    - Required for **DNA synthesis** (via ribonucleotide reductase enzyme).
    - Essential for rapidly dividing cells (bone marrow, fetal tissues).
    - Deficiency leads to:
        - Impaired growth
        - Reduced cognitive development in children
        - Decreased immunity

Applied: Iron Deficiency Anaemia







4

- **Causes**
  - **Nutritional deficiency**

        - Poor dietary intake.
        - Diet low in heme iron (vegetarian diets without adequate supplementation).
        - Common in children and low socioeconomic groups.
    - **Blood loss**
        - Chronic gastrointestinal bleeding.
        - Menstrual blood loss (menorrhagia).
        - Hookworm infestation.
        - Repeated blood donation.
    - **Malabsorption**
        - Celiac disease.
        - Post-gastrectomy state.
        - Achlorhydria (? gastric acid ? ? Fe^{3}? to Fe^{2}? conversion).
    - **Increased requirement**
        - Pregnancy.
        - Lactation.
        - Infancy and adolescence (rapid growth phase).
- **Pathophysiology**
    - ? Iron stores ? ? serum ferritin.
    - ? Iron availability for hemoglobin synthesis.

    - Impaired heme formation.
    - Reduced hemoglobin production in developing RBCs.
    - Result: smaller, paler red cells.

- **Microcytic hypochromic anemia**
    - **Microcytic** ? decreased MCV.
    - **Hypochromic** ? decreased MCH/MCHC.
    - Peripheral smear shows:
        - Small RBCs.
        - Increased central pallor.
        - Anisopoikilocytosis (variation in size and shape).

- **Clinical features**
    - Pallor (skin, conjunctiva).
    - Fatigue and weakness.
    - Dyspnea on exertion.
    - Palpitations.
    - Koilonychia (spoon-shaped nails).
    - Angular cheilitis.
    - Glossitis.
    - Pica (craving for non-food items).

- **Laboratory findings**
    - ? Hemoglobin.
    - ? Serum iron.
    - ? Serum ferritin (early marker).
    - ? TIBC.
    - ? Transferrin saturation.
    - ? MCV, ? MCH.
- **Prevention principles**
    - Iron-rich diet (green leafy vegetables, meat, liver).
    - Iron supplementation in:
        - Pregnancy.
        - Infants and adolescents.
    - Deworming in endemic areas.
    - Early detection and treatment of chronic blood loss.