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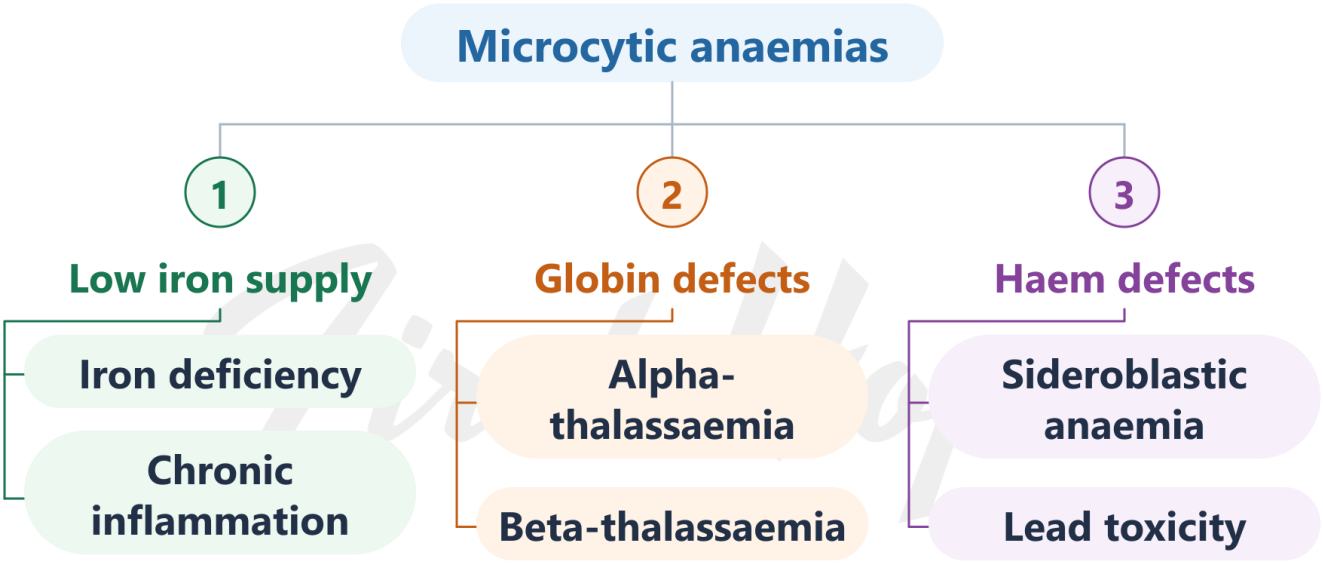
# Pathology - Topic 14 - Microcytic anemia

## Microcytic Hypochromic Anaemia

- **Microcytosis** means that red cells are smaller than expected, while **hypochromia** means that they contain less haemoglobin and show increased central pallor.

### Meaning and Main Causes

- In adults, microcytosis usually corresponds to an MCV below about 80 fL, but children require age-appropriate ranges.
- Reduced haemoglobin synthesis allows extra cell divisions during erythroid development and produces smaller mature cells.
    - The defect may involve iron availability, globin-chain production or haem synthesis.




1. **Iron Deficiency**
    - ➢ Insufficient available iron limits haem formation and eventually lowers haemoglobin concentration.
        - Chronic blood loss is an important cause and must be investigated rather than assuming that diet is always responsible.
2. **Thalassaemia**
    - ➢ An inherited reduction in alpha- or beta-globin production produces marked microcytosis.
        - A thalassaemia trait can cause very small red cells with only mild anaemia and a relatively preserved or high red-cell count.
3. **Inflammation and Impaired Iron Use**
    - ➢ Chronic inflammation restricts iron delivery to erythroid cells and suppresses erythropoiesis.
        - The anaemia is often normocytic initially but can become mildly microcytic.

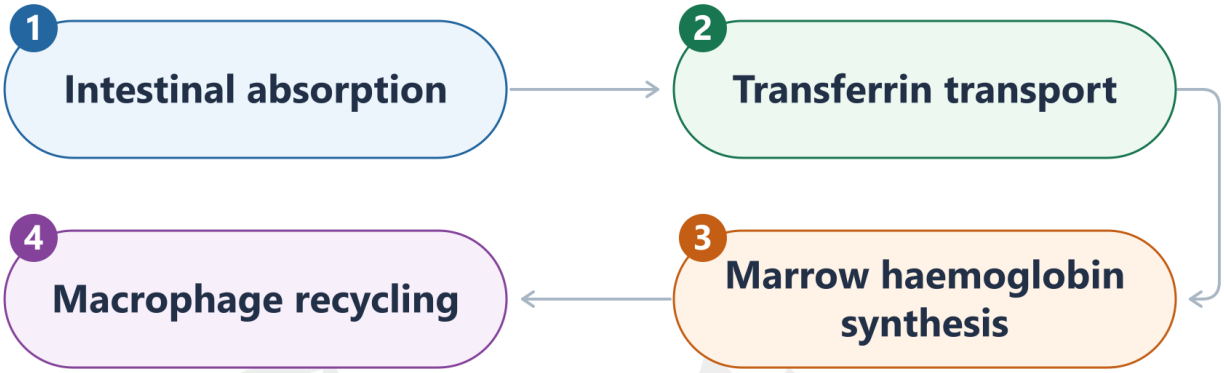
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### 4. Defective Haem Synthesis

- Sideroblastic disorders and lead toxicity can impair haem synthesis despite available iron.
    - These causes are less common than iron deficiency and thalassaemia but become important when the initial results do not fit either pattern.

## Iron Metabolism

- Iron metabolism coordinates intestinal absorption, transport, storage and recycling to support haemoglobin production while limiting iron-related injury.




### Intestinal Absorption

- Iron is absorbed mainly in the duodenum and proximal small intestine.
    - Haem iron and non-haem iron enter intestinal cells by different processes, and non-haem ferric iron must be made available in a reduced form for efficient uptake.
- Absorbed iron is either stored within the enterocyte as ferritin or exported into blood through **ferroportin**.
    - Iron retained in an intestinal cell is lost when that cell is shed.

#### Apical Uptake and Basolateral Export

- Duodenal surface ferrireductase activity converts ferric iron to ferrous iron, which can enter through the divalent metal transporter DMT1.
- Iron exported by ferroportin is oxidised to the ferric state by ferroxidases such as hephaestin so that it can bind transferrin.
- Gastric acidity and ascorbate can improve the availability of non-haem iron, while phytates and some other dietary constituents reduce uptake.
- The final amount absorbed reflects both diet composition and systemic regulation rather than total dietary iron alone.

### Transport and Recycling

#### Plasma Transport and Macrophage Recycling

- **Transferrin** transports iron in plasma and delivers it to cells through transferrin receptors.

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- Developing erythroid cells use a large proportion of delivered iron to make haemoglobin.
- Macrophages remove ageing red cells and recycle their iron.
- Daily recycling supplies much more iron to the marrow than daily intestinal absorption does.

### Iron Balance and Cellular Uptake

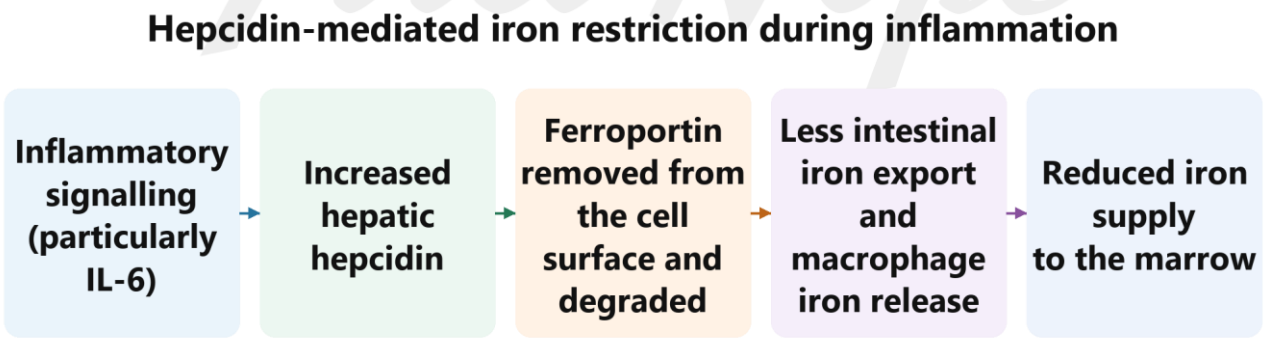
- The body has no major regulated pathway for iron excretion, so absorption is tightly controlled.
- Transferrin binds its receptor on erythroid precursors and is taken into an endosome, where iron is released for cellular use.
- Recycled iron returns to plasma through macrophage ferroportin, linking red-cell destruction directly to supply for new erythropoiesis.
- Normal small losses occur through epithelial shedding and bleeding, so prolonged negative balance gradually exhausts reserves.

## Iron Stores and Hepcidin

### Storage Forms

- **Ferritin** stores iron in an available form, while larger aggregates of storage iron form haemosiderin.

### Hepcidin and Ferroportin




- The liver produces **hepcidin**, which binds ferroportin and promotes its internalisation and degradation, reducing iron export from enterocytes and macrophages.
- High hepcidin reduces intestinal iron absorption and traps iron within macrophages.
- Inflammation increases hepcidin, whereas iron deficiency and increased erythropoietic demand generally suppress it.
- This explains why a patient with inflammation can have iron in storage but too little iron reaching the marrow.

### Inflammatory and Erythroid Regulation

- Inflammatory cytokine signalling, particularly through IL-6, increases hepatic hepcidin production.

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- Erythroid signals such as erythroferrone suppress hepcidin during increased erythropoietic demand and can contribute to excessive absorption in ineffective erythropoiesis.

# Iron Deficiency Anaemia

- Iron deficiency anaemia develops when available iron is insufficient for normal haemoglobin synthesis.

## Causes and Development

### 1. Blood Loss

- Menstrual loss and gastrointestinal bleeding are common sources of chronic iron loss.
  - Gastrointestinal causes include ulcers, tumours and parasitic infection, depending on the patient's setting and exposure.
- Repeated donation and other repeated small losses can also deplete stores.
  - An apparently small daily loss becomes important when it continues over months.

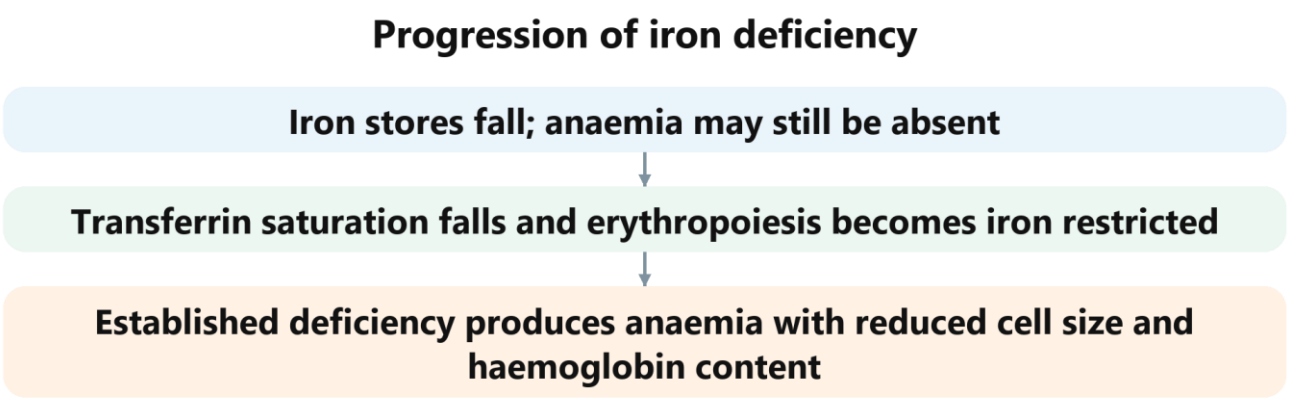
### 2. Increased Requirement or Reduced Intake

- Rapid childhood growth, adolescence and pregnancy increase the iron requirement.
- A diet with insufficient bioavailable iron can contribute, especially when requirements are high.
  - Dietary deficiency and blood loss may coexist, so finding one cause does not automatically exclude another.

### 3. Malabsorption

- Coeliac disease, some gastric or intestinal operations and other absorptive disorders can impair iron uptake.
  - Failure of an expected response to replacement should prompt reassessment of adherence, absorption, ongoing loss and the original diagnosis.

## Stages of Deficiency




*Progression of iron deficiency*

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- Iron stores fall before the haemoglobin concentration becomes low.
    - A patient can therefore have iron deficiency without anaemia.
- As available iron falls further, transferrin saturation decreases and erythropoiesis becomes iron restricted.
- Established deficiency produces anaemia with reduced cell size and reduced haemoglobin content.
    - Early iron deficiency can remain normocytic, so a normal MCV does not rule it out.

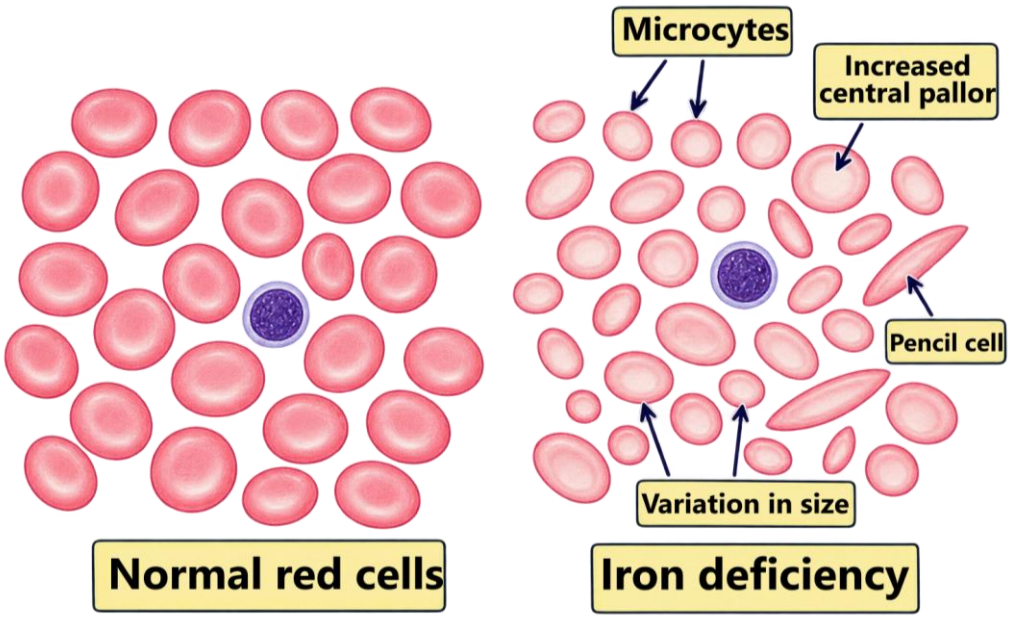
## General Symptoms and Their Severity

- General features include fatigue, pallor, reduced exercise tolerance and palpitations.
- Tissue symptoms can precede pronounced microcytosis because iron-containing enzymes and other cellular functions are affected as reserves decline.
- The speed of haemoglobin decline and cardiopulmonary reserve influence symptoms as much as the final concentration.

## Tissue Features and Associated Syndromes

- Some patients develop pica, which is a craving for non-food substances or unusual items such as ice.
- Glossitis, angular cheilitis and brittle or spoon-shaped nails may occur in longstanding deficiency.
    - These signs support the possibility of deficiency but are not present in every case and are not independently diagnostic.
- Plummer–Vinson syndrome combines iron-deficiency anaemia with dysphagia and upper oesophageal webs.

## Peripheral Smear and Marrow




*Small pale red cells and pencil cells in iron deficiency anaemia*

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