Case

- 35 year old woman is seen for easy fatigue for many months. She is now 24 weeks pregnant with her 3rd child in 3 years. She does not see any obstetrician and does not take any vitamins. Lately, she has developed a taste for eating ice. She has no other complaint. Family and past history are negative. She does not smoke or drink. Physical examination is positive for pale conjunctiva, mild spooning of nails, and a II/VI systolic murmur at left lower sternal border. Stools are negative for occult blood.

- Craving and **chewing ice** (pagophagia) is often associated with iron deficiency, with or without anemia, although the reason is unclear.

- A 10-year-old girl presented with excessive tiredness, poor appetite, inability to concentrate and tingling sensations. On examination, there was pallor. Laboratory examination revealed decrease in hemoglobin, ferritin and MCV. Total iron binding capacity (TIBC), transferrin were increased. What is the likely diagnosis?

MINERALS

Minerals are inorganic compounds that are required for the body as one of the nutrients

MINERALS

Macrominerals

Required in excess of 100mg/day

Ca^{++}, P, S, Mg, Cl, Na, K.

Microminerals

Required in amounts less than 100mg/day

Fe, Cu, Zn, Mo, I, Fl, Cr, CO, Mn


10 x 10 Tablets
Iron, Folic Acid,
Cyanocobalamin with Zinc Tablets
IROFEM-12

IRON

Sources

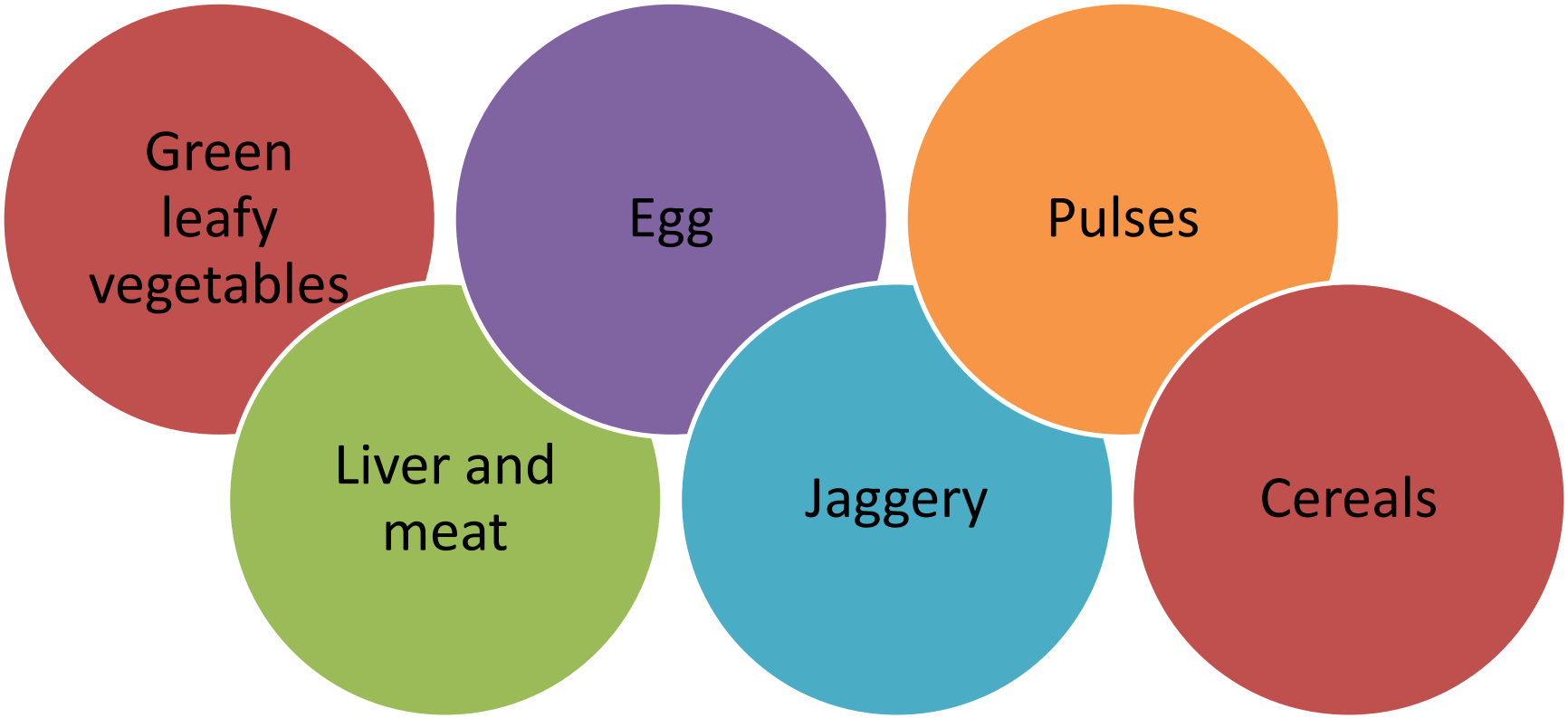
RDA

Metabolism

Functions

Disorders

IRON - SOURCES



IRON - RDA

Adults

10-20 mg/day

Pregnancy

40mg/day

IRON - METABOLISM

IRON - ABSORPTION

Site

Upper part of the duodenum

Forms

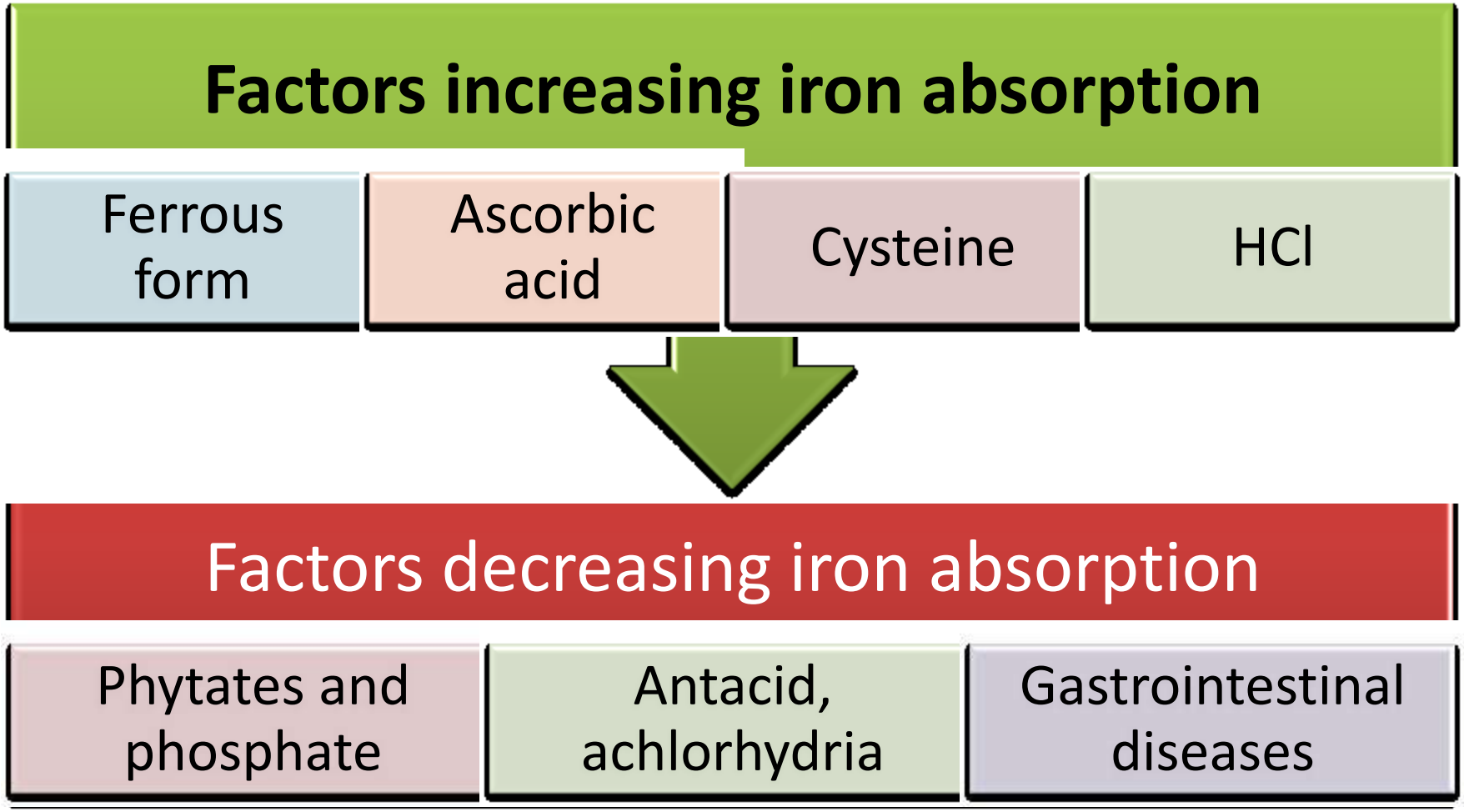
Heme

Non-haem

Efficiency

About 10% of total food iron is absorbed

FACTORS AFFECTING IRON ABSORPTION



MECHANISM OF IRON ABSORPTION

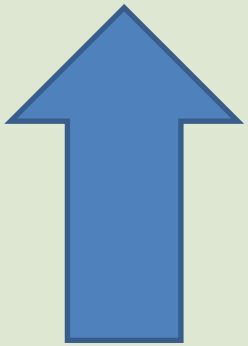
MUCOSAL BLOCK THEORY

- Duodenum and jejunum are the sites of absorption.
- Iron metabolism is unique because homeostasis is maintained by regulation at the **level of absorption** and not by excretion
- No other nutrient is regulated in this manner. **In other words, iron is a oneway element.**

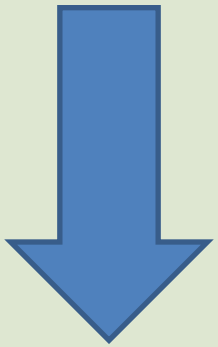
- When iron stores in the body are depleted, absorption is enhanced. When adequate quantity of iron is stored, absorption is decreased. This is referred to as “**mucosal block” of regulation of absorption of iron.**

MUCOSAL BLOCK THEORY

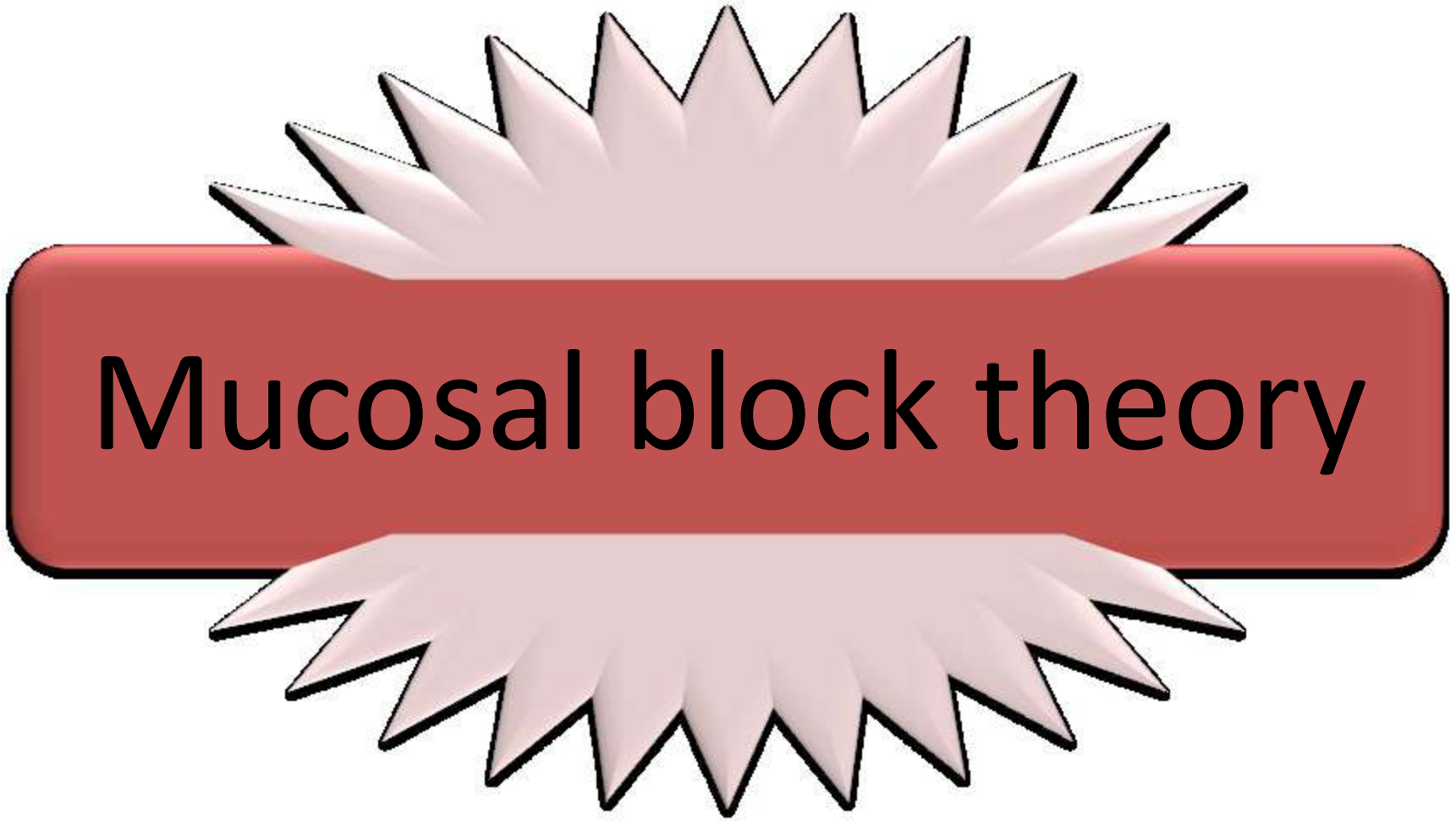
When iron stores in the body are depleted, absorption is enhanced

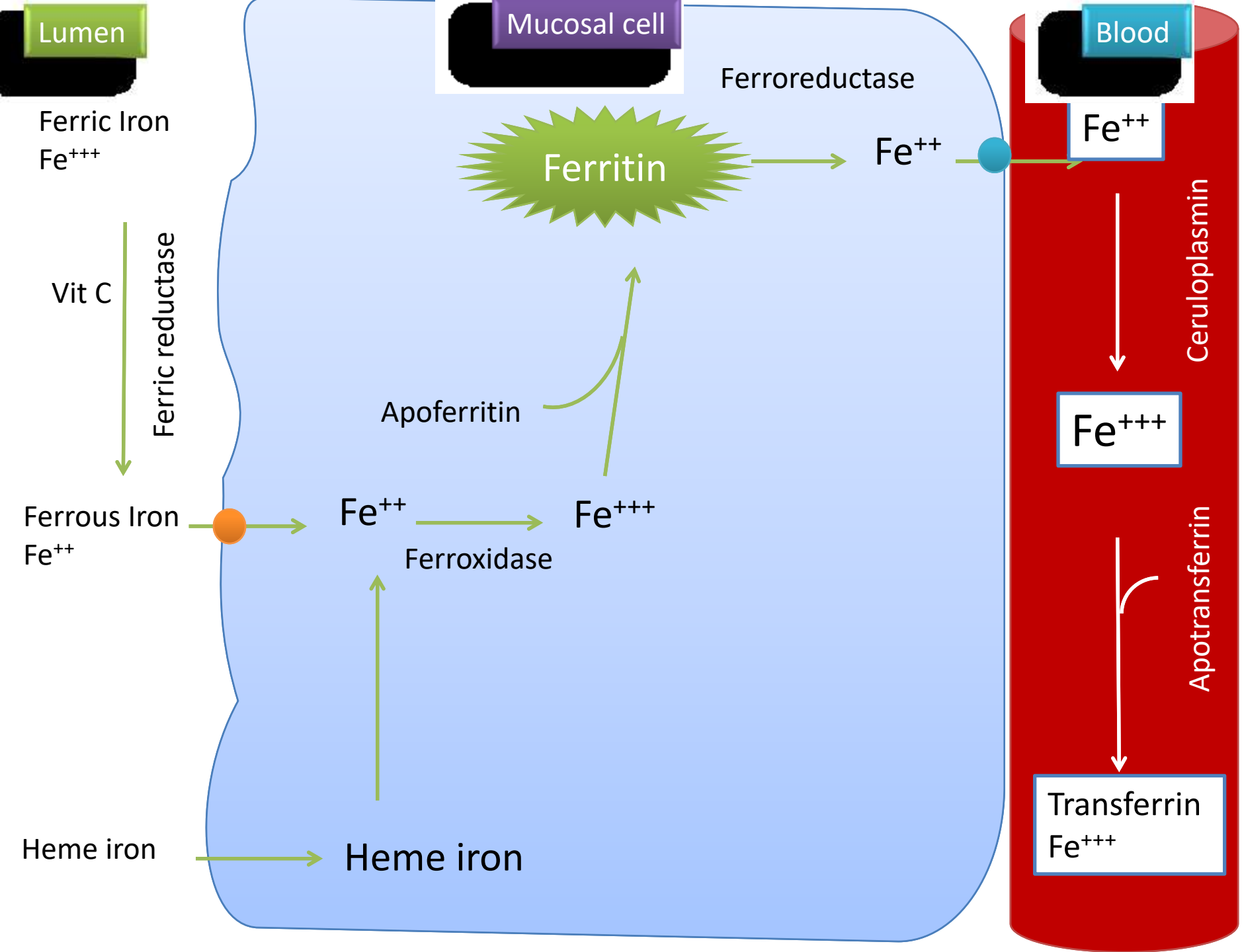


When adequate quantity of iron is stored, absorption is decreased.



REGULATION OF IRON ABSORPTION




Lumen
Mucosal cell
Blood
Ferroreductase
Ferric Iron
Fe+++
Ferritin
Fe++
Fe++
Ceruloplasmin
Vit C
Ferric reductase
Fe+++
Apoferritin
Ferrous Iron
Fe++
Fe++
Fe+++
Ferroxidase
Apotransferrin
Transferrin
Fe+++
Heme iron
Heme iron

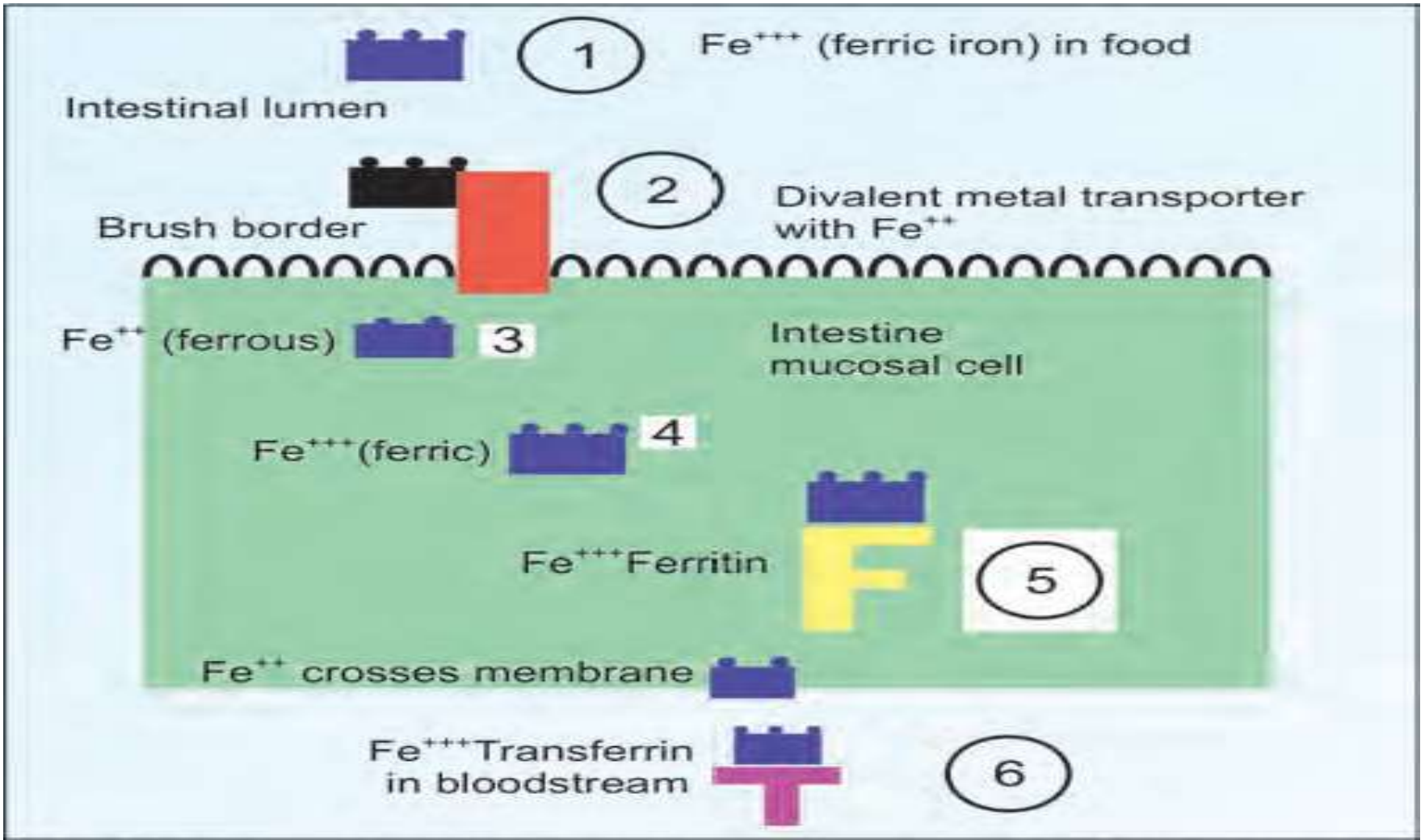
- Only ferrous (and not ferric) form of iron is absorbed.
- Ferric iron is reduced to ferrous iron by ***ferric reductase,*** **an enzyme present on the surface of** enterocytes.
- **Ferrous iron in the intestinal lumen** binds to mucosal cell protein, called divalent metal transporter-1 **(DMT-1).**
- **This bound iron is then** transported into the mucosal cell. The rest of the unabsorbed iron is excreted.

- Inside the mucosal cell, iron is oxidized to ferric state, and is complexed with apoferritin to form **ferritin.**

- The fraction of iron absorbed and retained is decided by the iron status. When iron is in excess, absorption is reduced; this is the basis of “mucosal block”

- This mechanism of iron absorption from **intestinal lumen to the mucosal cell** is different from the iron release from intestinal cell to the bloodstream

- Iron in the ferritin is released, then crosses the mucosal cell with the help of a transport protein called, **ferroportin. But this can happen only when** there is free transferrin in plasma to bind the iron.



1= Fe^{+++} (ferric iron) in food. 2= Iron is reduced to Fe^{++} (ferrous) state, and attaches to divalent metal transporter on the mucosal surface. 3= Ferrous iron is internalized. 4= Iron is oxidized to ferric state. 5= Ferric iron binds with ferritin for temporary storage. 6=Ferric iron released, reduced to ferrous state crosses the cell membrane, re-oxidized to ferric state by ceruloplasmin. In the bloodstream, ferric iron is bound with transferrin.

IRON TRANSPORT IN BLOOD AND UPTAKE BY CELLS

- Transport form of iron is **transferrin.** It is synthesized in liver.
- Normal plasma level of transferrin is 250 mg/100 mL.
- In iron deficiency, this level is increased. One molecule of transferrin can transport 2 ferric atoms.

- **Total iron binding capacity (TIBC) in plasma is** 400 mg/100 mL; this is provided by the transferrin.
- In iron deficiency anemia, TIBC is increased (transferrin level is increased); but serum iron level is reduced.
- Transferrin has a half life of 7–10 days, and is a useful index of nutritional status.

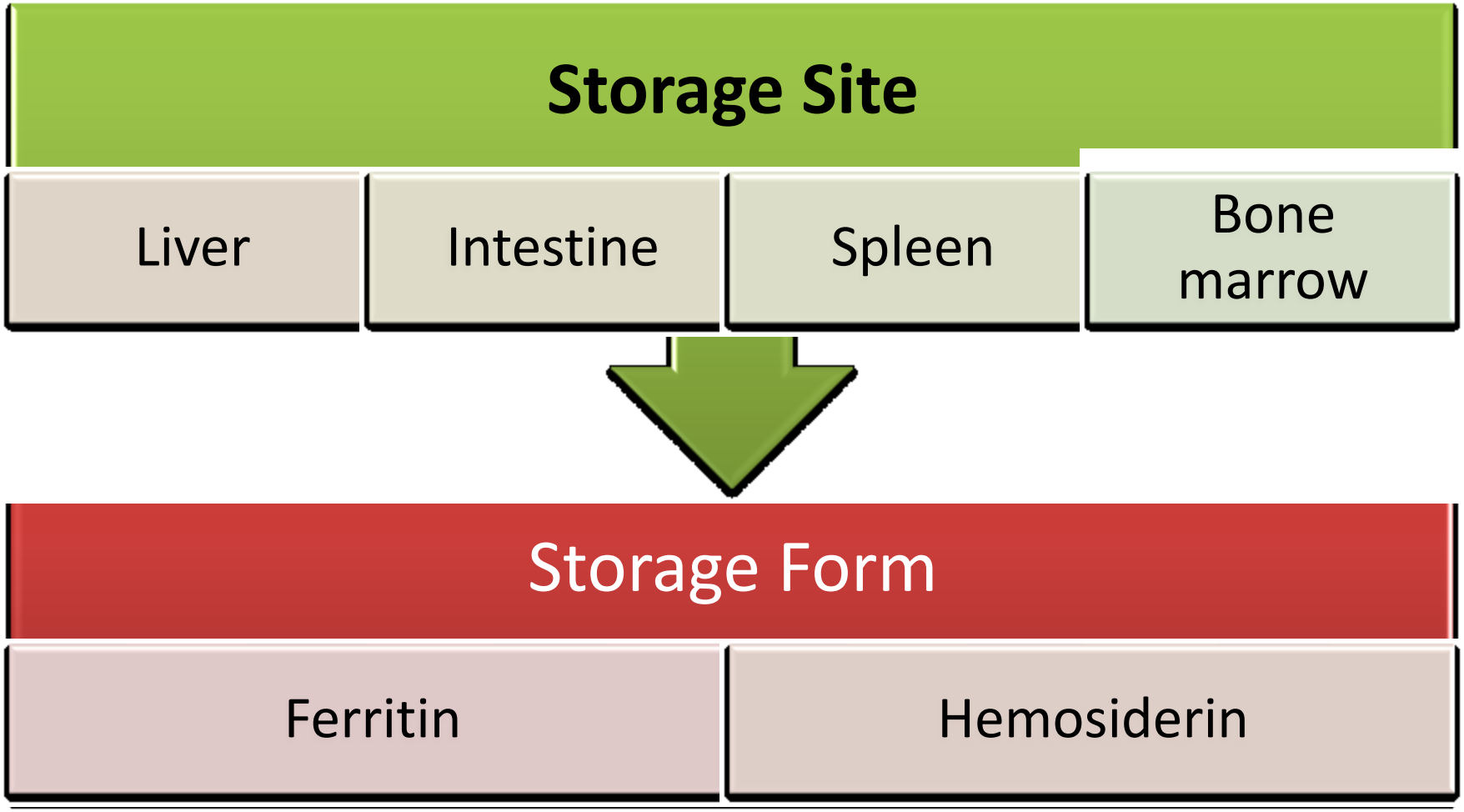
- One molecule of transferrin can bind two ferric ions.

In blood, **ceruloplasmin is the ferroxidase, which** oxidizes ferrous to ferric state.

Ferroxidase

Apo-transferrin + 2 Fe++ → Transferrin combined with 2 Fe+++

STORAGE OF IRON



EXCRETION OF IRON

Normal excretion

- Very little
- About 1mg/day

Stool

- 0.7 mg/day

Physiological loss

- Menstruation 20-30mg/cycle
- Delivery 750mg

FUNCTIONS OF IRON

Iron is a component of several functionally important compounds

Heme compounds

Non-heme compounds

FUNCTIONS OF IRON

Haem compounds

- Haemoglobin
- Myoglobin
- Cytochrome
- Catalase

Non-haem compounds

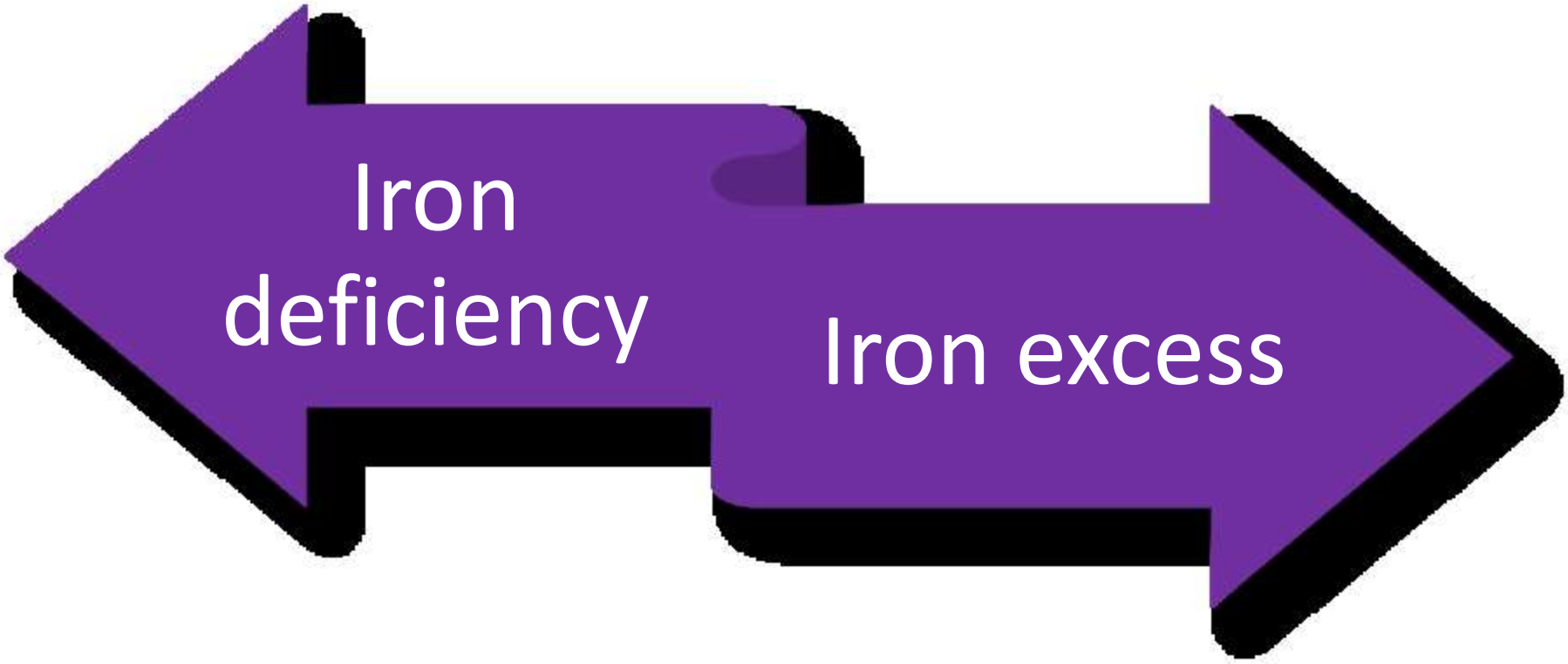
- Succinate dehydrogenase
- Xanthine oxidase
- Iron sulfur proteins

IRON IS CONSERVED

- When RBC is lysed, haemoglobin enters into circulation.
- Being a small molecular weight substance, Hb will be lost through urine.
- To prevent this loss, Hb is immediately taken up by **haptoglobin (Hp)**

- When the globin part is removed from Hb, the heme is produced, and is released into circulation.
- In order to prevent its excretion through urine, heme is bound with **hemopexin**

DISORDERS OF IRON METABOLISM



IRON DEFICIENCY ANEMIA

CAUSES:

1. **Nutritional deficiency of iron**

2. **Lack of absorption: Subtotal gastrectomy and hypochlorhydria**

3. **Hookworm infection: One hookworm will cause the loss of** about 0.3 mL of blood per day. Calculation shows that about 300 worms can produce a loss of 1% of total body iron per day

4. **Repeated pregnancies: About 1g of iron is lost from the** mother during one delivery

5. **Chronic blood loss: Hemorrhoids (piles), peptic ulcer,** Menorrhagia

6. **Nephrosis: Haptoglobin, hemopexin and transferrin are loss** in urine, along with loss of iron

7. **Lead poisoning: Iron absorption and hemoglobin synthesis** are reduced. In turn, iron deficiency causes more lead absorption. It is a vicious cycle.

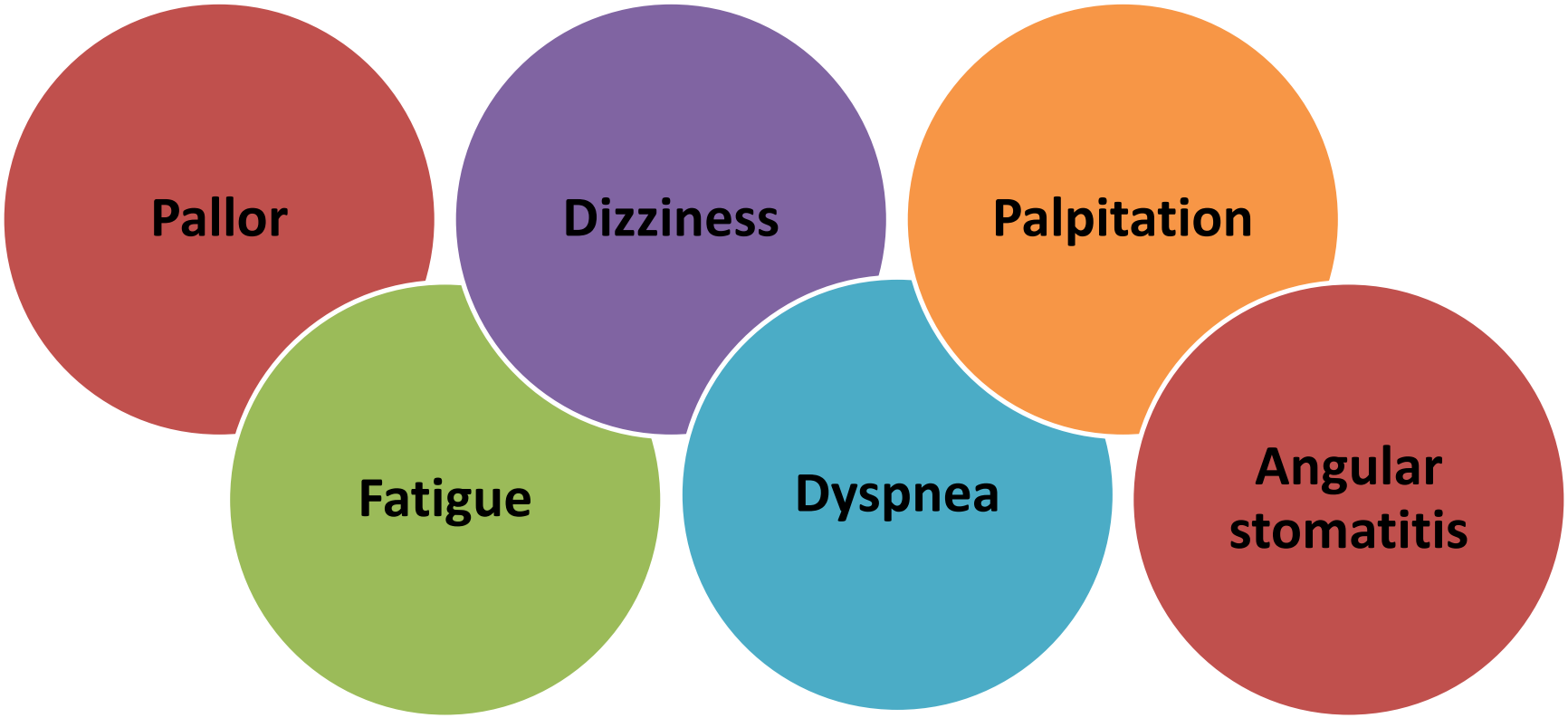
FEATURES

- When the level is lower than 10 g, body cells lack oxygen and patient becomes uninterested in surroundings (**apathy).**
- **Since iron is an important** constituent of cytochromes, their deficiency leads to derangement in cellular respiration and all metabolic Processes become sluggish.

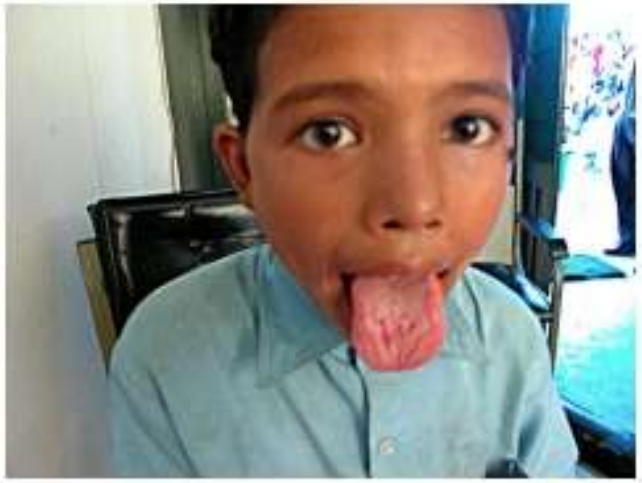
- Prolonged iron deficiency causes atrophy of gastric epithelium leading to **achlorhydria, which in turn** causes lesser absorption of iron, aggravating the anaemia.

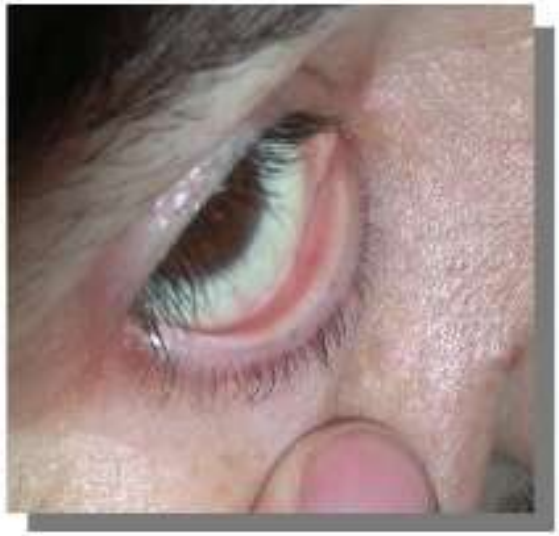
- Similar atrophy of epithelium in oral cavity and esophagus causes dysphagia termed **Plummer- Wilson syndrome, which is a known precancerous** condition.

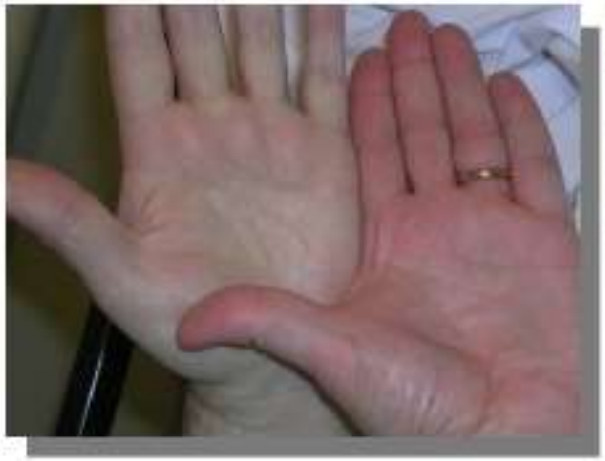
IRON DEFICIENCY – FEATURES



Clinical presentation of IDA







Laboratory Findings

- i. **Serum iron level: It is depressed in iron deficiency, acute** and chronic infections, carcinomas, hypothyroidism and Kwashiorkor.

- **Total iron binding capacity (TIBC): It is elevated in** hypochromic anemias, acute hepatitis and pregnancy.

IRON DEFICIENCY – LAB FINDINGS

Decreased hemoglobin

Microcytic hypochromic anemia

Decreased serum iron

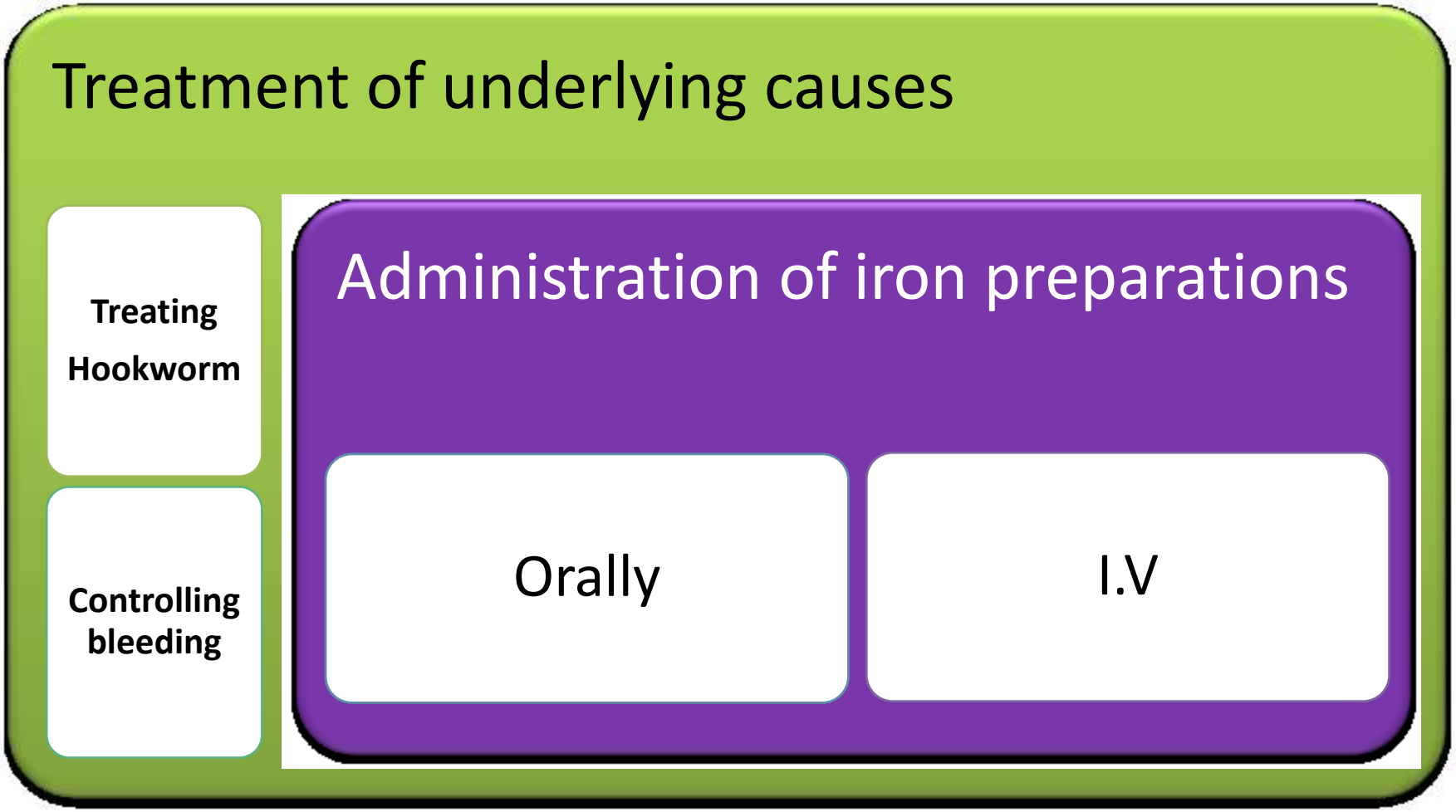
Increased serum total iron binding capacity

Decreased plasma ferritin

IRON DEFICIENCY - CAUSES

Decreased intake of iron	Decreased absorption of iron	Increased loss of Iron	Increased iron requirement
Mal-nutrition	**Achlor-hydria and chronic diarrhea**	**Bleeding, hookworm infestation**	**Pregnancy, infancy**

IRON DEFICIENCY – TREATMENT



- 100 mg of **iron + 500 mg of folic acid are given to pregnant women**

- 20 mg of iron + 100 mg folic acid to children. Iron tablets are usually given along with **vitamin C, to convert** it into ferrous form, for easy absorption.
- Unabsorbed iron may generate **free radicals and so, it is advisable to give vitamin E (to prevent free radical generation) along with** iron.

IRON OVERLOAD

Haemosiderosis

Increase in iron stores as haemosiderin

Without associated with tissue injury

Haemochromatosis

Excessive deposition of iron in the tissue

Associated with tissue injury

- **Iron vessels: Cooking in iron vessels increases the** availability of iron.
- **Bantu siderosis: Bantu tribe in Africa is prone to** hemosiderosis because the staple diet, corn, is low in phosphate content.

Prevention of IDA in infants

- Breastfeeding
- or iron-fortified formula for the first year.
- Cow's milk isn't a good source of iron for babies
- Iron from breast milk is more easily absorbed than the iron found in formula.

Iron obtained from animal products is much more easily absorbed by the body than iron from plant sources,

MCQ

Trushna Shah

Asst.Prof.in

Dept. of Biochemistry

S.B.K.S.MI&R.C,Pipariya

1.The daily iron requirement of an adult man is about

- (A) 10-20 mg% (B) 70 mg%
- (C) 40 mg% (D) 80 mg%

- **2.** Increase in iron stores as haemosiderin is called

  (A) Haemosiderosis
- (B) Hypercalcaemia
- (C) Alkalosis
- (D) Hypocalcaemia and alkalosis

- **3. Intestinal absorption of iron is hampered by**
- (A) Phosphate (B) Phytate
- (C) Proteins (D) Lactose

- **4. The daily iron requirement in pregnancy and lactation is about**
- (A) 40 mg (B) 80 mg
- (C) 50 mg (D) 100 mg

- **5. Storage form of iron is**
- (A) ferritin
- (B) heme
- (C) apoferritin
- (D) None of above


Thank you


thank you
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2. ATP Used in Gluconeogenesis

a) 50

b) 100

c) 6

d) 2

3. Shuttle used in Gluconeogensis

a) Malate

b) Carnitine

c) Pyruvate

d) Lactate

4. How many steps are irreversible in Gluconeogenesis

a) 10

b) 5

c) 6

d) 4

5. Substrate for Gluconeogenesis

a) Pyruvate

b) Glycerol

c) Lactate

d) All of above


Thank you


thank you
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THANK YOU