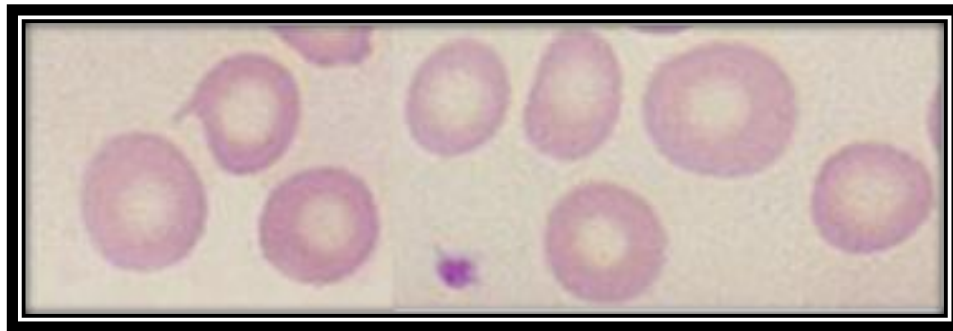


Microcytic Anemia: Iron Deficiency (IDA) and ACD*

IDA: iron deficiency anemia

*ACD: anemia of chronic disease



Howard J. Sachs, MD
www.12daysinmarch.com

Microcytic Anemia, IDA and ACD

- Part One
 - Anemia overview
 - Iron homeostasis

- Part Two
 - Iron Deficiency Anemia, diagnostics
 - Anemia of Chronic Disease

Anemia
Hgb < 12g/dL; HCT <37%

Microcytic
<80 fL

Normocytic
80-100 fL

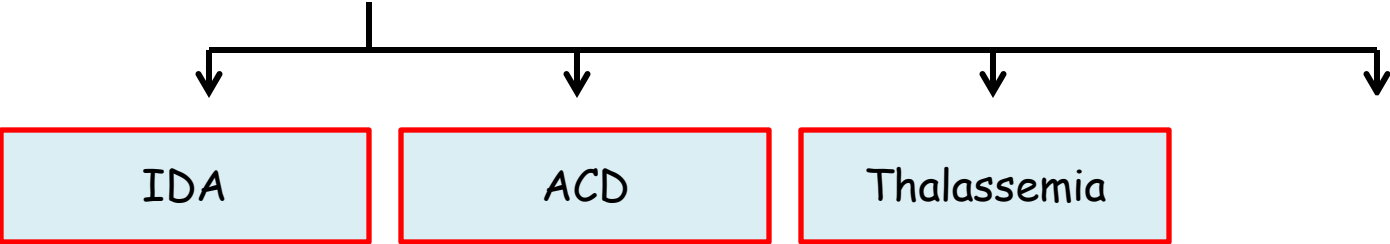
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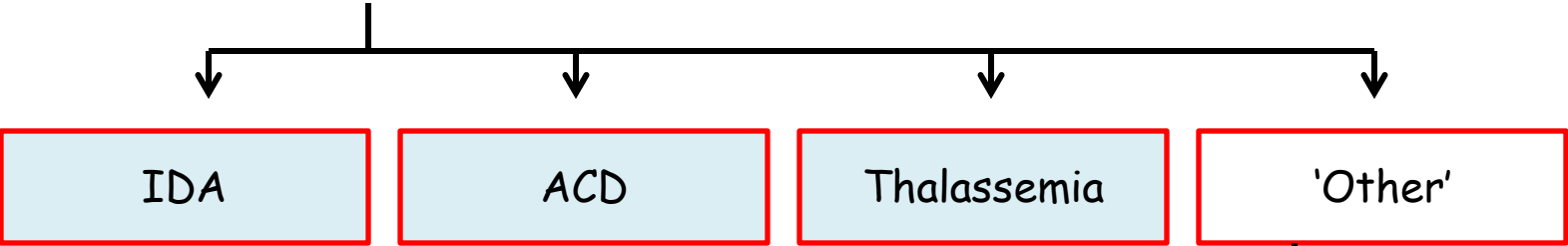
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Spherocytosis:
A disease of the red cell membrane (ankyrin)

Sideroblastic

Spherocytosis

Not hypochromic
↑ MCHC

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ACD: anemia of chronic disease
MCHC: mean cell hemoglobin concentration

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IDA

ACD

Thalassemia

'Other'

Hemoglobin	9.9 g/dL	12.0-16.0
Hematocrit	33.2 %	37.0-47.0
MCV	71.1 fl	83.0-101.0

Sideroblastic

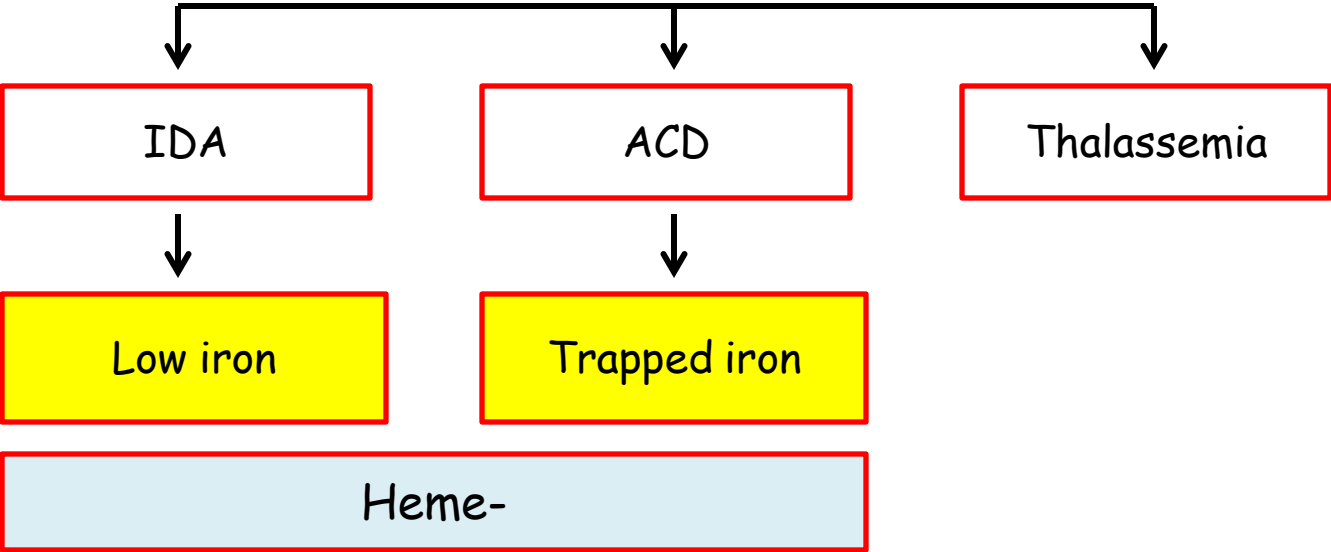
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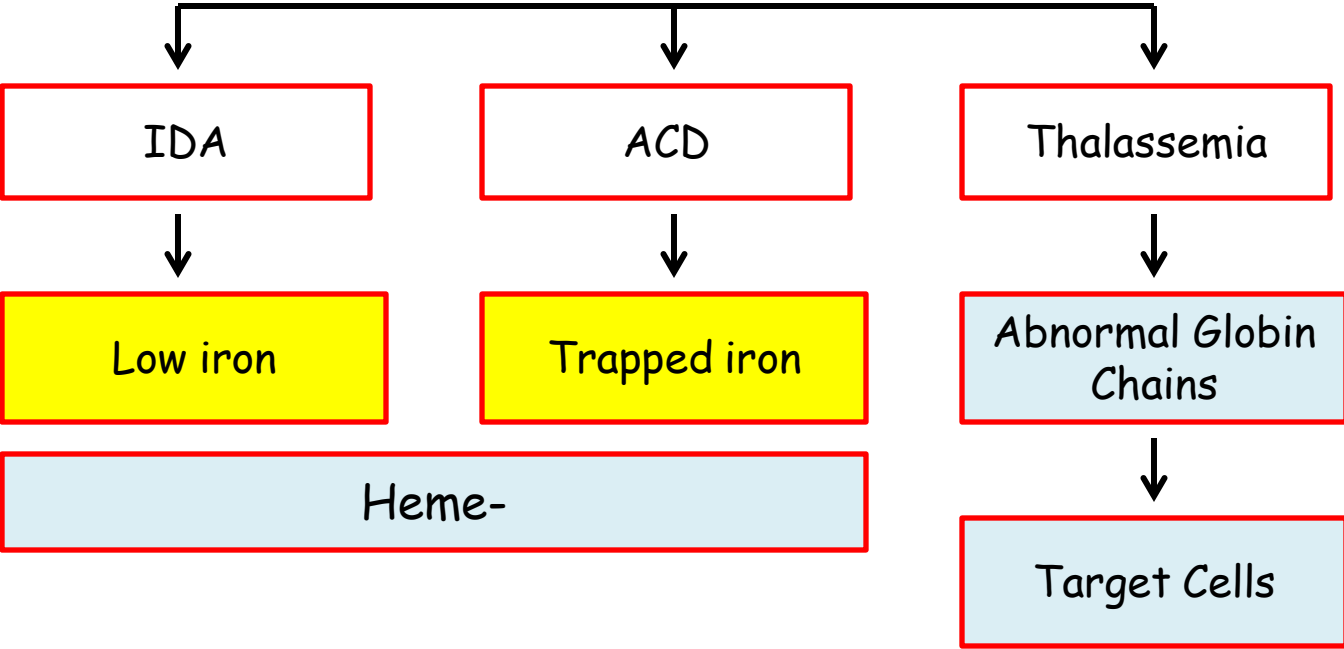
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IDA

ACD

Low iron

Trapped iron

NBME Goals:

1. Identify the presence of IDA
2. Distinguish from ACD

Presentation, IDA Overview

Low MCV and Anemia

Hemoglobin	9.9 g/dL	12.0-16.0
Hematocrit	33.2 %	37.0-47.0
MCV	71.1 fl	83.0-101.0

Smear, Indices

Diagnostics, IDA

Diagnostics, Etiologies

Treatment



Symptoms of Anemia
Low oxygen content and
CV response

Symptoms of Blood loss
GYN, GI

Symptoms of
Malabsorption

Physical Stigmata of IDA
Pale, koilonychia, glossitis

Presentation, IDA Overview

Low MCV and Anemia

Iron Homeostasis

Symptoms of Anemia
Low oxygen content and
CV response

Symptoms of Blood loss
GYN, GI

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Malabsorption

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Smear, Indices

Diagnostics, IDA

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Iron Metabolism

- Background
 - Only absorption and movement are regulated, **not excretion**.
 - Corollary 1: the body has no mechanism for excretion.
 - Corollary 2: iron deficiency must be pathologic.

Iron Metabolism

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Pathologic Mechanisms:

- Iron (blood) loss: GI, GYN, blood donor
- Increased utilization: Pregnancy, EPO rx
- Failure of: consumption or absorption

Iron Metabolism

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- Key Players in Regulation
 - **Divalent Metal Transporter** (DMT; absorption)
 - Iron regulatory protein, Iron response element
 - **Hepcidin** (movement)
 - Ferroportin

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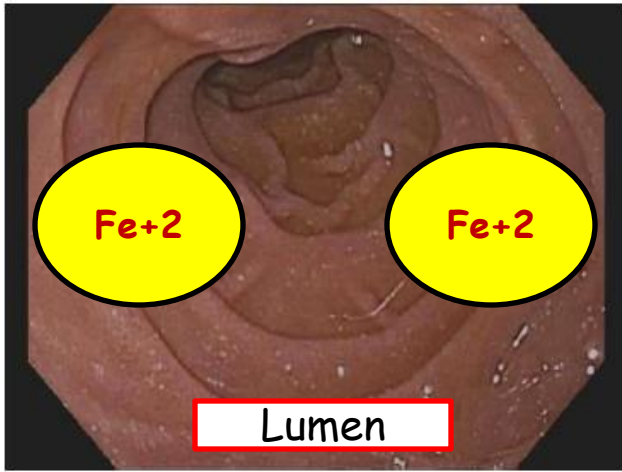
Iron homeostasis is regulated strictly at the level of intestinal absorption (DMT) and release of iron (hepcidin)

Iron Metabolism

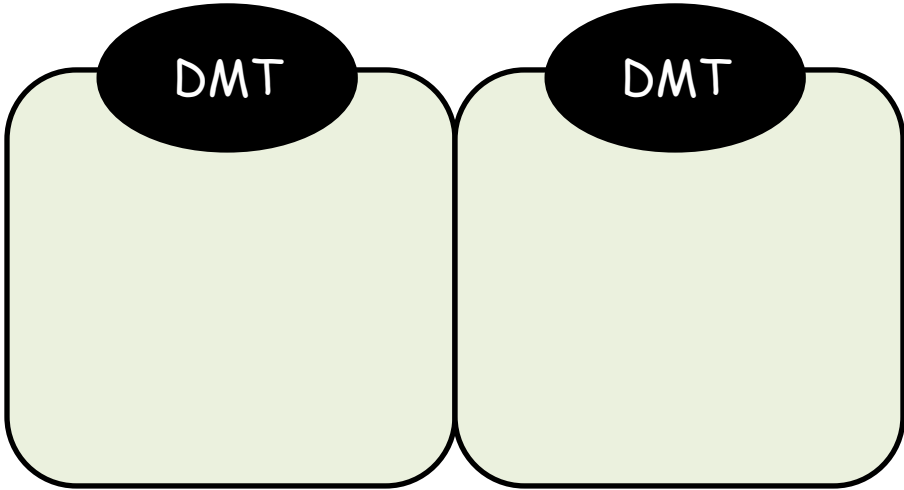
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- Key Players in **Transport and Storage**
 - Transferrin
 - Ferritin
 - Hemosiderin

Iron Metabolism

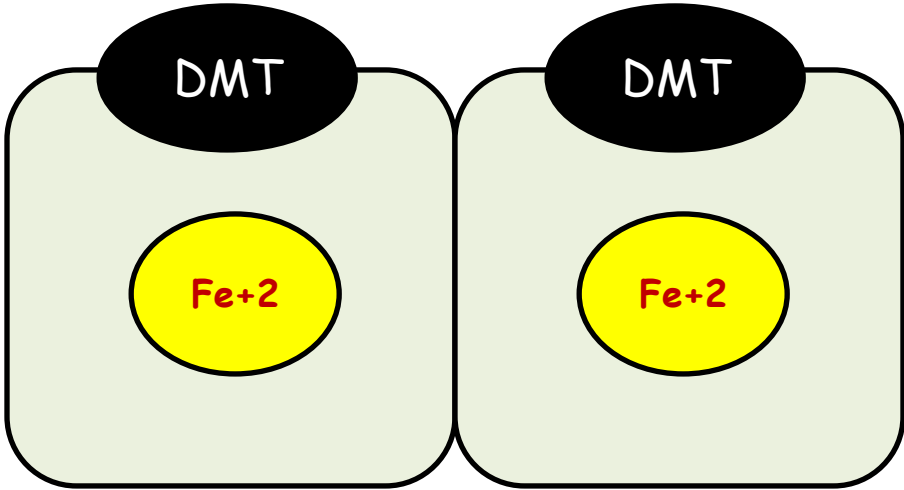
- Key Players in Regulation
 - Divalent Metal Transporter (DMT; **absorption**)
 - Iron regulatory protein (IRP), Iron response element (IRE)
 - Hepcidin (**movement**)
 - Ferroportin



Regulators



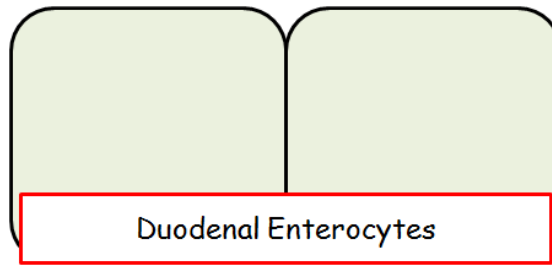
Duodenal Enterocytes



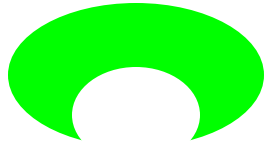
Duodenal Enterocytes

How is the DMT (divalent metal transporter) regulated?

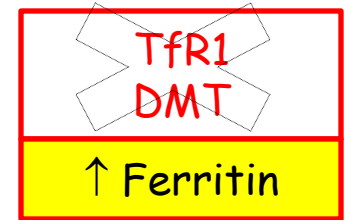
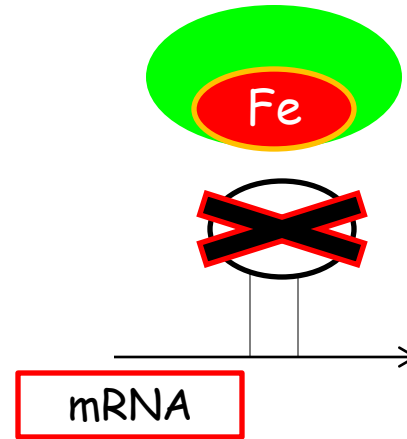
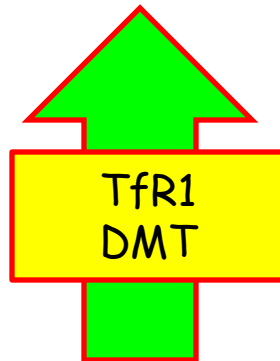
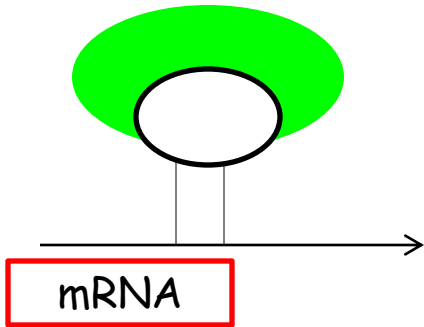
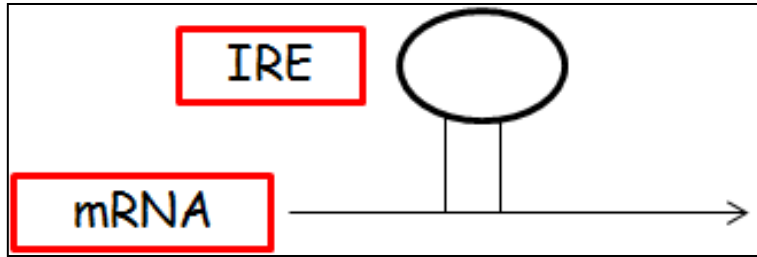
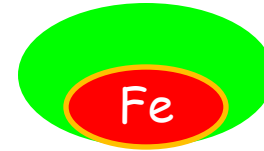
Low Fe



High Fe



IRP



Duodenal Lumen

Fe+2

DMT

Enterocyte

DMT

Fe+2

?

Iron absorption is regulated (DMT).

Movement is also regulated.

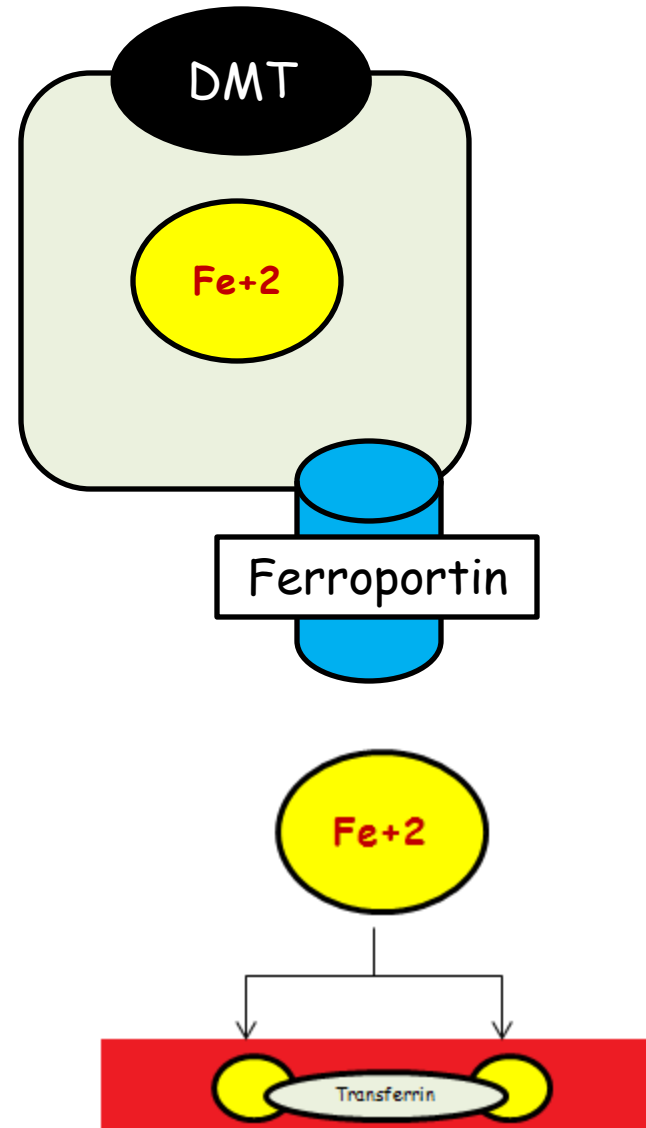
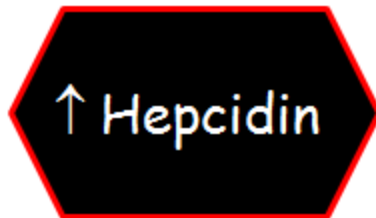
Which hepatocyte hormone regulates movement AND how is it accomplished?

Hepcidin

A polypeptide synthesized in the liver.

It regulates the **MOVEMENT** of iron through regulation of ferroportin.

When iron is abundant, hepcidin increases and **leads to degradation of ferroportin channel.**



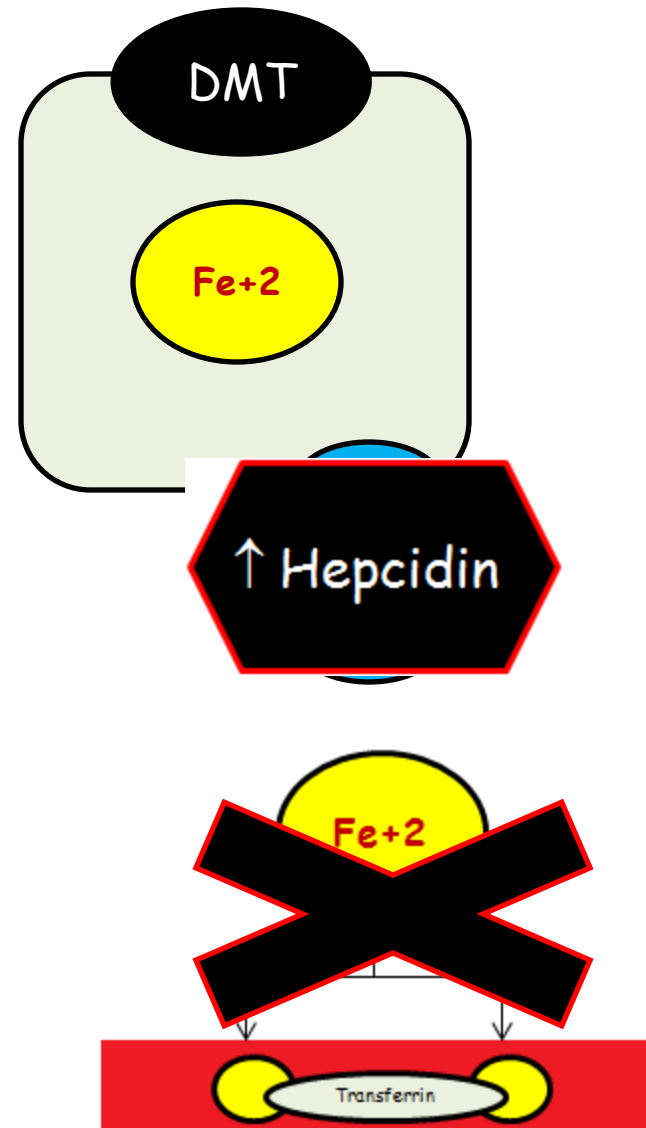
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Increased Hepcidin when iron is abundant



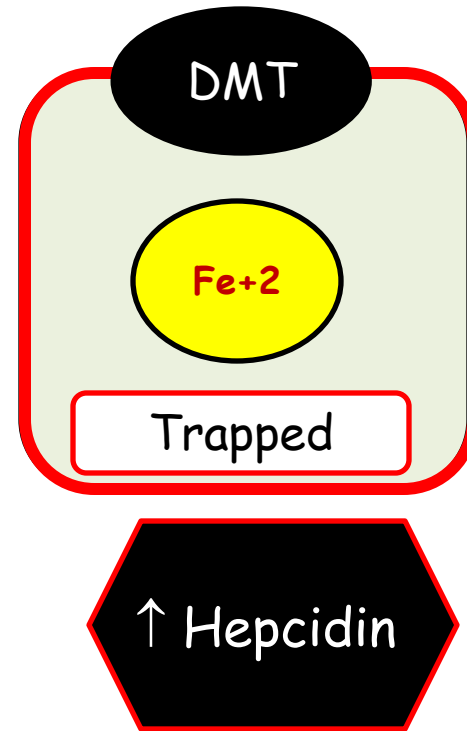
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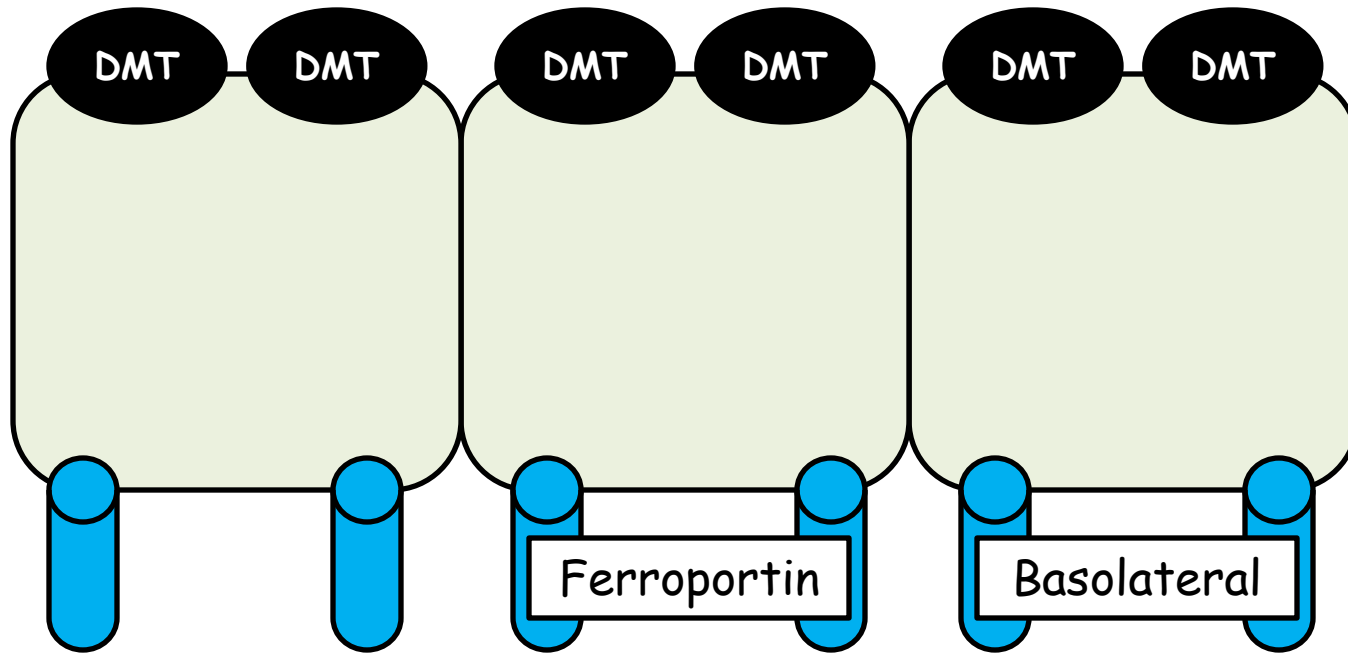
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Iron becomes 'trapped' in enterocyte and RES.



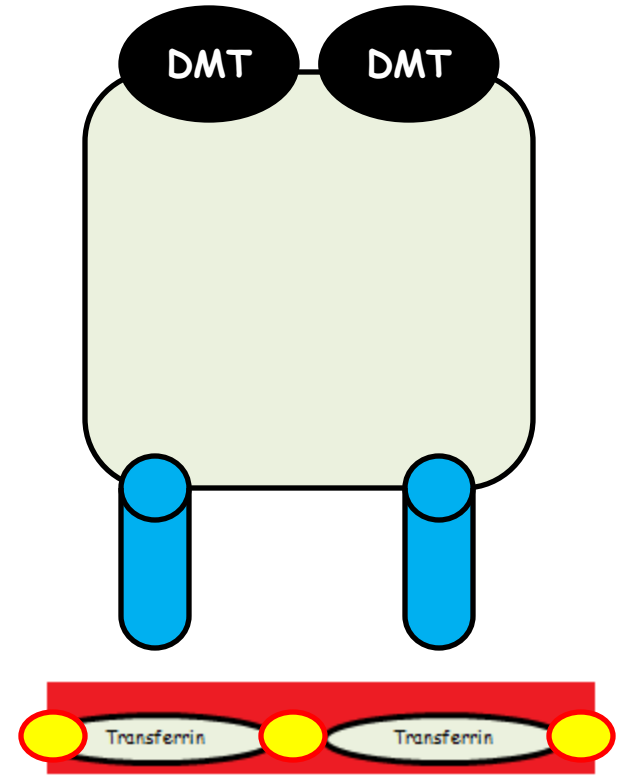
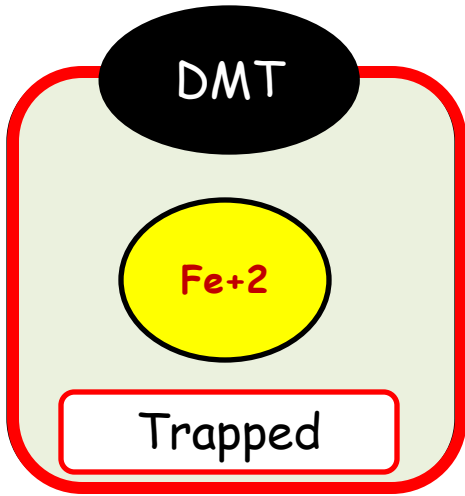
So what happens in IDA when iron is not abundant?



IDA and Regulators:

Upregulation of DMT (stimulated by IRP, IRE)
Downregulation of Ferritin
Decreased level of hepcidin





Anemia of
Chronic Disease

↑ Hepcidin

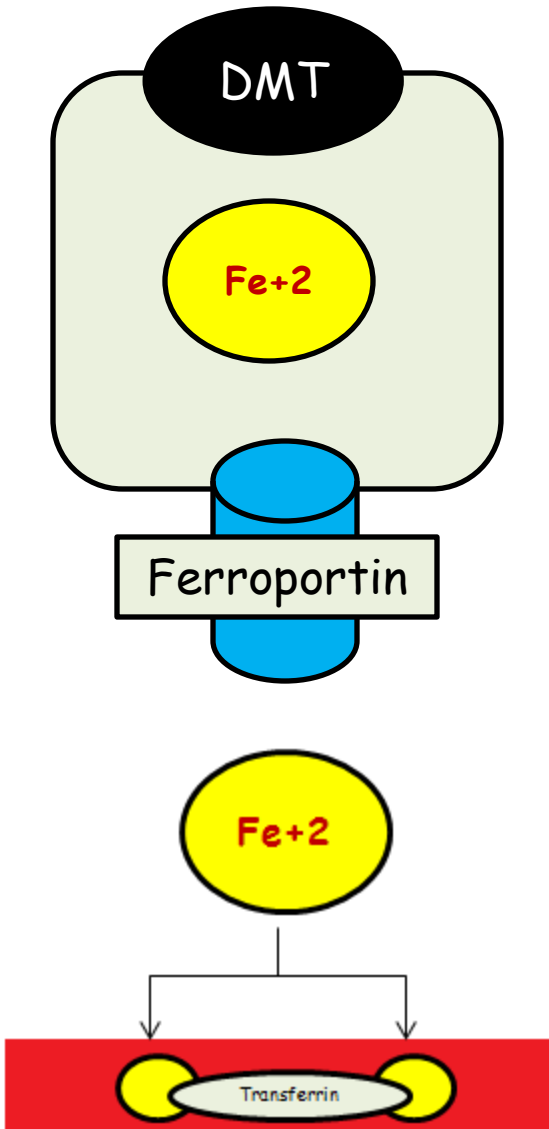


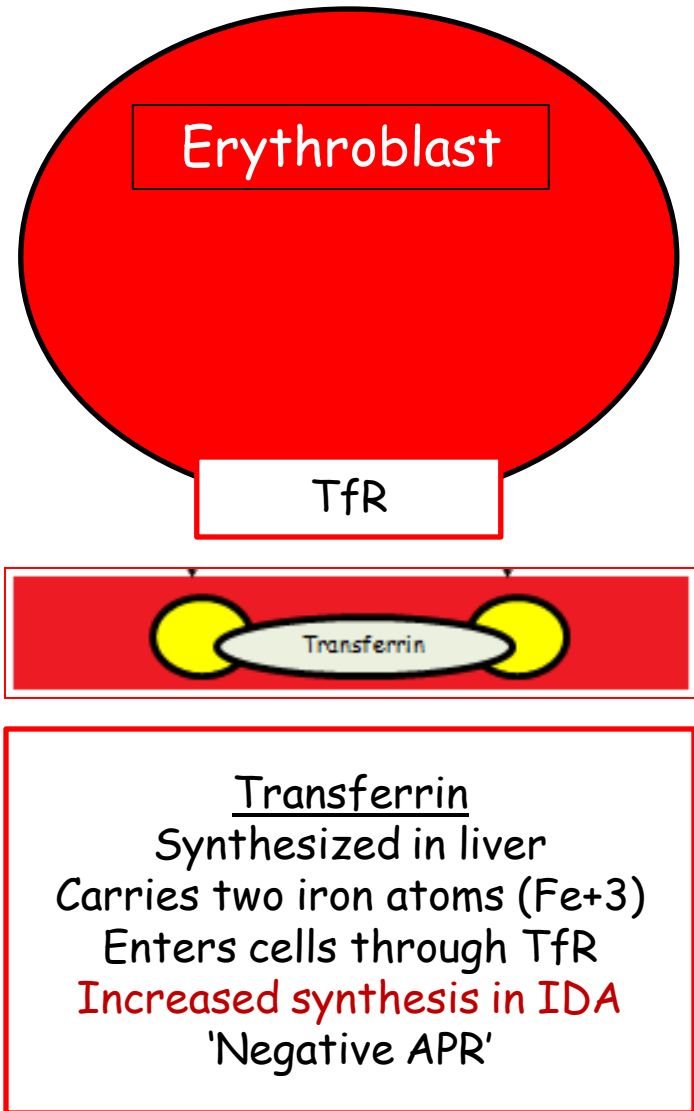
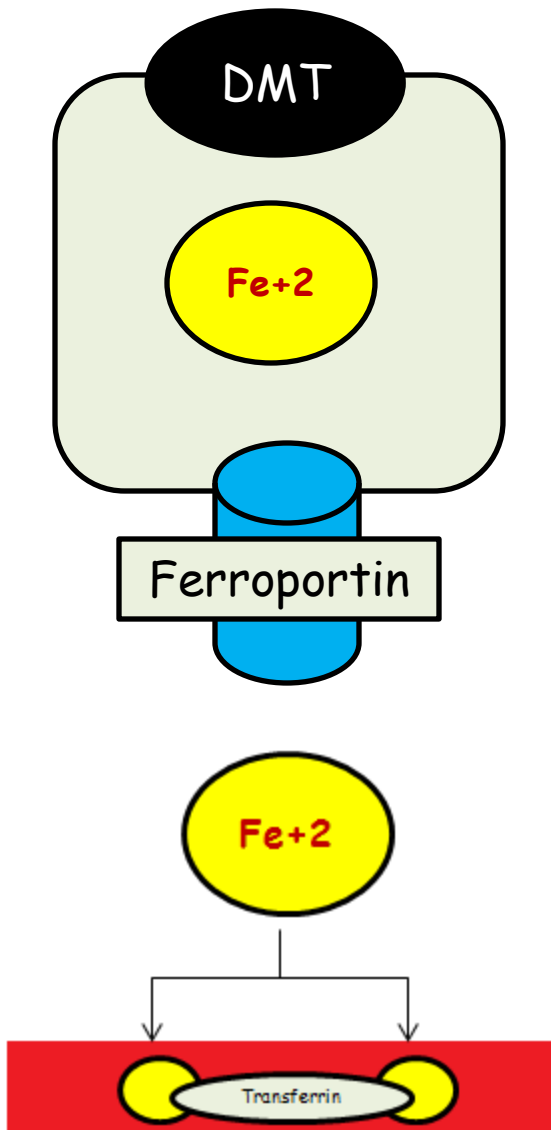
Hemochromatosis

↓ Hepcidin

Iron Metabolism

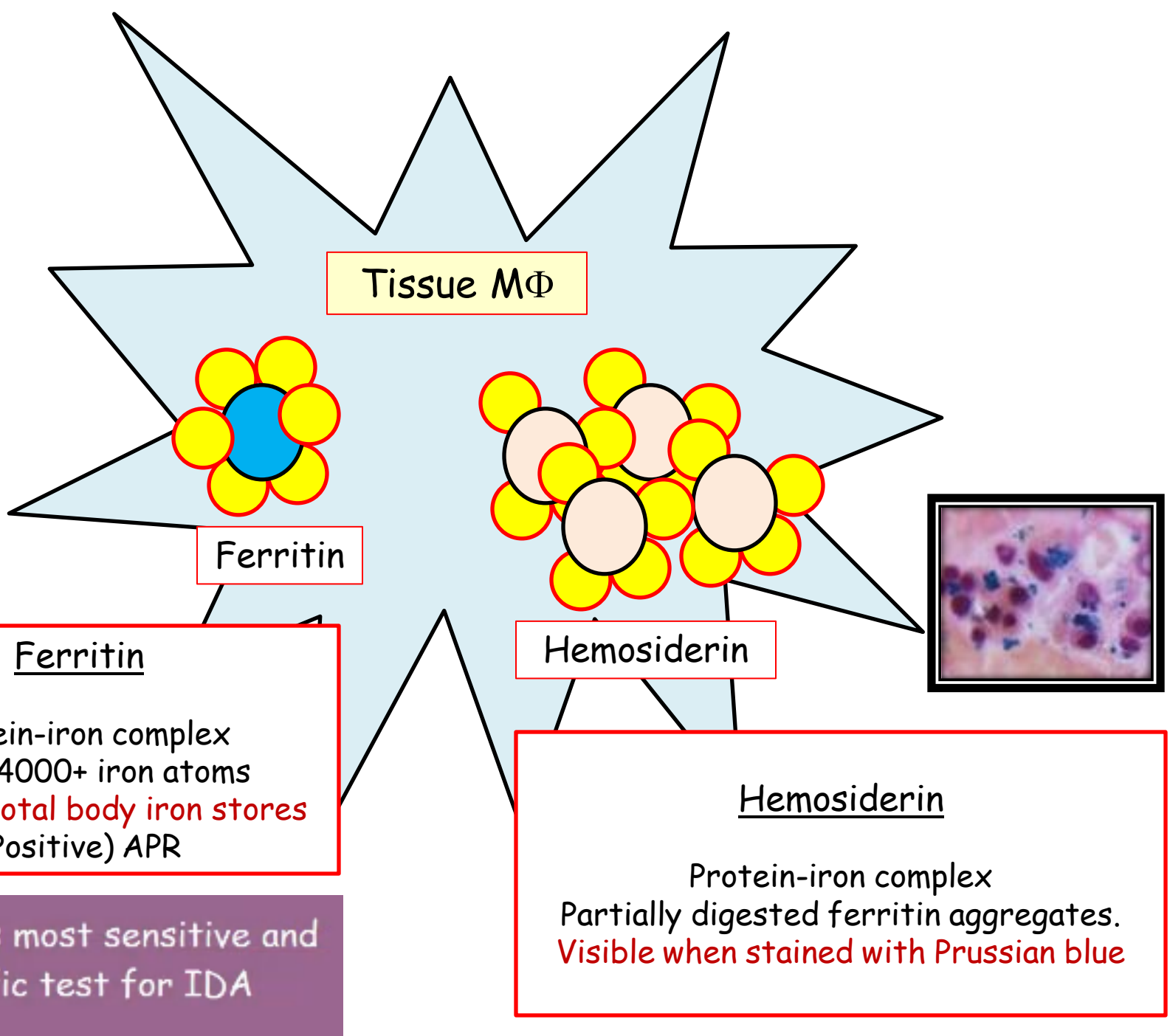
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 - Transferrin
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Transferrin
 Synthesized in liver
 Carries two iron atoms (Fe^{+3})
 Enters cells through TfR
 Increased synthesis in IDA
 'Negative APR'

TfR: transferrin receptor
 APR: acute phase reactant



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Part One:
Anemia Overview
Iron Homeostasis

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