

Microcytic Anemia: Iron Deficiency (IDA) and ACD*

IDA: iron deficiency anemia

*ACD: anemia of chronic disease

Part Two:
IDA: key diagnostic features
ACD overview

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Presentation, IDA Overview

Low MCV and Anemia

Symptoms of Anemia
Low oxygen content and
CV response

Symptoms of Blood loss
GYN, GI

Symptoms of
Malabsorption or Pica

Physical Stigmata of IDA
Pale, koilonychia, glossitis

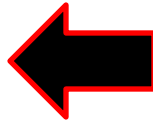
Iron Homeostasis

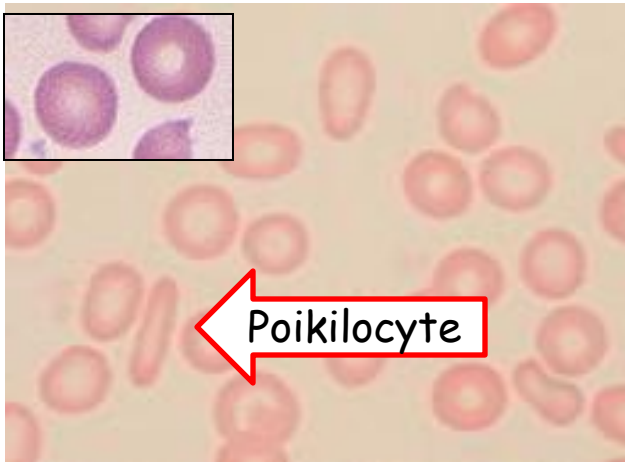
Smear, Indices

Diagnostics, IDA

Diagnostics, Etiologies

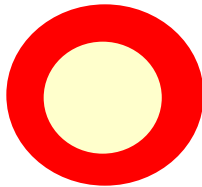
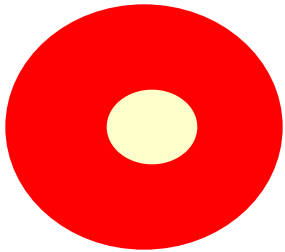
Treatment





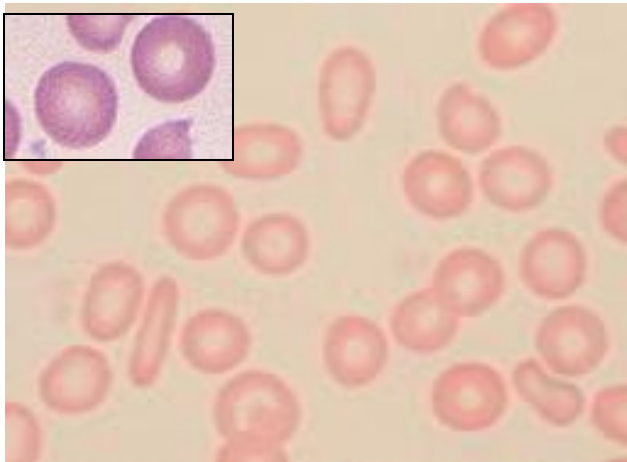
Low MCV and Anemia

Smear, Indices



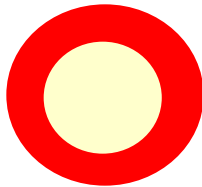
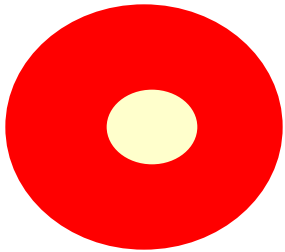
Normocytic
(inset above)
Normal zone of
central pallor
(~1/3 size of cell)

Microcytic
Hypochromic
Increased zone
of central pallor



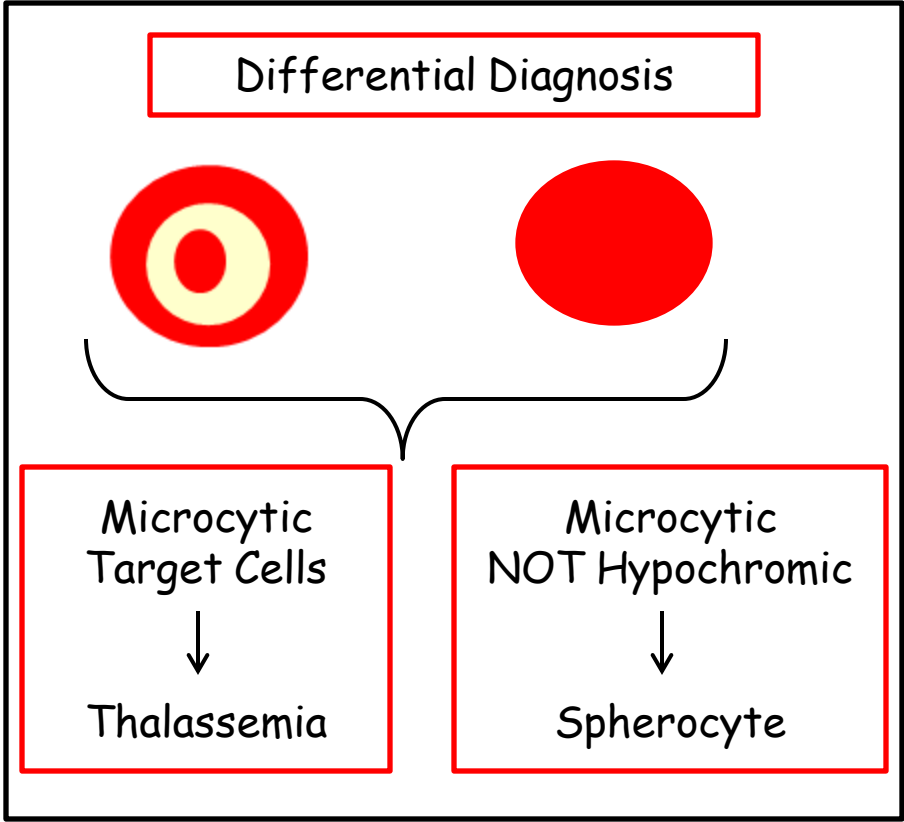
Low MCV and Anemia

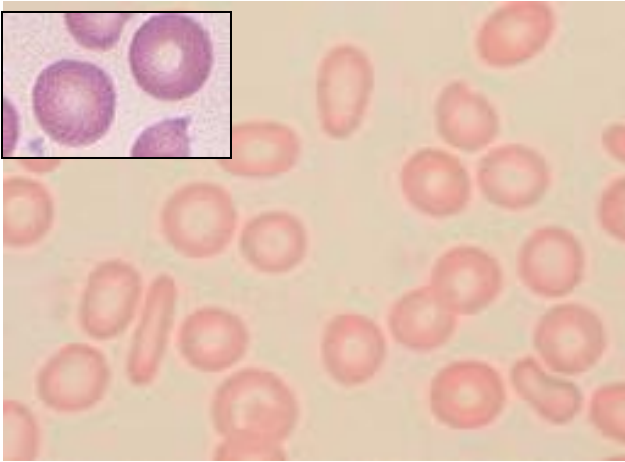
Smear, Indices



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(inset above)
Normal zone of
central pallor
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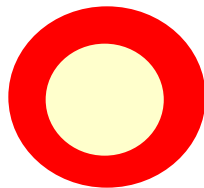
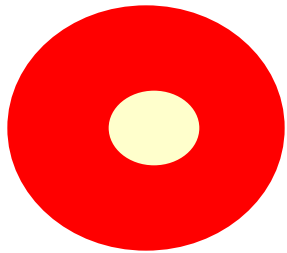
Microcytic
Hypochromic
Increased zone
of central pallor





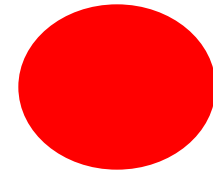
Indices: MCHC (mean cell hgb concentration)

The average concentration of hemoglobin
in a given volume of packed red cells
(expressed as gm/dL)



Normocytic
(inset above)
Normal zone of
central pallor
(~1/3 size of cell)

Microcytic
Hypochromic
Increased zone
of central pallor



Microcytic
Target Cells

↓
Thalassemia

Microcytic
NOT Hypochromic

↓
Spherocyte

Differential Diagnosis

NI



MCHC



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GYN, GI

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Pale, koilonychia, glossitis

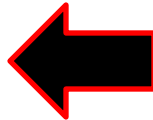
Iron Homeostasis

Smear, Indices

Diagnostics, IDA

Diagnostics, Etiologies

Treatment



Diagnostics, Iron Deficiency Anemia (IDA)

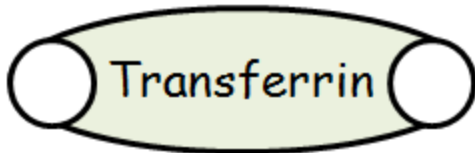
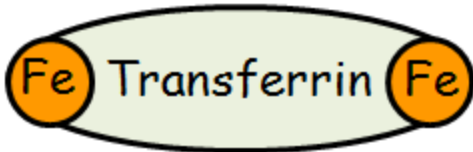
Summary:

1. Low Serum Iron level
2. High total iron binding capacity (TIBC)
 - 'Functional assessment' of transferrin
3. Low Iron (transferrin) Saturation (Fe/TIBC)
4. Low Ferritin
5. Bone marrow iron stores (hemosiderin) depleted

Previously reviewed:

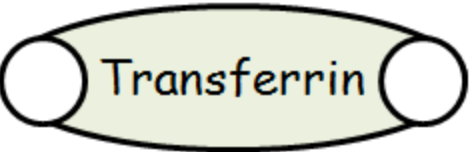
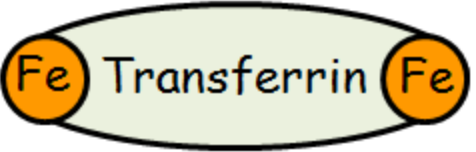
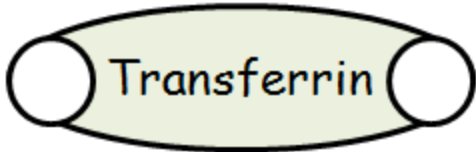
Smear: Microcytic, Hypochromic RBC
Indices: ↓ MCH/MCHC

Total Iron Binding Capacity (Transferrin)



Normal iron binding capacity is $\sim 1/3$

Total Iron Binding Capacity (Transferrin)

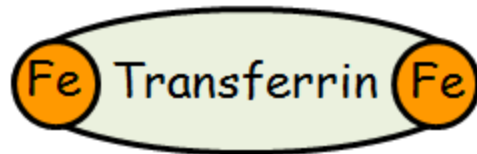


Normal iron binding capacity is ~1/3

Binding capacity refers to these 'empty seats'
There is room to accommodate more iron travelers



In IDA, the transferrin level actually rises,
further increasing the IBC.

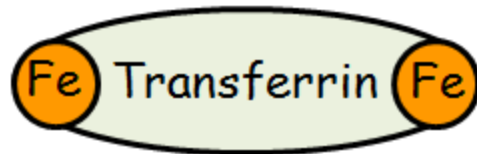


Normal

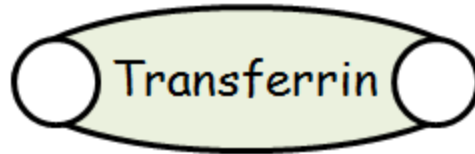


IDA
↑ TIBC

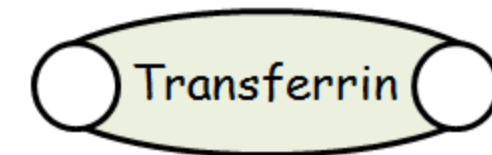
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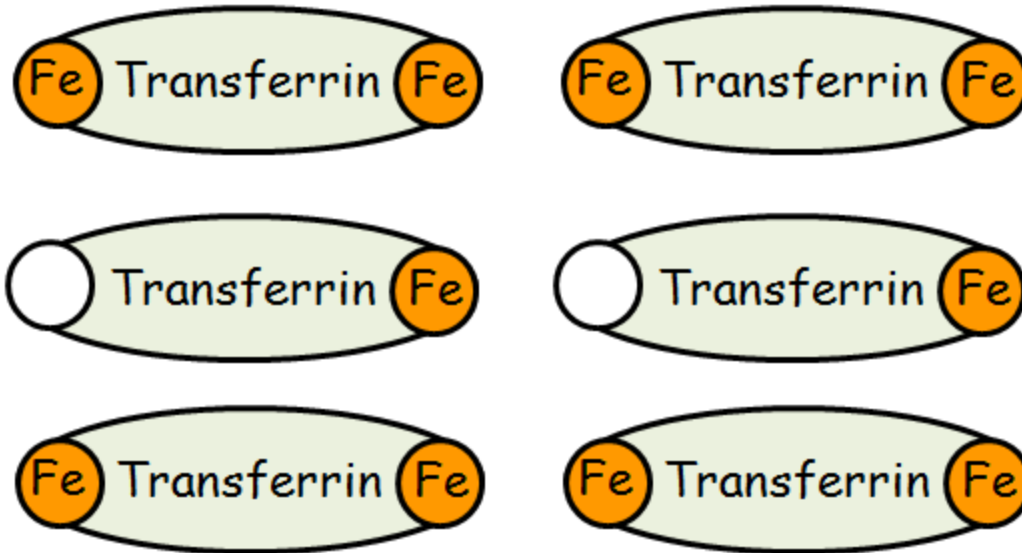
Normal



IDA
↑ TIBC



In IDA, there is an elevated TIBC
(Plenty of available seats)



Iron Overload (Hemochromatosis):

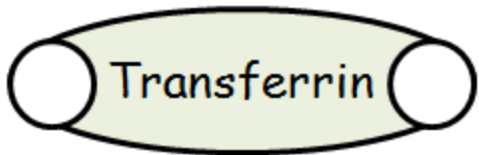
TIBC is ↓↓

Transferrin is saturated with iron;
there is no place for iron to bind (low capacity)

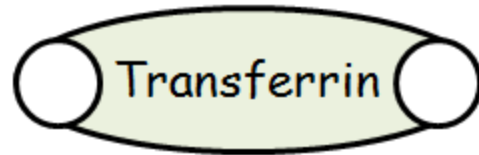


Sorry, we're full.
No more capacity

$$\text{Iron (transferrin) Saturation} = \text{Fe} / \text{TIBC}$$



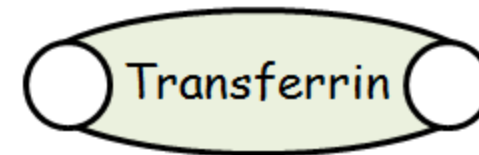
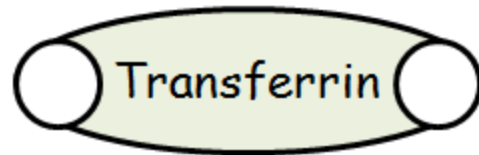
Low



High



Low



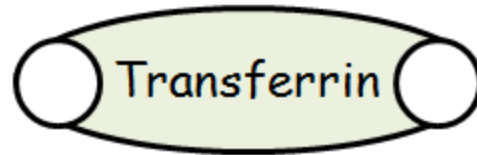
Test	Result	Reference
Iron	18 mcg/dL	28-170
Iron Binding Capacity	511 mcg/dL	255-450
Iron Saturation	4 %	20-50

IDA: <10% (ACD: 10-20%)

$$\text{Iron (transferrin) Saturation} = \text{Fe} / \text{TIBC}$$



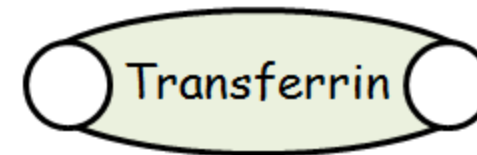
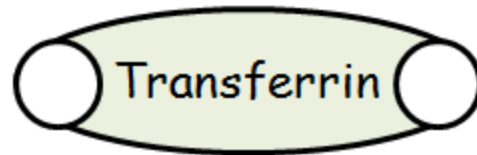
Low



High



Low

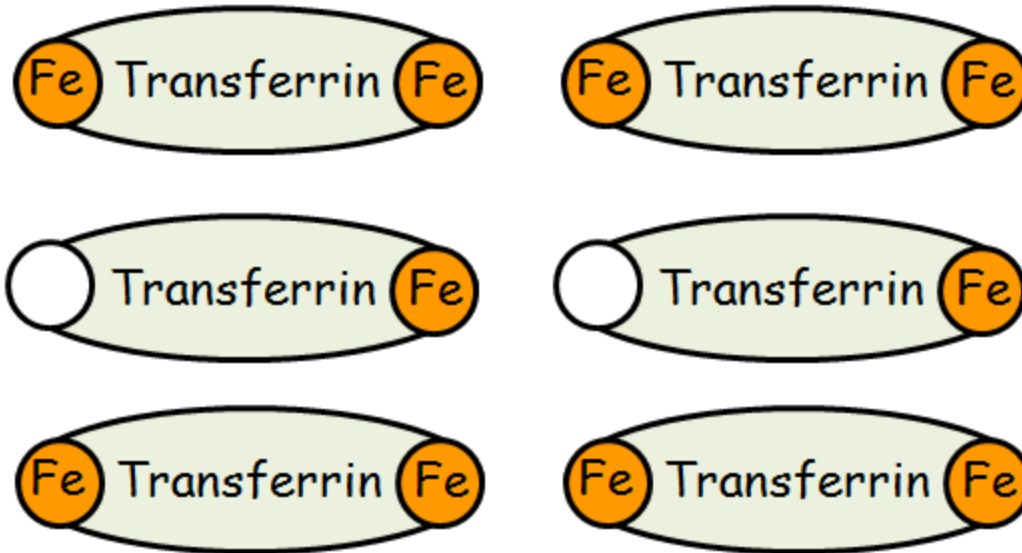


Test	Result	Reference
Iron	18 mcg/dL	28-170
Iron Binding Capacity	511 mcg/dL	255-450
Iron Saturation	4 %	20-50

IDA: <10% (ACD: 10-20%)

Serum Ferritin Level

Test	Result	Reference
Ferritin	5 ng/mL	11-306



Iron Overload (Hemochromatosis):

Iron is elevated

TIBC is ↓↓

Iron Saturation = $\text{Fe}\uparrow / \text{TIBC}\downarrow = \text{elevated } (>50\%)$

Presentation, IDA Overview

Low MCV and Anemia

Iron Homeostasis

Smear, Indices

Diagnostics, IDA

Summary:

1. Low serum iron level
2. High total iron binding capacity (TIBC)
 - Indirect measure of transferrin
3. Low iron saturation (Fe/TIBC)
4. Low Ferritin
5. Bone marrow iron stores (hemosiderin) depleted

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GYN, GI

Symptoms of
Malabsorption

Physical Stigmata of IDA
Pale, koilonychia, glossitis

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Diagnostics, Etiologies

Treatment



IDA, Etiologies

- Blood Loss (any source including pulmonary, GU)
 - GI, acute
 - GI, chronic

Chronic GI blood loss is big money.

They'll present indices of IDA

You'll be proud to figure it out 😊.

Then they ask most likely underlying etiology???

Language: chronic GI blood loss, colon cancer (right sided)

IDA, Etiologies

- Blood Loss (any source including pulmonary, GU)
 - GI, acute
 - GI, chronic
 - GYN, menstruation

They'll present indices of IDA
You'll be proud to figure it out.

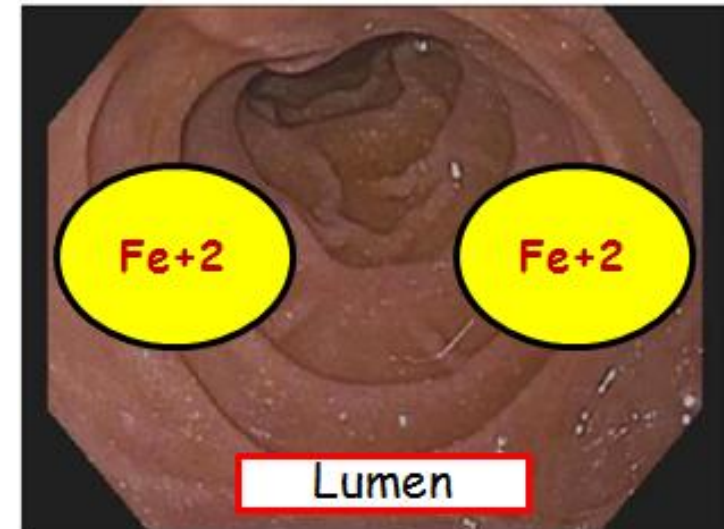
Then they ask most likely underlying etiology???

Language: look for the occult such as fibroid

(other options will include all kinds of bone marrow junk and you'll be tempted.
The vignette might include SLE or RA and you'll think hemolysis or ACD).

IDA, Etiologies

- Blood Loss (any source including pulmonary, GU)
 - GI, acute
 - GI, chronic
 - GYN, menstruation
- Nutritional
- Malabsorption syndrome
 - GI: Celiac disease, Gastric bypass



IDA, Rx

- Identify and Rx underlying cause
 - This is the majority
- Supplemental iron
 - Reticulocytosis: 10 d
 - Replenishment: 6 mos (assuming underlying cause corrected)
- Special notes:
 - Be familiar with the oxygen content section and cardiovascular response to anemia (previously covered).
 - Reactive thrombocytosis may be seen in ~10%

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Anemia of Chronic (Inflammatory) Disease

Anemia of Chronic (Inflammatory) Disease

- Background:
 - Best to consider it an inflammatory disorder with manifestations and lab parameters 2° to elevated cytokines
 - IL-6 ↑ raises hepcidin → iron trapping (in MΦ of RES)
 - Transferrin ↓: it is a **negative** acute phase reactant (APR)

Anemia of Chronic (Inflammatory) Disease

- Background:
 - Best to consider it an inflammatory disorder with manifestations and lab parameters 2° to elevated cytokines
 - IL-6 ↑ raises hepcidin → iron trapping (in MΦ of RES)
 - Transferrin ↓: it is a **negative** acute phase reactant (APR)
- Data
 - HCT ~ 30%; **MCV >75**; Reticulocytes low
 - Transferrin ↓ → low TIBC
 - Iron Saturation (Fe ↓/IBC ↓) mildly decreased: >10% (normal ~20%)
 - Ferritin: normal or elevated
 - Bone marrow: normal iron stores (hemosiderin in MΦ)

Lab Parameters: Anemia of Chronic (Inflammatory) Disease

Iron trapped due to high hepcidin

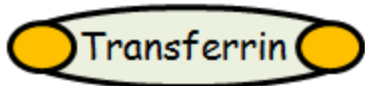
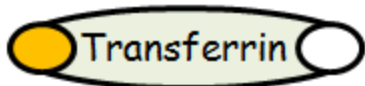
- Serum iron: low (its trapped)

Transferrin, negative APR \Rightarrow low

- **TIBC** (transferrin availability) low

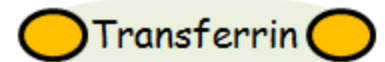
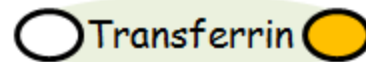
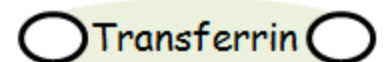
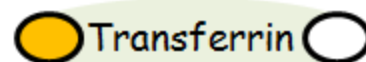
Fe Saturation: 'Normal-ish'

Both iron and transferrin are proportionately low



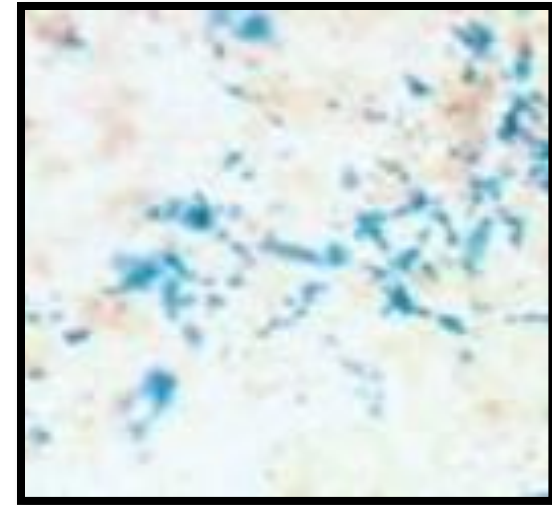
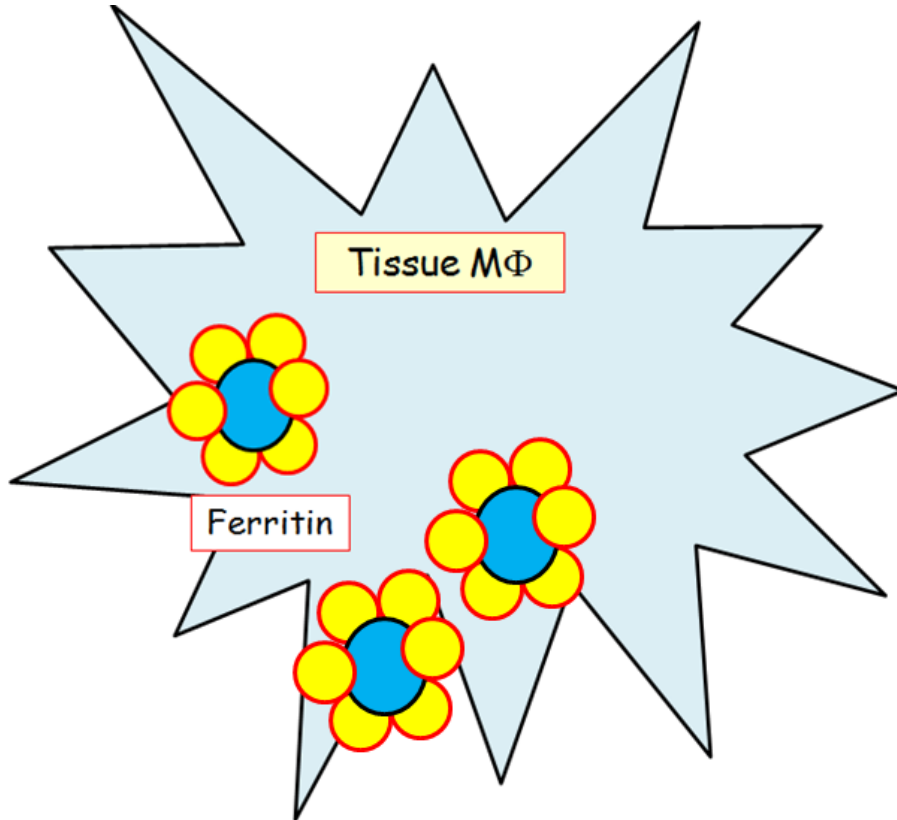
Low

TIBC



Fe/TIBC \Rightarrow 'Normal' Saturation

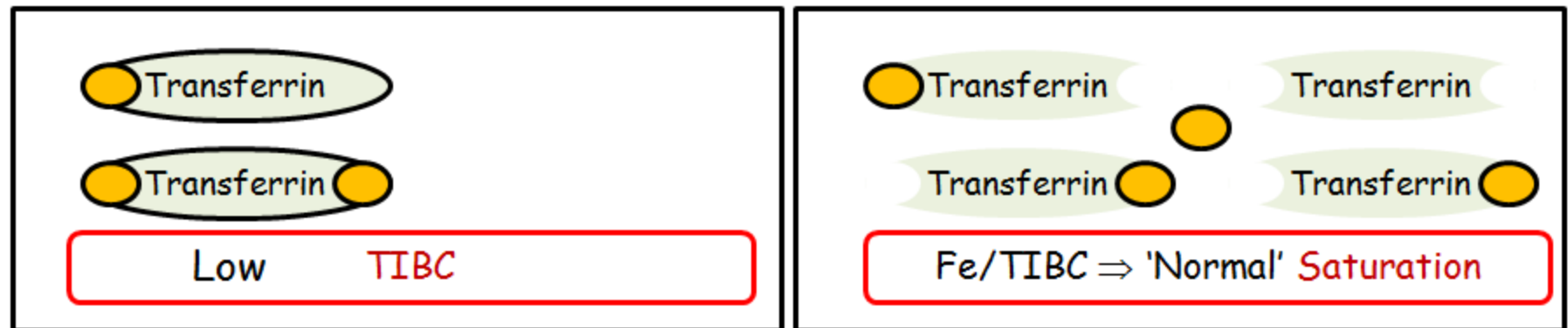
Lab Parameters: Anemia of Chronic (Inflammatory) Disease



↑ Ferritin in ACD
It is an APR
Not useful diagnostically
(low in IDA)

Bone Marrow
Stains normal (Prussian blue)
Iron trapped in MΦ (not erythroblast)
(If they report normal BM, it isn't IDA)

IDA

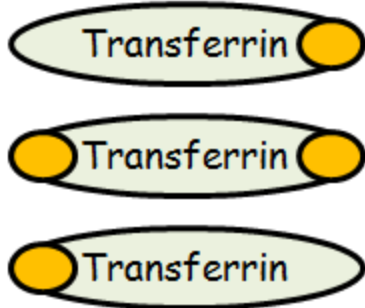


ACD

Low Ferritin

IDA

Bone Marrow
Decreased iron stores



TIBC High



Fe/TIBC \Rightarrow Low Saturation



Low TIBC



Fe/TIBC \Rightarrow 'Normal' Saturation

High-ish Ferritin

ACD

Bone Marrow
Normal iron stores

IDA

Classic Question

They will come after you with an old, tired weak patient with inflammatory symptoms such as hand and wrist pain/swelling. She will be anemic. MCV will be 75. The serum iron will be low. They will give you **TIBC and/or iron (transferrin) saturation**.

You will need to choose the underlying cause of her anemia:

Rheumatoid arthritis
Chronic GI blood loss (GI neoplasm)

ACD

IDA

Classic Question

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You will need to choose the underlying cause of her anemia:

Rheumatoid arthritis
Chronic GI blood loss (GI neoplasm)

IDA: low iron, high binding capacity (transferrin elevated), low Fe saturation (<10%)

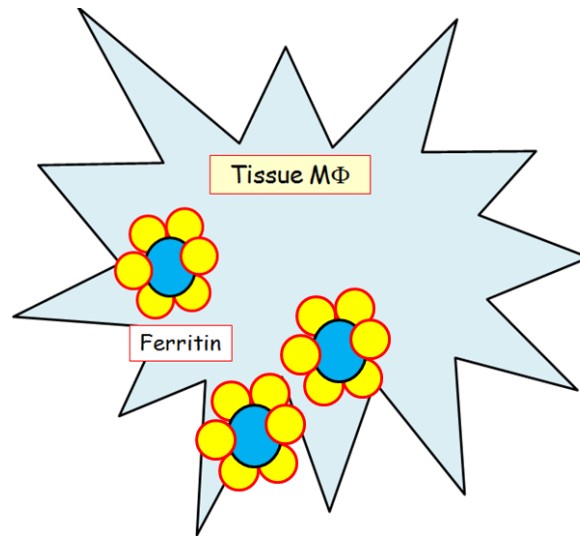
ACD: low iron, low binding capacity (transferrin decreased), Fe saturation (10-20%)

ACD

Anemia of Chronic (Inflammatory) Disease

- Background:
 - Best to consider it an inflammatory disorder with manifestations and lab parameters 2° to elevated cytokines
 - IL-6 ↑ raises hepcidin → iron trapping (in MΦ of RES)
 - Transferrin ↓ because it is a negative acute phase reactant (APR)
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 - HCT ~ 30%; MCV >75; Reticulocytes low
 - Transferrin ↓ → low TIBC
 - Iron Saturation (Fe ↓/IBC ↓) mildly decreased: >10% (normal ~20%)
 - Ferritin: normal or elevated
 - Bone marrow: normal iron stores (hemosiderin in MΦ)
- Notes
 - EPO: reduced; does not respond to ↓ oxygen content 2° to inflammatory cytokines (IL-1, TNF)

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