

# Anemias and "All that Jazz"

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## Objectives

- Understand pathophysiology of RBC production/destruction
- Evaluate components of CBC for preliminary diagnosis of anemia
- Select and interpret complementary lab studies to systematically diagnose anemias

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Concept #1 Let's start from the beginning!

## Where do RBCs come from?

- a. Liver
- b. Spleen
- c. Kidney
- d. Bone marrow

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**Why does the bone marrow  
make RBCs?**

...because erythropoietin told it to!

RBCs

Erythropoietin (EPO) is an endocrine hormone made in the kidney!

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**When bone marrow is  
exposed to EPO...  
RBC production can  
increase 5 fold!**

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**What makes a kidney  
release EPO?**

After several days of low O<sub>2</sub>, and when detected by kidneys, EPO is released.  
The more EPO that is released, the more RBCs are produced!

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**True or False**

**A patient who has COPD probably has an elevated hematocrit.**

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**Concept #1**

**RBCs are produced by the bone marrow in response to EPO.**

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**True or False:**

**A reticulocyte is an immature RBC.**

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## Reticulocytes

Erythrocyte

Reticulocytes = 1% of circulating RBCs

Spend about 3 days in the bone marrow, then are released into circulation. After the 4<sup>th</sup> day.....

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## ...reticulocyte becomes an ERYTHROCYTE!

- NO nucleus!
- Biconcave discs
- Very flexible and can change shape to get thru capillaries

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## Lifespan of RBCs

Live for about 100-120 days and then are "eaten" by macrophages and removed from circulation.

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**As long as.....**

**Rate of RBCs**

Removed (1%) = Rate produced (1%)

All is good!

No anemia, no polycythemia!

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**“Mrs. Boudreaux”**

42 year old female, otherwise healthy, non-smoker

**CC:** Fatigue for the past 4-6 weeks; attempted to donate blood and was refused related to “low blood count”

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**Rule 1:**

**Anemia is**

**Never Normal!**

*Always suspect that something is going on with your patient!*

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**“Mrs. Boudreaux”**

42 year old female, otherwise healthy

**CC:** Fatigue for the past 4-6 weeks; attempted to donate blood and was deferred related to “low blood count”

**History:** SOB when walking up stairs, denies chest pain, *no history of recent weight loss, loss of appetite, denies fever/night sweats*

**denies dark or bloody stools; reports heavy monthly menses R/T uterine fibroid**

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**So, the anemia appears to be something of recent onset. If this had been lifelong, what might be part of your differential?**

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**“Mrs. Boudreaux”**

42 year old female, otherwise healthy

**Meds:** none (no ASA, no herbals, no OTCs)

**FH:** Adopted, does not know FH (thinking of thalassemias, hemoglobinopathies, etc.)

**PE:** Pale conjunctiva, Grade I/VI systolic murmur, no lymphadenopathy, no jaundice or hepatosplenomegaly, *denies bone pain*

**Rectal exam WNL, stool: brown, heme negative**

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**Mrs. Boudreaux' CBC**  
**Is our patient anemic?**

CBC	Patient	Normal Values
WBC	8.0	4-10 million/mm <sup>3</sup>
Hgb	8.1 g/dL	12.6-16.1 g/dL
Hct	24.3%	38-47.7 %
RBC	3.8	3.93 – 5.69 million/mm <sup>3</sup>
MCV	60	80-99.5 fL
MCH	20	27.5-33.3 pg/cell
MCHC	34.2	33.3-35.5 g/L
RDW	16.5	11.4-14.4%
Platelets	500,500	150,000-400,000x10 <sup>3</sup> uL
Reticulocyte count	3%	0.5-1.5%
Absolute Retic count	40,000	25,000-75,000 uL

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**Mrs. Boudreaux' CBC**  
**What kind of anemia?**

CBC	Patient	Normal Values
WBC	8.0	4-10 million/mm <sup>3</sup>
Hgb	8.1 g/dL	12.6-16.1 g/dL
Hct	24.3%	38-47.7 %
RBC	4.1	3.93 – 5.69 million/mm <sup>3</sup>
MCV	60	80-99.5 fL
MCH	20	27.5-33.3 pg/cell
MCHC	34.2	33.3-35.5 g/L
RDW	16.5	11.4-14.4%
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**Peripheral Smear**  
**“Window to the bone marrow”**

Normocytic, normochromic  
Red Blood Cells

Microcytic, hypochromic  
Red Blood Cells

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**Mrs. Boudreaux' Blood Smear:**  
**microcytic, hypochromic red cells**

Normocytic, normochromic Red Blood Cells	Microcytic, hypochromic Red Blood Cells
Normal	"Mrs. Boudreaux"

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**Microcytic,  
Hypochromic anemia**

**Differential Diagnosis:**

- Iron deficiency
- Thalassemia
- Anemia of chronic disease
- Sideroblastic anemia

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**Mrs. Boudreaux' CBC**

**What does the increased RDW indicate?**

CBC	Patient	Normal Values
WBC	8.0	4-10 million/mm <sup>3</sup>
Hgb	8.1 g/dL	12.6-16.1 g/dL
Hct	24.3%	38-47.7 %
RBC	4.1	3.93 – 5.69 million/mm <sup>3</sup>
MCV	60	80-99.5 fL
MCH	20	27.5-33.3 pg/cell
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Platelets	500,400	150,000-400,000x10 <sup>3</sup> uL
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## RDW

**RDW (red cell distribution width):**  
**indicates degree of variation in**  
**RBC size (<15% is normal)**

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## Anisocytosis

**Red cells are not the same size!**

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### Mrs. Boudreaux' CBC

**What does the increased PLT count indicate?**

CBC	Patient	Normal Values
WBC	8.0	4-10 million/mm <sup>3</sup>
Hgb	8.1 g/dL	12.6-16.1 g/dL
Hct	24.3%	38-47.7 %
RBC	4.1	3.93 – 5.69 million/mm <sup>3</sup>
MCV	60	80-99.5 fL
MCH	20	27.5-33.3 pg/cell
MCHC	34.2	33.3-35.5 g/L
RDW	16.5	11.4-14.4%
<b>Platelets</b>	<b>500,400 uL</b>	150,000-400,000x10 <sup>3</sup> uL
Reticulocyte count	3%	0.5-1.5%
Absolute Retic count	40,000	25,000-75,000 uL

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## Thrombocytosis? Why?

**“Poor Man’s Sed Rate”**

- Chronic IDA
- Chronic infection
- Inflammatory disorders (“Poor man’s sed rate”)
- Malignancy

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## What might Thrombocytopenia (in the presence of anemia) indicate?

- Aplastic anemia
- Hypersplenism
- Marrow involvement with malignancy
- Autoimmune platelet destruction
- Folate, B12 deficiency

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## Mrs. Boudreaux’ CBC

**Should pancytopenia be part of diff?**

CBC	Patient	Normal Values
WBC	8.0	4-10 million/mm <sup>3</sup>
Hgb	8.1 g/dL	12.6-16.1 g/dL
Hct	24.3%	38-47.7 %
RBC	4.1	3.93 – 5.69 million/mm <sup>3</sup>
MCV	60	80-99.5 fL
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RDW	16.5	11.4-14.4%
Platelets	500,400	150,000-400,000x10 <sup>3</sup> uL
Reticulocyte count	3%	0.5-1.5%
Absolute Retic count	40,000	25,000-75,000 uL

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**Mrs. Boudreaux' CBC**

**Is hemolysis occurring in this patient?**

CBC	Patient	Normal Values
WBC	8.0	4-10 million/mm <sup>3</sup>
Hgb	8.1 g/dL	12.6-16.1 g/dL
Hct	24.3%	38-47.7 %
RBC	4.1	3.93 – 5.69 million/mm <sup>3</sup>
MCV	60	80-99.5 fL
MCH	20	27.5-33.3 pg/cell
MCHC	34.2	33.3-35.5 g/L
RDW	16.5	11.4-14.4%
Platelets	500,400	150,000-400,000x10 <sup>3</sup> u/L
Reticulocyte count (uncorrected)	3%	0.5-1.5%
Absolute Retic count	40,000	25,000-75,000 u/L
LDH	220	0-300 U/L

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**What is Hemolysis?**

Responsible for about 5% of anemias

**Premature destruction of RBCs:**

- Inherited disorders (Sickle cell anemia, thalassemia)
- Malaria
- Hemolytic anemia (G6PD deficiency)

Consider hemolysis if rapid fall in hemoglobin, reticulocytosis, and/or abnormally shaped RBC-spherocytes or RBC fragments-on peripheral smear

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**What lab tests indicate Hemolysis?**

The most sensitive measure is LDH.  
Reticulocyte count may indicate hemolysis.

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## LDH

- Lactate dehydrogenase (lactic acid dehydrogenase)
- Enzyme that is abundant in all body tissues
- RBCs are LOADED with LDH; but only small amounts in the blood!!!

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## What causes rises in LDH?

- Hemolysis → RBCs are LOADED with LDH
- Tissue damage → MI
- Tumor production → Malignancies

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## LDH

- Criterion for hemolysis
- Highly sensitive for hemolysis
- NOT specific: LDH could be released from neoplastic cells, liver, or other damaged organs
- LDH 1 and 2 are specific for RBC destruction but also present in patients who have an MI

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**Normal LDH: Hemolysis unlikely. What about retics?**

CBC	Patient	Normal Values
WBC	8.0	4-10 million/mm <sup>3</sup>
Hgb	8.1 g/dL	12.6-16.1 g/dL
Hct	24.3%	38-47.7 %
RBC	4.1	3.93 – 5.69 million/mm <sup>3</sup>
MCV	60	80-99.5 fL
MCH	20	27.5-33.3 pg/cell
MCHC	34.2	33.3-35.5 g/L
RDW	16.5	11.4-14.4%
Platelets	500,400	150,000-400,000x10 <sup>3</sup> uL
Reticulocyte count (uncorrected)	3%	0.5-1.5%
Absolute Retic count	40,000	25,000-75,000 uL
LDH	220	0-300 U/L

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**Mrs. Boudreaux' CBC**

**Is the retic count appropriate?**

CBC	Patient	Normal Values
WBC	8.0	4-10 million/mm <sup>3</sup>
Hgb	8.1 g/dL	12.6-16.1 g/dL
Hct	24.3%	38-47.7 %
RBC	4.1	3.93 – 5.69 million/mm <sup>3</sup>
MCV	60	80-99.5 fL
MCH	20	27.5-33.3 pg/cell
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RDW	16.5	11.4-14.4%
Platelets	500,400	150,000-400,000x10 <sup>3</sup> uL
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**What are reticulocytes?**

- Reticulocytes are immature RBCs
- Measure of bone marrow's ability to produce RBCs when they are needed

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## Reticulocyte counts

- Normal % of retics is about 1%
- During anemia, retic % should be at least 2% if bone marrow is functioning properly (and has the ingredients needed to make new RBCs)

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### What's the difference between retic count and absolute retic count?

CBC	Patient	Normal Values
WBC	8.0	4-10 million/mm <sup>3</sup>
Hgb	8.1 g/dL	12.6-16.1 g/dL
Hct	24.3%	38-47.7%
RBC	4.1	3.93 – 5.69 million/mm <sup>3</sup>
MCV	60	80-99.5 fL
MCH	20	27.5-33.3 pg/cell
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RDW	16.5	11.4-14.4%
Platelets	500,400	150,000-400,000x10 <sup>3</sup> uL
Reticulocyte count	3%	0.5-1.5%
Absolute Retic count	40,000	25,000-75,000 uL

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## Reticulocyte Count

- During anemic states, retic % may appear increased and not reflect the true response of the bone marrow to the anemia. It has to be corrected....

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## Absolute Reticulocyte Count

- This is the corrected count!!!
- Uses the patient's hematocrit to calculate (takes the anemia into account)
- It is reported as the absolute retic count

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## Absolute Reticulocyte Count

- This is part of initial evaluation to determine whether anemia is due to loss of RBCs or inadequate production

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## ↑ Reticulocyte count with anemia

- ↑ RBC production
- ↑ Bleeding
- ↑ Hemolysis

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**↓ Reticulocyte count with anemia**

**Bone marrow failure**

**↓ RBC production**

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**So, her absolute retic count was normal...significance?**

CBC	Patient	Normal Values
WBC	8.0	4-10 million/mm <sup>3</sup>
Hgb	8.1 g/dL	12.6-16.1 g/dL
Hct	24.3%	38-47.7%
RBC	4.1	3.93 – 5.69 million/mm <sup>3</sup>
MCV	60	80-99.5 fL
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Absolute Retic count	40,000	25,000-75,000 uL

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**Normal or Decreased Reticulocyte Count**

- IDA, B12, folate anemia *without supplementation*
- Chronic renal failure
- Aplastic anemia
- Lymphoma
- Post-radiation

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**So, if she has IDA and we supplement with iron, what *should* happen to her retic count?**

- a. Increase
- b. Decrease
- c. Stay the same

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**So, here's what we know...**

- Microcytic, hypochromic anemia
- RDW elevated (IDA?)
- NO hemolysis
- Retic count appropriate

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### **Microcytic, Hypochromic Anemia**

***Differential Diagnosis:***

- *Iron deficiency:* micro, hypo, RDW elevated
- *Thalassemia:* micro, hypo, RDW normal
- *Anemia of chronic disease:* 80% normochromic, normocytic; 20% micro, hypo
- *Sideroblastic anemia:* macro or micro

\* Most common anemias IDA, ACD

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## Patient Iron Studies

Study	Patient	Normal Value
Serum Fe	30	60-152 ug/dL
TIBC	510	300-360 ug/dL
Serum Ferritin	6	40-202 ng/mL

Stools for occult blood: Negative x 3

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### Iron Measures: Serum Fe

**Serum iron: Decreased in IDA**

- Amount of iron in circulation

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### Iron Measures: *Don't get tricked!!!*

**Serum iron: Decreased in IDA**

- Should be decreased in IDA unless..... patient took iron supplement and then serum iron is measured
- Serum Fe level effected if patient takes oral Fe supplement within 24-48 hours of serum level

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**Iron Measures: Serum Ferritin**

**Serum ferritin: Decreased in IDA**

- Amount of iron in storage
- This will take 4-6 months of supplementation to replenish storage

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**Iron Measures:**

***Don't get tricked!!!***

**Serum ferritin: Decreased in IDA**

- Serum ferritin is an acute phase reactant, so if low, then really low
- Increased serum ferritin seen in inflammatory states, hyperthyroidism, and neoplasm

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**Iron Measures:**

***Don't get tricked!!!***

**Serum ferritin: Take Home Point**

- Normal serum ferritin does not rule out IDA

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## Iron Measures: TIBC

### TIBC: Increased in IDA

- Total iron binding capacity is the “capacity to bind iron”

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## RBC Timeline

- Reticulocytosis: 3-10 days
- Increased Hemoglobin: 2-4 weeks
- Replace iron stores: 4-6 months

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## Causes of IDA

- Heavy blood loss from fibroid is most likely cause
- Start treatment now for IDA
- Once this is corrected, anemia should resolve

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## Take Home Point

GI workup always mandatory if source of bleeding not identified: GI bleed, GI malignancy

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## Be Consistent in Approach

- Is the patient anemic?
- What kind of anemia?
- Peripheral smear OK?
- What does RDW indicate?
- What do platelets indicate?
- Is hemolysis occurring?
- What does retic count indicate?
- What else?

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### “Earl”

72 year old male, underweight, poor nutritional status, poor historian, VSS

**CC:** Fatigue and weakness for the past 4-6 weeks; brought in to clinic by adult daughter who thinks he looks “pale and sick”

**History:** Patient consumes 8-10 EtOH drinks daily, admits to very poor dietary habits, *denies fever/night sweats, denies dark or bloody stools*

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**“Earl”**

72 year old male, underweight, poor nutritional status, poor historian

**Meds:** Inconsistently takes lisinopril for HTN

**FH:** Daughter has been estranged, patient is poor historian

**PE:** Ill-appearing, looks older than his stated age, pale conjunctiva, no lymphadenopathy, no jaundice or hepatosplenomegaly, *denies joint, bone pain*, BMI = 18; rectal exam WNL, stool: brown, heme negative

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**Earl’s CBC**

**Is our patient anemic? What Kind?**

CBC	Patient	Normal Values
WBC	8.0	4-10 million/mm <sup>3</sup>
Hgb	9.1 g/dL	12.6-16.1 g/dL
Hct	27.3%	38-47.7 %
RBC	3.9	3.93 – 5.69 million/mm <sup>3</sup>
MCV	90	80-99.5 fL
MCH	30	27.5-33.3 pg/cell
MCHC	34.2	33.3-35.5 g/L
RDW	14.2	11.4-14.4%
Platelets	300,500	150,000-400,000x10 <sup>3</sup> uL

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**Earl’s CBC**

**I was expecting a macrocytic anemia**

CBC	Patient	Normal Values
WBC	8.0	4-10 million/mm <sup>3</sup>
Hgb	9.1 g/dL	12.6-16.1 g/dL
Hct	27.3%	38-47.7 %
RBC	3.9	3.93 – 5.69 million/mm <sup>3</sup>
MCV	90	80-99.5 fL
MCH	30	27.5-33.3 pg/cell
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RDW	14.2	11.4-14.4%
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## Normocytic, Normochromic Anemia

### ***Vast Differential Diagnosis:***

- Anemia of chronic disease (infection, inflammation, malignancy)
- Acute blood loss
- Early IDA
- Malignancy
- Chronic renal insufficiency
- Poorly managed chronic disease
- Other less common diseases

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### **FYI:**

#### **Chronic Diseases NOT associated with Anemia of Chronic Disease**

- **COPD**
- **HF**
- **HTN**

**If a patient with one of these diseases  
presents with anemia, look for  
another etiology!**

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## Normocytic, Normochromic Anemia

### ***Vast Differential Diagnosis:***

- Anemia of chronic disease (infection, inflammation, malignancy)
- Acute blood loss
- **Early IDA**
- Malignancy
- Chronic renal insufficiency
- Poorly managed chronic disease
- Other less common diseases

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## FYI on Normocytic Anemias

Mild IDA can be normocytic, normochromic

MCV becomes microcytic when Hct  $\leq$  30

Hgb	9.1 g/dL	12.6-16.1 g/dL
Hct	27.3%	38-47.7 %
RBC	3.9	3.93 - 5.69 million/mm <sup>3</sup>
MCV	90	80-99.5 fL
MCH	30	27.5-33.3 pg/cell
MCHC	34.2	33.3-35.5 g/L
RDW	14.2	11.4-14.4%

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## Take Home Point!

Normocytic, Normochromic Anemia

Don't ever just look at the serum Fe and make a diagnosis!

ACD vs IDA Labs

Test	ACD	IDA
Serum Fe	Decreased	Decreased
TIBC	Decreased	Increased
Serum Ferritin	Increased	Decreased

Consider measuring a ESR or CRP for inflammation

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### *Peripheral Blood Smear:*

Microcytic, hypochromic RBCs  
Macrocytic, normochromic RBCs

### *Dimorphic Smear:*

2 distinct populations of red blood cells

**Dx: Mixed Anemia**

**We need to workup BOTH!**

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## Take Home Point

In patients who have “Mixed Anemias”

Most valuable tool is peripheral smear!!!

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## Mixed Anemias “Another Clue”

RDW	Causes of Normocytic Anemia
Normal	ACD, acute blood loss
Elevated	Early IDA, incompletely treated IDA, Megaloblastic anemia

Hgb	9.1 g/dL	12.6-16.1 g/dL
Hct	27.3%	38-47.7 %
RBC	3.9	3.93 – 5.69 million/mm <sup>3</sup>
MCV	90	80-99.5 fL
MCH	30	27.5-33.3 pg/cell
MCHC	34.2	33.3-35.5 g/L
RDW	14.2	11.4-14.4%

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## Iron Studies indicate IDA

- Very likely etiology of the microcytic cells!!!
- What about the macrocytic cells?

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### Most Common Causes of Macrocytic Anemias

- **Vitamin B12 deficiency**
- **Folic acid deficiency**

These are megaloblastic anemias.

Megaloblastic means that there is an error in DNA synthesis resulting in impaired maturation of the RBC nucleus.

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### Macrocytic Anemias (not megaloblastic)

- Alcoholism
- Liver Disease
- Hypothyroidism
- Pregnancy
- Myeloma
- Others

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**Earl's Peripheral Blood Smear:**  
Microcytic, hypochromic RBCs  
Macrocytic, normochromic RBCs

Macroovalocytes,  
hypersegmented neutrophils

**What does THAT mean?**

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## Megaloblastic vs Not

- **Megaloblastic: Peripheral smear may differentiate (macroovalocytes and hypersegmented neut)**
- **Non-M: Neutrophil hyperseg is usually absent**
- **Order B12 and folate levels, if normal, then non-megaloblastic**

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## Folate Deficiency

**Not characterized by neuro changes like B12 deficiency**

Decreased Intake	Malabsorption	Impaired Metabolism	Increased Needs
Alcoholics Elderly	Sprue Gastrectomy	TMP-SMX Methotrexate	Pregnancy Lactation Hyperthyroidism Others

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## Serum Folate Levels

- **Serum folate levels should be gotten fasting because serum folate levels can normalize after eating a meal**
- **Many shortcomings with serum folate levels**

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## If you really want to know if someone.....

is folate deficient, measure a homocysteine level (it's elevated if deficient).

Homocysteine needs folic acid to be converted to methionine. If folic acid is not present, homocysteine levels increase.

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## Serum B12 Levels

Low serum B12 levels can indicate B12 deficiency, but other things can decrease B12 levels

Causes of B12 Level Decreases
Vitamin B12 deficiency
Folic acid deficiency (33% of patients)
Pregnancy
Multiple Myeloma
HIV
Others

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## B12 Deficiency

Characterized by neuro changes

Decreased Intake	Malabsorption	Impaired Metabolism	Increased Needs
Alcoholics Strict vegetarians	Sprue Ileitis Diverticulosis	TMP-SMX Methotrexate	Pregnancy Lactation Post Gastrectomy Cancer Hyperthyroidism

Other: Colchicine

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## Serum B12 Levels

Normal or elevated serum B12 levels don't  
RULE OUT B12 deficiency

### Causes of False Normal B12 Levels

- Lymphomas
- Liver Disease
- IDA
- Hemoglobinopathy

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## The Workup

- Neuro symptoms/changes are present
- Check serum Folate and B12 levels
- If normal or low normal, then homocysteine and MMA levels

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## The Workup

MMA	Homocysteine	Diagnosis
Normal	Normal	Unlikely B12 or Folate deficiency
Normal	Elevated	Likely Folate deficiency
Elevated	Elevated	B12 deficiency, maybe Folate deficiency

Folate Deficiency: Homocysteine increased  
 B12 Deficiency: Homocysteine and MMA levels increased

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## Earl's labs

Vitamin B12	Folate
Normal	Normal

MMA	Homocysteine
Elevated	Elevated

What's your diagnosis?

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## "John"

34 year old, healthy male

**CC:** Fatigue for the past 4-6 weeks

**History:** SOB when walking up stairs, denies chest pain, denies dark or bloody stools but diarrhea 2-3 times daily for several weeks

**Meds:** multivitamin (no ASA, no herbals, no OTCs)

**FH:** Mother has lupus, male cousin with RA & Sjogren's syndrome

**PE:** Pale conjunctive, sclera slightly yellow, no apparent hepatosplenomegaly

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## John's Labs

CBC	Patient	Normal Values
WBC	8.0	4-10 million/mm <sup>3</sup>
Hgb	7.1 g/dL	12.6-16.1 g/dL
Hct	21.3%	38-47.7 %
RBC	2.9	3.93 - 5.69 million/mm <sup>3</sup>
MCV	105	80-99.5 fL
MCH	30	27.5-33.3 pg/cell
MCHC	34.2	33.3-35.5 g/L
RDW	14.5	11.4-14.4%
Platelets	500,400	150,000-400,000x10 <sup>3</sup> uL

What do we know from lab analysis?

- Patient is anemic
- Macrocytic, normochromic anemia, elevated platelets
- RDW is a little elevated
- What about the peripheral smear?

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## Thrombocytosis? Why?

**“Poor Man’s Sed Rate”**

- Chronic IDA
- Chronic infection
- Inflammatory disorders (“Poor man’s sed rate”)
- Malignancy

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## John’s Labs

CBC	Patient	Normal Values
WBC	8.0	4-10 million/mm <sup>3</sup>
Hgb	7.1 g/dL	12.6-16.1 g/dL
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RDW	14.5	11.4-14.4%
Platelets	500,400	150,000-400,000x10 <sup>3</sup> u/L

*What do we know from lab analysis?*

- Patient is anemic
- Macrocytic, normochromic anemia, elevated platelets
- **RDW is a little elevated**
- What about the peripheral smear?

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## RDW

**RDW (red cell distribution width):**  
**indicates degree of variation in**  
**RBC size (<15% is normal)**

RDW	14.5	11.4-14.4%
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## John's labs

Vitamin B12	Folate
Normal	Normal

MMA	Homocysteine
Normal	Normal

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## John's Labs

CBC	Patient	Normal Values
WBC	8.0	4-10 million/mm <sup>3</sup>
Hgb	7.1 g/dL	12.6-16.1 g/dL
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RBC	2.9	3.93 – 5.69 million/mm <sup>3</sup>
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RDW	14.5	11.4-14.4%
Platelets	500,400	150,000-400,000x10 <sup>3</sup> u/L

*What do we know from lab analysis?*

- Patient is anemic
- Macrocytic, normochromic anemia, elevated platelets
- RDW is a little elevated
- **What about the peripheral smear?**

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**John's (Preliminary) Peripheral Blood Smear:**

**Macrocytic, normochromic RBCs**

**Nucleated red blood cells**

**Neutrophils: WNL**

**What does THAT mean?**

**2 things**

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## First: It's a Macrocytic Anemia (It's non-megaloblastic)

### Non-Megaloblastic Initial Differential:

- Alcoholism
- Liver Disease
- Hypothyroidism
- Pregnancy
- Myeloma
- Others

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## Megaloblastic vs Not

- **Megaloblastic: Peripheral smear may differentiate (macroovalocytes and hypersegmented neuts)**
- **Non-M: Neutrophil hyperseg is usually absent**
- **Order B12 and folate levels, if normal, then non-megaloblastic**

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## Second: Peripheral Smear

- Peripheral smear: demonstrates nucleated red blood cells
- This indicates marrow "stress"
- Red cell has extruded its nucleus after maturation

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## John's Labs

CBC	Patient	Normal Values
WBC	8.0	4-10 million/mm <sup>3</sup>
Hgb	7.1 g/dL	12.6-16.1 g/dL
Hct	21.3%	38-47.7 %
RBC	2.9	3.93 – 5.69 million/mm <sup>3</sup>
MCV	105	80-99.5 fL
MCH	30	27.5-33.3 pg/cell
MCHC	34.2	33.3-35.5 g/L
RDW	14.5	11.4-14.4%
Platelets	500,400	150,000-400,000x10 <sup>3</sup> u/L
LDH	800	0-300 U/L

LDH is elevated! What does that mean?

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### What causes rises in LDH?

- Hemolysis → RBCs are LOADED with LDH
- Tissue damage → MI
- Tumor production → Malignancies

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### LDH

- Criterion for hemolysis
- Sensitive for hemolysis
- NOT specific: LDH could be released from neoplastic cells, liver, or other damaged organs
- LDH 1 and 2 are specific for RBC destruction but also present in patients who have an MI

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## Elevated LDH

- Patient is having hemolysis of RBCs

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## What *else* indicates hemolysis?

*Serum haptoglobin*: low levels indicate moderate to severe hemolysis

- Haptoglobin is an acute phase reactant; so if inflammation is present, levels can be normal or elevated in the presence of hemolysis

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## What *else* indicates hemolysis?

### Elevated Indirect bilirubin

- Indirect bilirubin = unconjugated
- Direct bilirubin = conjugated
- *Elevated Direct* = hepatobiliary disease
- *Elevated Indirect* = ??? Hepatobiliary disease

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## What else indicates hemolysis?

### *Elevated Indirect bilirubin*

- Usually < 3 mg/dL in hemolysis
- >3 mg/dL found in compromised hepatic function or cholelithiasis

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## John's Labs

Test	Patient	Normals
Total Bilirubin	5.0	0.2-1.2 mg/dL
Direct bili	0.2	0.0-0.3 mg/dL
AST	20	5-40 u/L
ALT	22	4-40 u/L
Alk Phos	7	30-115 u/L
TSH	2.2	0.5-4.5uU/mL
HIV	Negative	Negative

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## So, here's what we know:

### Patient DOES NOT have:

- *Liver disease*: liver disease can cause macrocytosis but normal LFTs excludes liver disease
- *Non-Megaloblastic disease*: B12 and folate levels are normal
- *HIV*: Infections can cause hemolytic anemia, but there is no evidence of infection; normal WBC

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**John's (Final) Peripheral Blood Smear:**

Macrocytic, normochromic RBCs  
Nucleated red blood cells  
Neutrophils: WNL

**Spherocytes present**

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## Spherocytes

**What are they and what's the significance?**

- Small, dense RBCs
- RBC loses its biconcave shape
- Immune mediated hemolytic anemia
- Autoimmune hemolytic anemia

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## What labs to help confirm AIHA diagnosis?

**Coombs test:** If this is autoimmune hemolytic anemia, direct Coombs could evaluate presence of either IgG or C3 (complement) on red cell surface.

**Indirect Coombs:** looks for antibodies in the plasma. Autoimmune hemolysis typically has positive direct Coombs test.

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### John's Lab

Test	Patient	Normal
Direct Coombs	Positive	Negative
Indirect Coombs	Negative	Negative

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### What is the likely cause of this anemia?

Patient has Autoimmune hemolytic anemia (AIHA):

- Coombs positive hemolytic anemia
- The evidence that supports this is jaundice, elevated indirect bili, elevated LDH, positive Coombs (IgG)
- Peripheral smear indicates spherocytes common in warm antibody hemolytic anemia

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## Summary and Take Home

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## Be Consistent in Approach

- Is the patient anemic?
- What kind of anemia?
- Peripheral smear OK?
- What does RDW indicate?
- What do platelets indicate?
- Is hemolysis occurring?
- What does retic count indicate?
- What else?

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## Take Home Point

Don't forget the peripheral smear!!!

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**Thank you!**

*To Reach me:*  
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