### How to Evaluate Anemia



Dayne Alonso, PA-C Heme Onc Call

### What I will be discussing

- Overview of anemia
  - How to organized the causes of anemia
- Iron deficiency anemia
- RBC Transfusions and transfusion refusal
- Hematologist's organized approach to anemia

### Hematology disorders

|           | Low              | High                     |
|-----------|------------------|--------------------------|
| RBC       | Anemia           | Polycythemia             |
| WBC       | Leukopenia       | Leukocytosis<br>Leukemia |
|           |                  | Leukeiiila               |
| Platelets | Thrombocytopenia | Thrombocytosis           |
| Clotting  | Bleeding and     | Thrombophilia            |
|           | Coagulopathy     | 3                        |

### What is anemia?

- Decreased number of RBC and
- Decreased amount of hemoglobin

- Anemia is:
  - a possible chief complaint
  - a "disease" itself
  - a consequence of a larger problem

### Low hemoglobin (anemia) conditions

| Iron deficiency           | Chronic bleeding or malabsorption |
|---------------------------|-----------------------------------|
| Erythropoietin deficiency | Renal dysfunction                 |
| MDS                       | Bone marrow dysfunction           |
| Myeloma                   | Heme malignancy                   |

### High hemoglobin conditions

| Polycythemia vera        | Low erythropoietin  JAK-2 mutation positive |
|--------------------------|---|
| Chronic hypoxia          | High erythropoietin                         |
| (secondary polycythemia) | Pulmonary disease                           |
|                          | Altitude                                    |

### Why do we care about anemia?

- Why does the patient have anemia?
- Does the patient have cancer?
- Do they feel ill because of anemia?
- Do they need treatment for anemia?
- Do they need blood transfusions?
- Do they need a hematology referral?
- Do they need a bone marrow biopsy?

# Symptoms & signs that could prompt evaluation for anemia

- Fatigue
- Dyspnea
- Bleeding/bruising

- Jaundice
- Dark urine
- Syncope
- Angina

### "Symptomatic" anemia

Asymptomatic

- "Symptomatic" anemia (e.g. with hemoglobin<8)</li>
  - Dyspnea or fatigue without exertion
  - Palpitations, bounding pulse, roaring in ears

- Special symptoms
  - Jaundice, dark urine, syncope, angina

### Why do we test CBC's?

- "Routine" CBC in healthy people
  - Screening for anemia or chronic bleeding
  - Screening for bone marrow disorders

     (i.e. heme malignancies)
- "Diagnostic" test for somebody who is ill
  - High WBC may be infection or heme malig
  - Anemia in somebody who is acutely or chronically ill
  - Heme malignancy may be discovered

### What is anemia?

HCT<40 or Hgb<13.5 in a man HCT<36 of Hgb<12 in a woman

- Hospitalized patients are different
- Severe anemia (requires transfusion):
  - Bleeding patients with HCT<20</li>
  - Bleeding CAD/CVD pts with HCT<25</li>
  - (not chronic or subacute anemia unless Sx's)

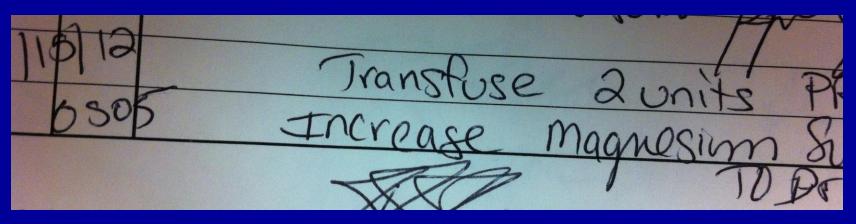
### Hematology consult for anemia

- 30yo AA woman
- 32 wks pregnant
  - Now pre-term labor
- c/o fatigue
- PMH: C section
- FHx "sickle cell"
- Exam: comfortable, no resp distress, HR 90



### Hematology consult for anemia

|          | 2012<br>15 May<br>04:16 |            |        | 2009<br>01 Feb<br>19:32<br> |
|----------|-------------------------|------------|--------|-----------------------------|
| 6.9 * LC |                         | Hemoglobin | 7.0 L  | 11.5 L                      |
| 21.5 L   |                         | Hematocrit | 21.7 L | 33.0 L                      |
| 17.8 H   |                         | WBC        | 11.6 H | 8.6                         |
| 194      |                         | platelets  | 182    | 213                         |
| 3.15 L   |                         | 140)/      | 3.14 L | 4.14                        |
| 68 L     |                         | MCV        | 69 L   | 80                          |



### Hematology consult for anemia



Diagnosis: severe iron deficiency

AND sickle trait/alpha thalassemia

### Interpreting anemia diagnostic tests

| Category                | Test   |
|-------------------------|--|
| Blood counts            | Hemoglobin, Hematocrit                                 |
| Microcytic/macrocytic   | MCV, Iron/TIBC, Retic, LDH, Vitamin 12, folate         |
| RBC production          | Retic  |
| RBC destruction         | LDH, Coombs (DAT), Haptoglobin                         |
| Bone marrow dysfunction | WBC differential, platelets Hemoglobin electrophoresis |

### MCV guides anemia evaluation

|            | Testing by Primary Care  |
|------------|--|
| LOW MCV    | Iron, TIBC, ferritin, retic Hgb electrophoresis (look for beta thal) GI, GU, or GYN referral     |
| NORMAL MCV | Iron, TIBC, ferritin, retic<br>B12, folic acid, TSH, Creat                                       |
| HIGH MCV   | Iron, TIBC, ferritin, retic<br>B12, MMA, folic acid, TSH, Liver<br>enzymes<br>LDH, Direct Coombs |

### Anemia: History and Physical Exam

- History: bleeding, fatigue, dyspnea, dark urine
- Physical: pallor, jaundice, hematoma, bruising, tachycardia, heart murmur





### Anemia patterns

- Always request a retic count and LDH
- If retic is not high: Fe, TIBC, Ferr
- If retic is high: hemolysis evaluation (LDH, DAT)
- If pt is a bleeder: iron studies
- It pt is a clotter: vitamin B12
- If pt is malnourished: folate
- If FHx or SHx: hemoglobin electrophoresis
- If all else normal and 2 lines down: BMBx

### What I will be discussing

- Overview of anemia
- Iron deficiency anemia
- RBC Transfusions and transfusion refusal
- Hematologist's organized approach to anemia

### Organized anemia evaluation

1. Is the patient bleeding? (RBC & iron loss) "acutely" bleeding vs. "chronically" bleeding

2. Low MCV vs. high MCV

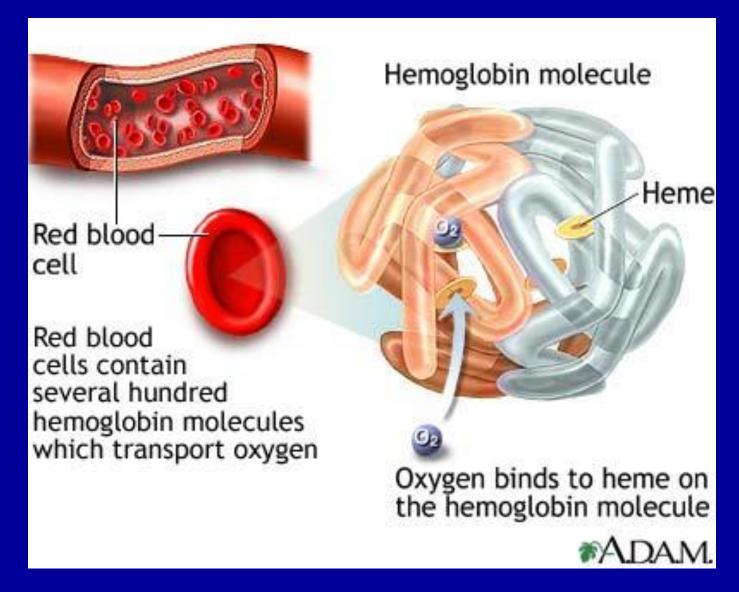
3. RBC production vs. RBC consumption/destruction

## Question 1 Is the patient (acutely or chronically) bleeding?

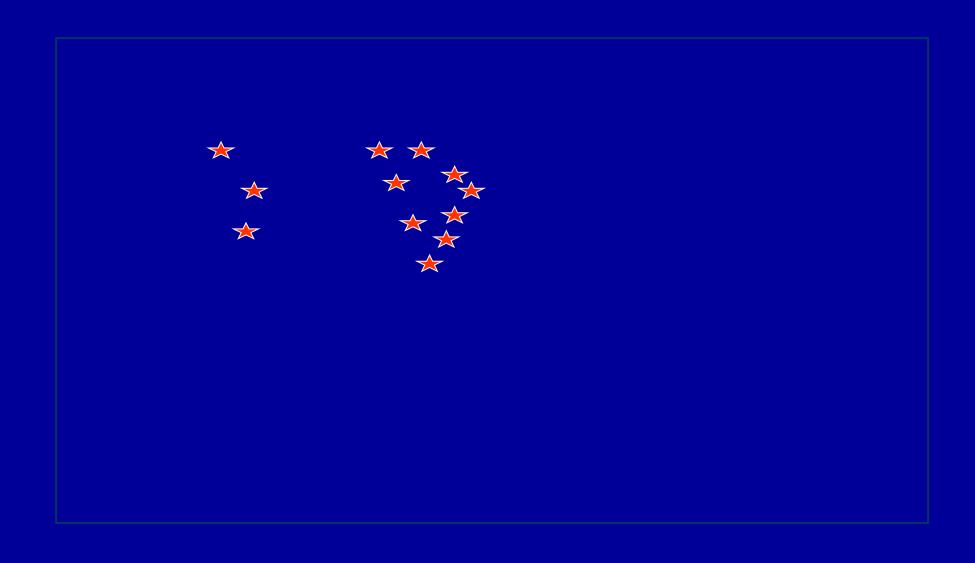
- > How acute is the anemia?
- Where is bleeding occurring?
- Is it GI tract bleeding related to IBD?
- Is it a heavy or irregular menstrual bleeding?
- Does the patient have "bleeding tendency"?
- > Is bleeding tendency due to medications?
- > Has iron deficiency been established?



### Iron is the oxygen carrier



### Erythropoietin and iron are both important



**Decreased iron intake Excess RBC/iron loss** 

#### **Decreased iron intake**

#### **Excess RBC/iron loss**

Chronic bleeding

#### **Decreased iron intake**

#### **Excess RBC/iron loss**

- Chronic bleeding
- Chronic wounds
- Excessive phlebotomy
- Chronic hemolysis
- Parasite
- Pregnancy

#### **Decreased iron intake**

- Malabsorption
- Malnutrition
- Acid suppression
- Gastric bypass surgery

#### **Excess RBC/iron loss**

- Chronic bleeding
- Chronic wounds
- Excessive phlebotomy
- Chronic hemolysis
- Parasite
- Pregnancy



**RUNNING OUT OF STEAM?** 

### Symptoms of iron deficiency

- Feeling tired and "weak"
- Palpitations
- Headache
- SOB with minimal exertion
- Brittle hair and nails
- Increased vulnerability to infection
- Craving ice
- Disturbed sleep, concentration, memory
- Abdominal pain



### Iron deficiency affects the whole body

#### Central Nervous System

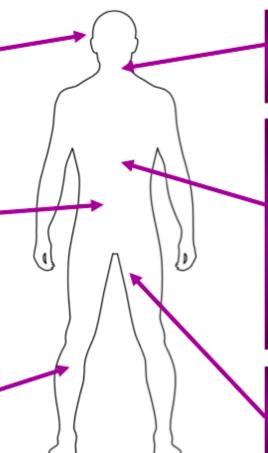
- Debilitating fatigue
- Depression
- Impaired cognitive function

#### Gastrointestinal System

- Anorexia
- Nausea

#### Vascular System

- Low skin temperature
- Pallor of skin, mucous membranes and conjunctiva



#### Immune System

 Impaired T cell and macrophage function

#### Cardio-respiratory System

- Exertional dyspnea
- Tachycardia, palpitations
- Cardiac enlargement, hypertrophy
- Increased pulse pressure, systolic ejection murmur
- Risk of cardiac failure

#### **Genital Tract**

- Menstrual problems
- Loss of libido

### Chewing Ice is Not Just a Habit





Pica, pagophagia

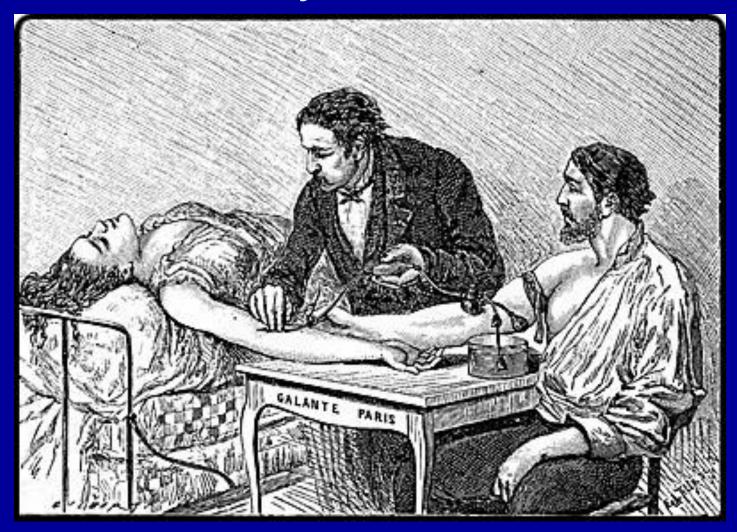
### How to treat iron deficiency

| Intervention                      | Hemoglobin      | Iron |
|-----------------------------------|-----------------|------|
| Address chronic or acute bleeding | Stop decreasing |      |
| Oral iron supplement              | Weeks-months    | Slow |
| IV iron supplement                | Days-weeks      | Fast |
| RBC transfusion                   | Hours           | Fast |

### What I will be discussing

- Overview of anemia
- Iron deficiency anemia
- RBC Transfusions and transfusion refusal
- Hematologist's organized approach to anemia

### 19th Century blood transfusion



1800's: direct transfusions used for several medical conditions

### History of transfusion

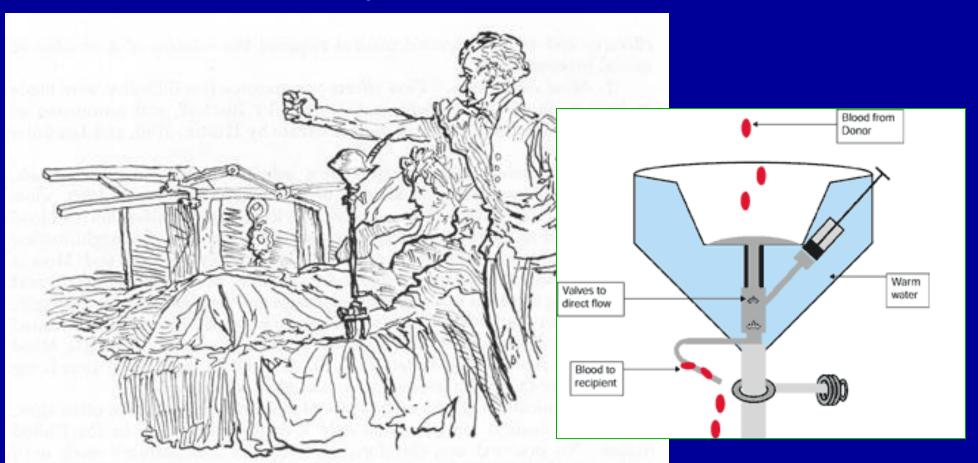


Figure 2.—Clinical transfusion with Blundell gravitator for transmitting "blood in a regulated stream from one individual to another" (3).

1800's: spouse blood transfused for postpartum hemorrhage

## 20th Century blood transfusion



Figure 80.—Fifth U.S. Army corpsmen administering blood plasma in open field to wounded comrade. In background is a war-ravaged town. Date is unknown, but the picture was taken before the introduction of large plasma bottles.

### Benefits of transfusion

| RBC       | Iron repletion for iron deficiency                              |  |
|-----------|---|--|
|           | Replace lost blood in bleeding pt                               |  |
|           | Supply oxygen-carrying capacity                                 |  |
|           | Treat "symptomatic" anemia in patients with RBC production prob |  |
|           | (or sometimes hemolytic anemia)                                 |  |
| Platelets | Stop or prevent bleeding  |  |
| Plasma    | Stop or prevent bleeding Special circumstances: TTP             |  |

### Who needs RBC transfusion?

Bleeding after trauma or surgery

Post-partum bleeding



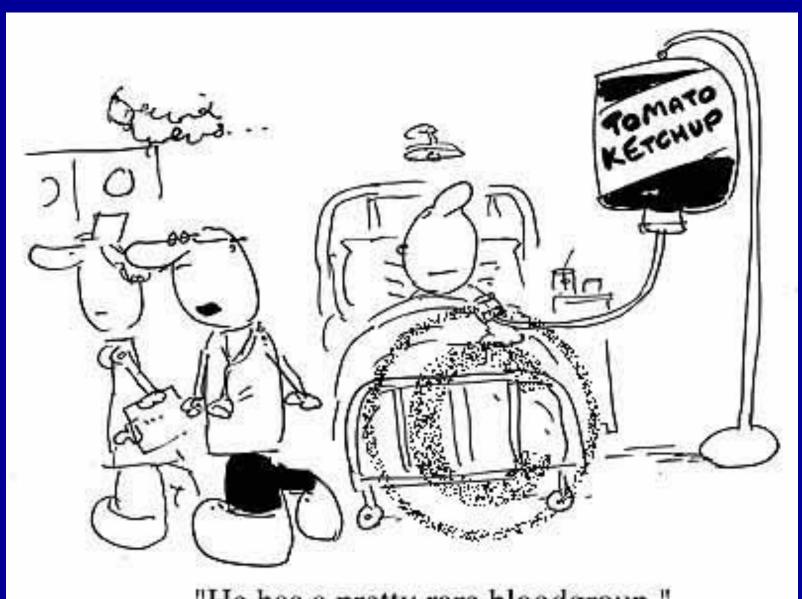


### Who needs RBC transfusion?

- Cancer patients receiving cytotoxic chemotherapy
- MDS patients receiving palliative treatment
- Thalassemia patients







"He has a pretty rare bloodgroup."

## Types of Transfusion Reactions

# Acute Reactions (Minutes to Hours)

- Anaphylaxis
- Other allergic reactions
- ABO incompatibility
- Bacterial contamination
- Febrile non-hemolytic transfusion reaction
- Transfusion-Related Acute Lung Injury (TRALI)

### **Delayed Reactions**

(Days to Weeks)

- Extravascular hemolysis
- Post-transfusion purpura
- Graft vs. host reaction
- Transmission of infectious agents
- Unrecognized risks



3

4



### Five Things Physicians and Patients Should Question

#### Don't transfuse more units of blood than absolutely necessary.

Each unit of blood carries risks. A restrictive threshold (7.0-8.0g/dL) should be used for the vast majority of hospitalized, stable patients without evidence of inadequate tissue oxygenation (evidence supports a threshold of 8.0g/dL in patients with pre-existing cardiovascular disease). Transfusion decisions should be influenced by symptoms and hemoglobin concentration. Single unit red cell transfusions should be the standard for non-bleeding, hospitalized patients. Additional units should only be prescribed after re-assessment of the patient and their hemoglobin value.

#### Don't transfuse red blood cells for iron deficiency without hemodynamic instability.

Blood transfusion has become a routine medical response despite cheaper and safer alternatives in some settings. Pre-operative patients with iron deficiency and patients with chronic iron deficiency without hemodynamic instability (even with low hemoglobin levels) should be given oral and/or intravenous iron.

#### Don't routinely use blood products to reverse warfarin.

Patients requiring reversal of warfarin can often be reversed with vitamin K alone. Prothromobin complex concentrates or plasma should only be used for patients with serious bleeding or requiring emergency surgery.

#### Don't perform serial blood counts on clinically stable patients.

Transfusion of red blood cells or platelets should be based on the first laboratory value of the day unless the patient is bleeding or otherwise unstable. Multiple blood draws to recheck whether a patient's parameter has fallen below the transfusion threshold (or unnecessary blood draws for other laboratory tests) can lead to excessive phlebotomy and unnecessary transfusions.



3

4



### Five Things Physicians and Patients Should Question

#### Don't transfuse more units of blood than absolutely necessary.

Each unit of blood carries risks. A restrictive threshold (7.0-8.0g/dL) should be used for the vast majority of hospitalized, stable patients without evidence of inadequate tissue oxygenation (evidence supports a threshold of 8.0g/dL in patients with pre-existing cardiovascular disease). Transfusion decisions should be influenced by symptoms and hemoglobin concentration. Single unit red cell transfusions should be the standard for non-bleeding, hospitalized patients. Additional units should only be prescribed after re-assessment of the patient and their hemoglobin value.

Don't transfuse red blood cells for iron deficiency without hemodynamic instability.

Blood transfusion has become a routine medical response despite cheaper and safer alternatives in some settings. Pre-operative patients with iron deficiency and patients with chronic iron deficiency without hemodynamic instability (even with low hemoglobin levels) should be given oral and/or intravenous iron.

- Don't routinely use blood products to reverse warfarin.
- Patients requiring reversal of warfarin can often be reversed with vitamin K alone. Prothromobin complex concentrates or plasma should only be used for patients with serious bleeding or requiring emergency surgery.
- Don't perform serial blood counts on clinically stable patients.

Transfusion of red blood cells or platelets should be based on the first laboratory value of the day unless the patient is bleeding or otherwise unstable. Multiple blood draws to recheck whether a patient's parameter has fallen below the transfusion threshold (or unnecessary blood draws for other laboratory tests) can lead to excessive phlebotomy and unnecessary transfusions.

### **Blood Transfusion Refusal**

| 2 .           | NO BLOOD TRANSFUSION!  As a God-fearing Christian and a believer of Jehovah's                          |
|---------------|--|
|               | word, the Bible, I hereby demand that blood, in any way, shape or form, is NOT to be fed into my body; |
| in the second | however, blood substitutes may be used in case of extreme loss of blood.                               |
|               | YOU MUST NOT EAT THE BLOOD OF ANY SORT OF FLESH' LEVITICUS 17:14 NW                                    |
|               | Signature (Over)   |

### Question 2: Low MCV vs. High MCV

### MCV < 80

#### MCV > 100

#### Hgb synthesis problems

--Iron-deficiencyabsolute iron deficfunctional iron defic"anemia of chronic dz"

--Thalassemiaalpha thalassemiabeta thalassemia"thalassemia major"

#### DNA synthesis problems

Drugs (cancer/HIV drugs)
Vitamin B12 deficiency
Folate deficiency
malnutrition, malabsorp
seizure meds
alcohol dependence

Hypothyroidism
Liver disease, hypersplenism
High retic counts

### Question 3: RBC production or destruction?

| Production   | Destruction   |
|--|---|
| Bone marrow failure  | Hemolytic anemia  |
| Thalassemia Nutrient defic (iron, B12, folate) Drugs, chemotherapy Epo defic (CRI or ESRD) Anemia of chronic disease MDS, Aplastic anemia "Sideroblastic" anemia = MDS | Intravascular RBC membrane Sickle cell disease Microangiopathic: DIC, TTP, HUS Extravascular AIHA, Drug-induced |

## What I will be discussing

- Overview of anemia
- Iron deficiency anemia
- RBC Transfusions and transfusion refusal
- Hematologist's organized approach to anemia

Iron deficiency

- Iron deficiency
  - Chronic bleeding
  - Iron malabsortion

- Iron deficiency
  - Chronic bleeding
    - GYN
    - GI tract
    - GU tract

(r/o malignancy)

- Iron malabsortion
  - GI tract surgery
  - Autoimmune disease

- Iron deficiency
  - Chronic bleeding
    - GYN
    - GI tract
    - GU tract

(r/o malignancy)

- Iron malabsortion
  - GI tract surgery
  - Autoimmune disease

- Iron deficiency
  - Chronic bleeding
    - GYN
    - GI tract
    - GU tract

(r/o malignancy)

- Iron malabsortion
  - GI tract surgery
  - Autoimmune disease

- Non-iron deficiency
  - What is the MCV?
  - Production problem or destruction problem?
  - Benign or malignant?

- Iron deficiency
  - Chronic bleeding
    - GYN
    - GI tract
    - GU tract

(r/o malignancy)

- Iron malabsortion
  - GI tract surgery
  - Autoimmune disease

- Non-iron deficiency
  - What is the MCV?
  - Low MCV alpha thal
  - High MCV
    - B12/folate
    - Liver dysfunctiojn
    - Hypothyroidism
    - Meds-antibiotics

- Iron deficiency
  - Chronic bleeding
    - GYN
    - GI tract
    - GU tract

(r/o malignancy)

- Iron malabsortion
  - GI tract surgery
  - Autoimmune disease

- Non-iron deficiency
  - Low MCV alpha thal
  - High MCV
    - B12/folate
    - Liver dysfunctiojn
    - Hypothyroidism
    - Meds-antibiotics
  - Production problem
    - Anemia of chronic dz
    - Epo deficiency CKD
  - Destruction problem
    - Autoimmune (AIHA)
    - Non-autoimmune

- Iron deficiency
  - Chronic bleeding
    - GYN
    - GI tract
    - GU tract

(r/o malignancy)

- Iron malabsortion
  - GI tract surgery
  - Autoimmune disease

- Low MCV alpha thal
- High MCV
  - B12/folate
  - Liver dysfunctiojn
  - Hypothyroidism
  - Meds-antibiotics
- Production problem
  - Anemia of chronic dz
  - Epo deficiency CKD
- Destruction problem
  - Autoimmune (AIHA)
  - Non-autoimmune
- Heme malignancy
  - Myeloma, lymphoma, MDS, MPD, leukemia

### What I've discussed

- Overview of anemia
  - Bleeding?
  - Low MCV or high MCV?
  - Production or destruction?
- Iron deficiency anemia
- RBC Transfusions and transfusion refusal
- Hematologist's organized approach to anemia
  - Iron deficiency vs. non-iron deficient

