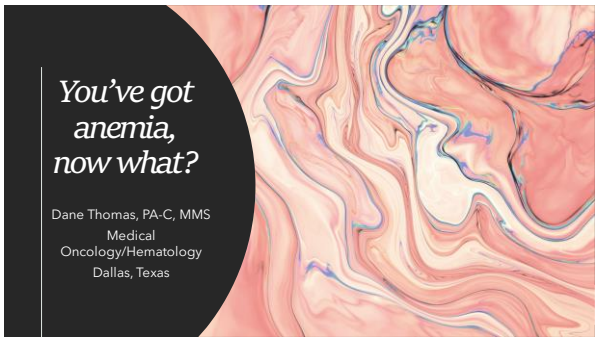


Disclosures

- None!

Disclaimer

- *This lecture is intended for informational purposes only. Individuals should use sound clinical judgement when evaluating all patients with hematological issues and err on the side of caution with any patient presenting with potential life-threatening hematological complaints.*

Objectives

1. Discuss how to identify anemia
2. Discuss the various causes of anemia
3. Discuss typical laboratory and clinical findings
4. Identify various treatment options for anemia for patients.
5. Identify when to refer to Hematology

What is anemia?

- Anemia is the reduction in one or more of the red blood cell (RBC) measurements obtained as a part of the complete blood count (CBC)
- Normal Ranges
  - Females: Hemoglobin > 11.9 g/dL and Hematocrit > 35%
  - Males: Hemoglobin > 13.6 g/dL and Hematocrit > 40%

Laboratory Evaluation

- CBC
  - Hemoglobin: Concentration of hemoglobin in whole blood
    - Binds to Oxygen and delivers to tissues
  - Hematocrit: Percentage of blood volume occupied by RBCs
  - Mean Corpuscular Volume (MCV): Average volume of RBCs
    - Normocytic (Normal): 80 – 100 fL
    - Microcytosis: < 80 fL
    - Macrocytosis: > 100 fL
  - Mean Corpuscular Hemoglobin (MCH) and Mean Corpuscular Hemoglobin Concentration (MCHC)
    - Average hemoglobin content/concentration per RBC
    - Low: iron deficiency anemia, thalassemia
    - High: Spherocytosis
- Reticulocyte Count
  - Elevated in anemia (Bone marrow increases the rate of RBC production in response to anemia)

What can cause anemia?

Case Study #1

34-year-old female presents in clinic for anemia. She reports that she has been dealing with anemia since childhood. She was never told the reason of her anemia from a young age. Her anemia was stable until after her pregnancy. She had a vaginal delivery and unfortunately lost a large amount of blood from a vaginal tear. At that time, her hemoglobin dropped to 6.0. She did not receive a blood transfusion at that time. She then continued to deal with her chronic anemia, but it remained mild. Approximately 6 months ago she started to experience increasing fatigue. She went to her primary care physician and underwent lab work which revealed:

- **Hemoglobin 10.9 (Normal ≥ 11.9)**
- **Hematocrit 33.3% (Normal ≥ 35%)**
- **MCV 78.8 (Normal between 80 – 100)**
- Platelet count of 320,000
- **Iron saturation 15% (Normal ≥ 20%)**
- **Ferritin 33 (Normal ≥ 40)**

She was then instructed to take OTC oral iron once a day which she did for 2 weeks. She was unable to tolerate her oral iron supplement due to constipation, bloating, and gas pains. She was then referred to Hematology for further evaluation of her iron deficiency anemia and to be evaluated for IV iron replacement therapy.

Iron Deficiency Anemia

- Common Causes
  - Menorrhagia
    - Uterine Fibroids/Endometriosis
  - Gastrointestinal blood loss
    - Peptic Ulcer Disease (PUD)
    - Arteriovenous Malformations (AVMs) of the small bowel
    - Ulcerative Colitis
    - Hemorrhoids/anal fissures
    - Hiatal hernia/Cameron's erosions
    - Colon Cancer
  - Genitourinary blood loss
  - Malabsorption
    - Irritable Bowel Syndrome (IBS)/Celiac Disease
    - Gastric bypass surgery
    - Chronic Proton Pump Inhibitor (PPI) use/Gastritis/H. Pylori infection
  - Pregnancy
- Rare Causes
  - Paroxysmal Nocturnal Hemoglobinuria (PNH)
    - May also cause iron overload due to hemolysis

Laboratory Findings in Iron Deficiency

- Microcytosis (MCV < 80)
- Hypochromia (Low MCH or MCHC)
- Reactive thrombocytosis (Platelet count > 400,000)
- Borderline low or high WBC
- Iron saturation < 20%
  - "Iron in your blood" or Checking account
  - Severe: < 10%
- Ferritin < 40 ng/mL
  - "Iron reserves" or Savings Account
  - Severe: < 10 ng/mL
- Elevated TIBC
  - "Lots of empty buckets trying to collect iron from your blood"
- Elevated soluble transferrin receptor or Transferrin (for patients with chronically elevated Ferritin secondary to acute phase reactant)

Clinical Findings

1. Fatigue/lethargy
2. Skin pallor
3. Brittle, spoon-shaped fingernails
4. Hair loss
5. Brain fog/short term memory loss
6. Shortness of breath on exertion
7. Dizziness and lightheadedness
8. Headaches
9. PICA (Ice, Dirt, Uncooked rice, Chalk, etc)
10. Restless legs/Muscle cramping
11. Tachycardia

Treatment Options for Iron Deficiency

- Iron supplementation
  - OTC or Prescription Pills/Liquid
    - Pros: Convenient for patient, more cost effective, not time consuming
    - Cons: most patients cannot tolerate it due to side effects (constipation, upset stomach, diarrhea, nausea/vomiting), not effective for severe iron deficiency or iron deficiency secondary to malabsorption
    - Numerous oral iron formulations are available and are almost equally effective
    - Avoid enteric-coated or sustained-release capsules (poorly absorbed due to iron released too far distally in intestinal tract)
    - Possible improved absorption when taken with Vitamin C
    - Avoid ingesting with food
    - Take 2 hours before or 4 hours after ingestion of antacids

- IV Iron
  - Pros: Side effects rare (nausea, diarrhea, headaches, muscle cramping, joint pain for 1 – 2 days after infusion), effective for patients with malabsorption, no need for daily consumption of oral iron, effective for severe iron deficiency
  - Cons: Not cost effective, time consuming and typically requires time off from work, higher chance of infusion reaction for patients with autoimmune disorders
  - No evidence that total doses above 1000 mg of elemental iron are clinically useful
    - Prevents iron overload
    - Exception is for severe ongoing blood loss
- IM Iron
  - Can raise iron level, but route of administration is painful, skin staining, and variable absorption
- Transdermal Iron
  - No clinical evidence of effectiveness or safety thus far in humans

Approaching Treatment Options with Patients

- Iron deficiency associated with no ongoing blood loss or etiology is secondary to malabsorption
  - Try oral iron (1 tablet/day, 1 tablet QOD or 1 tablet BID) with vitamin C for 3 months then recheck labs
    - If no improvement, Refer to Hematology for IV iron
- If Iron deficiency associated with ongoing blood loss
  - Mild iron deficiency: Try oral iron as above
  - Severe: Refer to Hematology for IV iron

Case Study #1 (Continued)

She reports that her menstrual cycles are regular and currently last 7 days. Previously, her periods were only lasting 5 days. She goes through 1 pad every 2 - 3 hours for the first 4 days of her menstrual cycle.

She received 4 Venofer 200 mg infusions which made her feel so much better. Labs after her infusions revealed:

Hemoglobin: 12.6
Hematocrit: 38.2%
Ferritin: 80
Iron Saturation: 29%

She then followed up with her gynecologist and was started on oral birth control which helped lighten her menstrual cycles.

Case Study #2

51-year-old female presents for recently diagnosed iron deficiency anemia. She reports that she has had decreasing energy levels for the past several years. Most recently, she has been dealing with intermittent chest pain for the past few months. She underwent cardiac work-up which was negative. She was diagnosed with iron deficiency anemia earlier this year and she started on oral iron supplementation for approximately 6 months but stopped due to constipation. She underwent lab work which revealed:

- **Ferritin of 15 (Normal ≥ 40)**
- **Iron saturation 10% (Normal ≥ 20%)**
- Serum folate 18.3
- TSH 2.36
- Hemoglobin 14.6
- Hematocrit 41.8
- Vitamin B12 446

Case Study #2 (Continued)

Past medical history is significant for gastric sleeve surgery performed 5 years ago as well as hiatal hernia repair during the same surgery. She unfortunately had her hiatal hernia reappear and her reflux got much worse. She then underwent gastric bypass surgery in 2019 and surgical repair of her hiatal hernia. She has seen GI in the past and underwent her last EGD in April 2021 which was only remarkable for GERD. She underwent a colonoscopy in September 2020 which was normal. She continues to take oral B12 supplements daily for her B12 deficiency.

She then received 2 FeraHeme infusions which she tolerated well.

Follow up labs reveal:

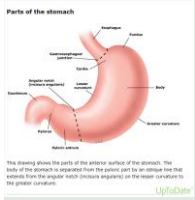
Hemoglobin: 15.6
Hematocrit: 44.4%
MCV: 89
Ferritin: 139
Iron Saturation: 32%

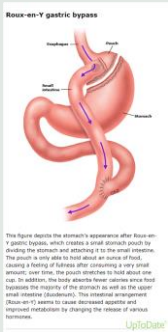
Malabsorption Syndromes

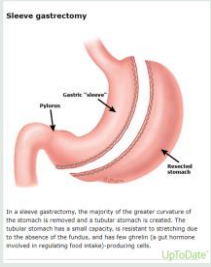
- Duodenum is the site of maximal iron absorption
- Common Causes
  - Disorders affecting the mucosal cells responsible for iron absorption
    - Bariatric Surgery
      - Gastric bypass/sleeve, duodenal switch, lap band
    - Celiac disease
    - Atrophic/autoimmune Gastritis
    - Helicobacter pylori
  - Chronic Proton Pump Inhibitor (PPI) Use
  - Irritable Bowel Syndrome (IBS)

Malabsorption Syndromes

- May not respond to oral iron supplementation or have intolerance to it
- Likely will need IV iron replacement therapy lifelong if found to have iron deficiency
- Average time from bariatric surgery to the need of iron replacement therapy varies, but on average it is 5 years
- About 50% of patients with malabsorption to iron will also have Vitamin B12 and folate deficiencies
  - Rare that B12 injections are needed
  - Oral B12 (tablet or sublingual) effective in raising B12 levels







B12 and Folate Deficiency

- B12 Deficiency
  - Textbook definition is B12 level below 300 (Below 500 in clinical practice)
  - Causes
    - IBS, Celiac disease, Gastric bypass, Medications (Metformin, PPIs, H2 receptor blockers, Antacids)
  - CBC
    - Macrocytic Anemia (MCV > 100)
      - Other causes: Copper deficiency, Myelodysplastic syndrome, Aplastic anemia, excess alcohol consumption, and hypothyroidism
    - Normocytic Normochromic Anemia
  - Elevated methylmalonic acid (MMA) and homocysteine
  - Treatment
    - Vitamin B12 1000 mcg tablet daily
      - Recommend sublingual for patients with suspected malabsorption
    - If not responding to oral supplementation, recommend B12 injections
      - B12 1000 mcg IM weekly for 4 weeks, then once a month
    - Intranasal route generally not used and transdermal route has not been validated clinically
  - Pernicious anemia
    - Autoimmune condition causing severely impaired B12 absorption
    - Diagnosis: Test for autoantibodies to intrinsic factor (auto-IF antibodies)
- Folate Deficiency
  - Below 4 ng/mL (9.1 nmol/L)
  - Treatment: Folic Acid 1 mg daily
  - Medications causing: Methotrexate, Bactrim, Phenytoin, Valproate, Carbamazepine

Case Study #3

67-year-old female with a past medical history significant for gastric sleeve surgery in 2015 presents with extreme fatigued, increased mental fogginess and cravings to eat various types of foods for the past year. She has never been diagnosed with iron deficiency anemia, leukocytosis or thrombocytosis in the past. She underwent lab work with her endocrinologist which revealed:

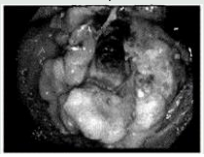
- **Ferritin of 5 (Normal ≥ 40)**
- **Iron saturation 7% (Normal ≥ 20%)**
- White blood cell count of 8.7
- **Hemoglobin 9.3 (Normal ≥ 11.9)**
- **Hematocrit 20.9 (Normal ≥ 35%)**
- MCV of 85.4
- MCH 27.5
- **MCHC of 32.2 (Normal between 32.5 and 35.2)**
- **Platelet count of 570,000 (Normal between 130,000 and 400,000)**

Case Study #3 (Continued)

- She received 2 FeraHeme infusions which she tolerated well.
- Follow up labs performed at her 2-month follow-up visit revealed:
  - White blood cell count of 7.8
  - **Hemoglobin 9.7 (Normal ≥ 11.9)**
  - **Hematocrit 30.5% (Normal ≥ 35%)**
  - MCV of 85.9
  - **Platelet count of 445,000 (Normal between 130,000 and 400,000)**
  - Ferritin 121
  - **Iron saturation of 17% (Normal ≥ 20%)**
- At her 2-month follow-up visit we checked Hemoccult stool which was positive x 3.

Case Study #3 (Continued)

- She was immediately referred to GI and underwent an EGD and colonoscopy which revealed gastritis, LA grade A esophagitis in the gastroesophageal junction, gastric sleeve anatomy, sigmoid colon mass which was biopsied, 1 polyp in the cecum and 1 polyp in the transverse colon
- Biopsy of the sigmoid mass was positive for adenocarcinoma



Case Study #3 (Continued)

- Underwent a robot-assisted sigmoid colectomy with low pelvic anastomosis.
- Pathology revealed moderately differentiated colonic adenocarcinoma extending entirely through the colonic wall and into the pericolonic adipose tissue
- Stage IIA T3N0cM0

Colon Cancer

- Approximately 150,000 cases diagnosed in the US annually
  - 20% have distant metastatic disease at time of presentation
- Common Symptoms/Signs
  - Hematochezia or melena
  - Abdominal pain
  - Unexplained iron deficiency anemia
    - Must rule out colon cancer if iron deficiency is found in Males
  - Change in bowel habits
- Testing
  - Fecal Immunochemical Test for Occult Blood (FIT)
    - 97% sensitive in one meta-analysis
  - Colonoscopy
    - Most accurate and versatile diagnostic test
  - Flexible sigmoidoscopy
    - Not recommended due to shift in right-sided or proximal colon cancers in the past 50 years
- Screening
  - US Preventive Services Task Force (USPSTF) recommends initiating screening at age 45 and end at age 75
  - Colonoscopy every 10 years or sooner if colon polyps are removed
  - FIT for occult blood annually if unable or unwilling to have colonoscopy
  - Multitarget stool DNA testing (Cologuard)
    - Combines fecal markers for hemoglobin and DNA mutation and methylation
    - USPSTF recommends screening every 1 – 3 years
    - More expensive than FIT
  - Computer Tomography Colonography (Virtual Colonoscopy)
    - Performed every 5 years

Pregnancy

- Physiologic or Dilutional Anemia
  - Maternal red cell mass increases but at the same time plasma volume increases to a greater degree
    - Causes hemoglobin and hematocrit to decrease to anemic levels
- Normal Hemoglobin Ranges
  - 1st Trimester: $\geq$ 11 g/dL
  - 2nd and 3rd Trimester: $\geq$ 10.5 g/dL
- Iron deficiency is a common cause of anemia in pregnancy
  - Treatment
    - 1st Trimester
      - Oral iron (Ferrous sulfate most common)
        - Best to take every other day to reduce gastrointestinal effects
      - IV iron contraindicated due to no safety data for first trimester use
    - 2nd and 3rd Trimester
      - Oral iron as above
      - Oral iron failure → IV iron (Venofer only product deemed safe)
        - Avoid Ferrlecit (contains benzyl alcohol as preservative)
      - IV iron is best to use from week 30 onwards due to insufficient time to replete iron orally
        - Avoid IV iron in late 3rd trimester to avoid risk of inducing labor (infusion reactions)
- Must rule out other causes of anemia (Folate deficiency, B12 deficiency, etc.)

Treating the Root Cause of Iron Deficiency

- Fecal Occult Blood Test (FOBT) to rule out GI blood loss
- Referral to Specialist (GI/GYN/Colorectal surgery)
  - EGD/Colonoscopy/PillCam Endoscopy
  - Surgery for large hiatal hernia
  - PPI for gastric bleed
  - Hemorrhoid banding/Hemorrhoidectomy
  - Menorrhagia
    - Oral contraceptives/Tranexamic acid/Gonadotropin-releasing hormone antagonist (Myfembree)
    - Uterine Ablation
    - Partial or total hysterectomy

Case Study #4

64-year-old male presents for recently diagnosed microcytic hypochromic anemia. He reports that he has been anemic for the past 3 years. For those 3 years, he has been taking 1 oral iron tablet daily which he tolerated well without any issues. He recently follow-up with his PCP and underwent lab work which revealed:

- White blood cell count of 5.1
- **Hemoglobin 12.1 (Normal ≥ 13.6)**
- **Hematocrit 37.5% (Normal ≥ 40%)**
- **MCV of 70.3 (Normal between 80 - 100)**
- **MCH of 22.7 (Normal between 27.0 and 31.0)**
- **MCHC of 32.3 (Normal between 32.5 and 35.2)**
- Platelet count of 203,000
- Ferritin 97.4
- Iron saturation 42%
- TIBC 301

He was referred to us for further evaluation of his microcytic hypochromic anemia.

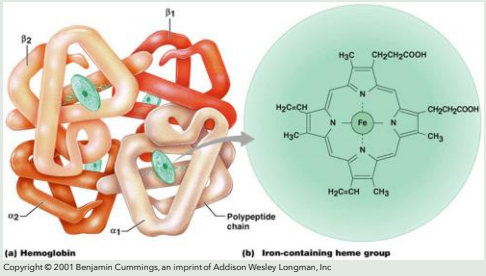
Case Study #4 (Continued)

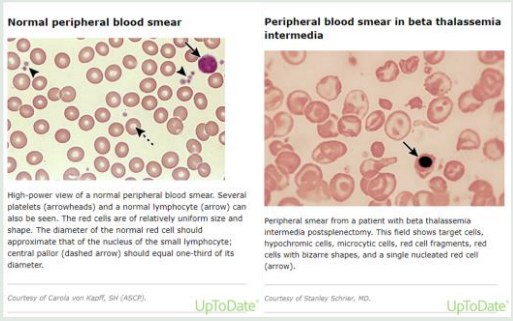
- We ordered an alpha globin DNA analysis laboratory test which revealed that he was homozygous positive for the alpha plus thalassemia mutation.
- He initiated folic acid 1 mg daily and stopped his oral iron supplementation.

Thalassemia

- One of the most common hemoglobinopathies (Second to Sickle Cell Disease)
- 5% of the world's population has at least one thalassemia variant allele
- Alpha Thalassemia
  - Highly prevalent in Southern China, Malaysia and Thailand
  - Mild forms common with African and Asian ancestry
  - 4 alpha globin genes
    - Alpha thalassemia is caused by reduced production of alpha chains and accumulation of excess beta-like chains
    - Severity increases with loss of one, two, three or four alleles
      - Alpha thalassemia minima: loss of 1 alpha chain gene
        - No anemia, normocytic, possible mild hypochromia
      - Alpha thalassemia minor: loss of 2 alpha chain genes
        - Mild anemia, hypochromia, microcytosis
      - Hemoglobin H disease: loss of 3 alpha chain genes
        - Mild anemia, microcytosis, neonatal jaundice, may require episodic transfusions during periods of increased hemolysis (Infection, Pregnancy, etc)
      - Hemoglobin Barts (Hb Barts): no alpha chains
        - Severe anemia during fetal development with hydrops fetalis; fatal before birth unless in utero transfusions are administered

- Beta Thalassemia
  - Present in Africa
  - 2 beta globin genes
    - Beta thalassemia caused by reduced production of beta chains and accumulation of excess alpha chains
    - Transfusion dependent beta thalassemia (Beta thalassemia major, Cooley's anemia, Mediterranean anemia)
      - Minimal to no beta chain production
      - Presents between 6 – 12 months of life with severe anemia
    - Non-transfusion dependent beta thalassemia (Beta thalassemia intermedia)
      - Homozygous or compound heterozygous for beta thalassemia variant
      - Presents between 2 – 4 years old
    - Beta thalassemia minor (Beta thalassemia trait)
      - Heterozygous for beta thalassemia mutation; carrier condition
      - Mild anemia with marked microcytosis
- Management
  - Suggest folic acid supplementation for all individuals with thalassemia major or thalassemia intermedia with evidence of chronic hemolysis with Folic acid 1 mg daily
    - Compensate for increased folate requirements associated with increased RBC turnover
    - Suggest Folic acid 4 – 5 mg daily during pregnancy
  - Need to avoid iron supplementation **UNLESS** they have documented iron deficiency
    - Increased iron absorption with thalassemia which can lead to iron overload
      - Ferritin can be elevated which is normal, unless ferritin is greater than 1000 and/or iron sat > 50%





Case Study #5

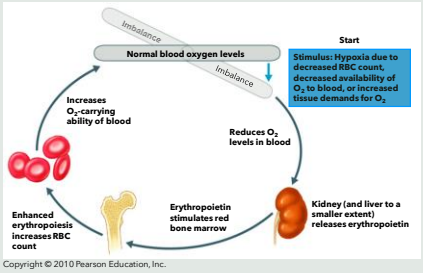
60-year-old female who presents with recently diagnosed normocytic normochromic anemia. She has stage V kidney disease with an eGFR of 13. She underwent lab work at her nephrologist office which revealed:

- White blood cell count of 9.2
- **Hemoglobin 9.6 (Normal ≥ 11.9)**
- **Hematocrit 29.5 (Normal ≥ 35%)**
- MCV of 87.5
- Platelet count of 202,000
- **BUN 32 (Normal 7 – 18)**
- **Creatinine 3.66 (Normal less than or equal to 1.30)**
- **eGFR 14 (Normal ≥ 60)**

We ordered a full peripheral laboratory anemia work-up which was only remarkable for vitamin B12 deficiency. Thus, it was confirmed that her anemia was secondary to anemia of chronic kidney disease and vitamin B12 deficiency.

Initiated Retacrit and B12 injections. Hemoglobin improved to as high as 11.4.

Erythropoietin Mechanism



Chronic Kidney Disease

- CKD Stage III – V (eGFR 59 and under) can cause anemia secondary to decreased production of erythropoietin
- Can cause normocytic normochromic anemia
- Work up requires Hematology referral to rule out other potential causes before confirming that anemia is secondary to kidney disease
- Treatment consists of Erythropoiesis-Stimulated Agents (ESA) (Examples: Procrit, Aranesp)
  - Side effects: HTN, increased risk of clotting (CVA)
  - Relative contraindications: History of CVA, bedbound status, dementia
  - Requirements for initiation at most institutions and insurance provider:
    - Hemoglobin and Hematocrit be less than 10 and 30 respectively
    - Ferritin > 100 or Iron Saturation > 20%
  - After initiation, can administer if H/H is less than 11/33 and iron studies at goal
- End Stage Renal Disease (CKD Stage 5)
  - ESA therapy under management of Nephrologist during hemodialysis
- Achieving optimal iron levels
  - Can develop functional iron deficiency while on ESA therapy
    - Iron stores may be available but their release into the circulation may not be rapid enough to support the increased erythropoietic rate
  - Supplement with iron if iron saturation < 30% (may have insufficient iron availability for erythropoiesis)

Anemia Secondary to Hemolysis

- Causes
  - Acquired
    - Liver disease (Cirrhosis)
    - Hypersplenism
    - Infections (Bartonella, clostridial sepsis, malaria, babesiosis)
    - Toxins (lead, copper, snake and spider bites)
  - Hereditary
    - Sickle cell disease, thalassemia, G6PD deficiency
  - Immune related
    - Drug induced
    - Hemolytic transfusion reactions (ABO incompatibility)
    - Autoimmune hemolytic anemia
  - Paroxysmal Nocturnal Hemoglobinuria (PNH)
- Symptoms/Signs
  - Dark urine
  - Jaundice
  - Gallstones
  - Anemia with certain food or drug exposures (fava beans, oxidant drugs)
- Labs
  - LDH (Increased)
  - Indirect Bilirubin (Increased)
  - Haptoglobin (Decreased)
  - Direct Coombs test (DAT) (Positive)
  - Peripheral Blood smear (spherocytic RBCs, schistocytes, bite cells)
- Treatment
  - Blood transfusion if Hgb < 6 g/dL
  - Treat the offending agent
  - Consult Hematology

Case Study #6

35-year-old female presents with recently diagnosed iron deficiency anemia. She states that she has been diagnosed with iron deficiency anemia in the past most notably during her pregnancy approximately 4 years ago. She took iron pills during that time and her anemia improved although she suffered from significant constipation issues. After her pregnancy, she was found to have continued iron deficiency anemia. She continued taking iron pills for some time but discontinued them due to constipation issues. Approximate 1 month ago, she started to notice that she was developing fatigue, dizziness and lightheadedness which progressively got worse over the following several weeks. She reports having a short syncopal episode for 1 to 2 seconds but regained consciousness quickly. She was evaluated at her urgent care approximately 2 weeks ago and was found to have an UTI. She was treated with antibiotics and her UTI was resolved. She underwent lab work at the urgent care which revealed:

- **Hemoglobin of 8.2 (Normal ≥ 11.9)**
- **Hematocrit 25.3 (Normal ≥ 35%)**
- **Platelet count of 450,000 (Normal between 130,000 and 400,000)**
- **MCV of 71.6 (Normal between 80 – 100)**
- **White blood cell count of 12.1 (Normal 4.8 – 10.8)**
- **Iron saturation of 5% (Normal ≥ 20%)**

She also reports having unintentional weight loss of 20 pounds over the past year. Her menstrual cycles have for the most part been regular. Her menstrual cycle has normal flow lasting 2 to 3 days and she goes through 3 pads per day. She was then referred to hematology for evaluation for IV iron replacement therapy.

Case Study #6 (Continued)

Lab testing at our office revealed:
- **White blood cell count of 11.0 (Normal 4.8 – 10.8)**
- **Hemoglobin 9.6 (Normal > 11.9)**
- **Hematocrit 31.6 (Normal > 35%)**
- **MCV of 76.9 (Normal between 80 – 100)**
- **Platelet count of 606,000 (Normal between 130,000 and 400,000)**
- ANC of 6.1
- BUN 13
- Creatinine 0.66
- TIBC 238
- **Iron saturation 9% (Normal ≥ 20%)**
- **Ferritin 219 (Normal ≥ 40)**
- Vitamin B12 997
- Folate 5.7
- **U/A: Microscopic Hematuria**

Further Testing Revealed:
- Direct antiglobulin test (DAT) negative
- TSH 1.23,
- Free T4 1.1
- Stool for occult blood x 3 negative
- PNH evaluation negative
- No monoclonal proteins detected on SPEP with immunofixation
- Free kappa light chain 70.9
- Free lambda light chains 44.1
- Free K/L ratio 1.61
- **IgG quantitative 3236 (Ref Range 600 – 1640)**
- **IgA quantitative 406 (Ref Range 47 – 310)**
- IgM quantitative 91
- Hemoglobin electrophoresis negative
- Alpha globin gene sequencing panel negative

Due to her elevated ferritin levels as well as elevated IgG and IgA levels, we performed a full rheumatological work up.

Case Study #6 (Continued)

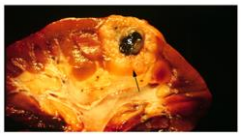
Her full Rheumatological work up was…..NEGATIVE except for….
- **Sedimentation rate 86 (Ref Range 0 - 20)**
- **C-reactive protein 3.4 (Ref Range 0 - 1.0)**

Malignancy work up
- Chest X-ray and CT scan of the Abdomen and Pelvis with IV and PO Contrast
  - CXR: No acute cardiopulmonary abnormality seen
  - CT
    - Right kidney is asymmetrically enlarged with severe hydronephrosis, calyceal dilatation and extensive uroepithelial thickening and inflammation to the level of an impacted stone at the right ureterovesical junction measuring 10 mm
    - Numerous parenchymal fluid collections present in the right kidney measuring up to 3.6 x 3.5 cm

Diagnosis:
- Xanthogranulomatous Chronic Obstructive Pyelonephritis of the right kidney with hydronephrosis and associated pyeloureteritis

Treatment
- ASAP Referral to Urology
- Due to high risk of kidney atrophy and destruction, she underwent right nephrectomy
- No longer has anemia!

Xanthogranulomatous PN gross

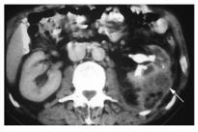


Gross specimen of a kidney with a segmental area of xanthogranulomatous pyelonephritis (arrow) surrounding a calcium stone (S). The yellow tissue in this area represents an inflammatory reaction with lipid-filled macrophages.

Courtesy of Helmut Rennke, MD.

UpToDate

Xanthogranulomatous pyelonephritis

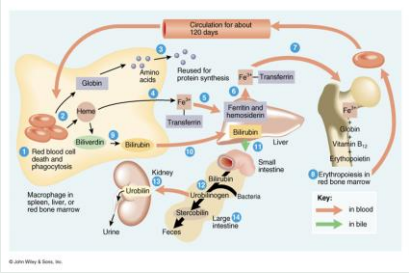


CT scan of xanthogranulomatous pyelonephritis with perinephric extension. There is diffuse enlargement of the left kidney and the renal tissue is replaced by multiple low-attenuation masses (arrow). A calcification is visible within the renal pelvis and there is posterior and pararenal extension of the pseudotumoral inflammatory tissue. The contralateral kidney is normal.

Courtesy of Alain Meyrier, MD.

UpToDate

Formation and Destruction of RBC's

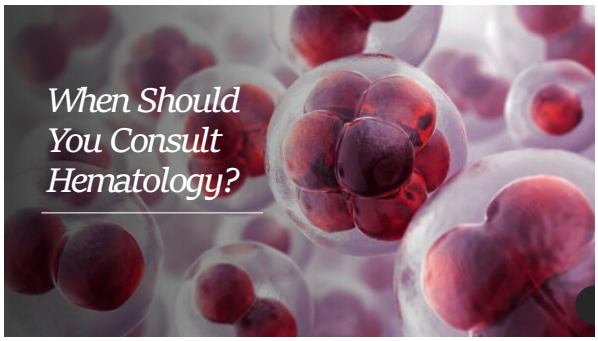


What are indications for a blood transfusion?

- Blood transfusion indicated typically if hemoglobin is less than 7 and the patient is symptomatic (severe shortness of breath, heart palpitations, lethargy, severe weakness, etc)
- If patient is clinically stable, shown to have iron deficiency and their hemoglobin is less than or around 7, they can be referred to Hematology for consideration of iron infusions ASAP
- Hematology can order outpatient blood transfusions if necessary, saving the patient an ER visit

Initial Approach to Anemia Work Up

- Questions to answer:
  - Is the bone marrow suppressed?
  - Is the patient bleeding (now or in the past)
  - Is there evidence of hemolysis?
  - Is there a vitamin deficiency (iron, B12, or folate)?
- Order appropriate laboratory testing
- If malignancy or organ dysfunction is suspected, order imaging
- Refer to specialists if necessary for further work up
- If cause is reversible, treat the underlying cause
- If you are still stumped, then, refer to Hematology!



Indications for Hematology Consult

- Unexplained anemia
- Unexplained microcytosis or macrocytosis
- Patient is not responding to oral iron supplementation
- Patient meets criteria for IV iron
- Concern for malignancy related anemia
- Severe anemia (Hemoglobin < 7)
- Patient with anemia of chronic kidney disease and persistent hemoglobin/hematocrit of less than 10/30 respectively

References

PubMed. *Chapter 1: Diagnosis and evaluation of anemia in CKD.* Kidney Int Suppl (2011). 2012;2(4):288.

PubMed. *Gastrointestinal causes of refractory iron deficiency anemia in patients without gastrointestinal symptoms.* Annibale B, Capurso G, Chistolini A, D'Ambra G, DiGiulio E, Monarca B, DelleFave G. Am J Med. 2001;111(6):439.

PubMed. *Iron deficiency anaemia.* Lopez A, Cacoub P, Macdougall IC, Peyrin-Biroulet L. Lancet. 2016 Feb;387(10021):907-16. Epub 2015 Aug 24.

PubMed. *Use of proton pump inhibitors and risk of iron deficiency: a population-based case-control study.* Tran-Duy A, Connell NJ, Vanmolkot FH, Souverein PC, de Wit NJ, Stehouwer CDA, Hoes AW, de Vries F, de Boer A. J Intern Med. 2019;285(2):205. Epub 2018 Sep 17.

PubMed. *Iron Deficiency and Iron Deficiency Anemia: Implications and Impact in Pregnancy, Fetal Development, and Early Childhood Parameters.* Nutrients. 2020;12(2) Epub 2020 Feb 11.

Means, Robert T, Brodsky, Robert A. *Diagnostic approach to anemia in adults.* UpToDate. Sept 2022

Means, Robert T, Fairfield, Kathleen M. *Clinical manifestations and diagnosis of vitamin B12 and folate deficiency.* UpToDate. June 2023

Auerbach, Michael. Causes and diagnosis of iron deficiency and iron deficiency anemia in adults. UpToDate. July 2023.

PubMed. *Effect of Low-Dose Aspirin Versus Placebo on Incidence of Anemia in the Elderly: A Secondary Analysis of the Aspirin in Reducing Events in the Elderly Trial.* McQuilten ZK, Thao LTP, Pasricha SR, Artz AS, Bailey M, Chan AT, Cohen HJ, Lockery JE, Murray AM, Nelson MR, Schneider HG, Wolfe R, Woods RL, Wood EM, McNeil JJ. Ann Intern Med. 2023;176(7):913. Epub 2023 Jun 20.

Thanks for listening!

Questions, comments, suggestions?

Please email me at:
danethomaspa@gmail.com
Or
DM me on LinkedIn
www.linkedin.com/in/dane-thomas-pac