Brigham and Women's Hospital
Founding Member, Mass General Brigham

Anemia: An Overview

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Disclosures

I have no relevant financial relationships with ineligible companies.

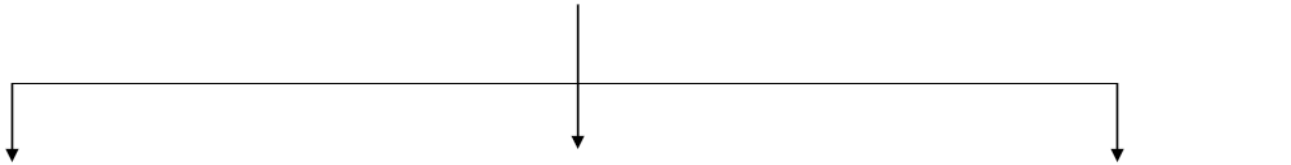
OBJECTIVES

Use case vignettes to:

- Review the work-up of anemia.
- Highlight the presentation and management of specific causes of anemia.

Anemia: An Overview

Morphological Classification of Anemia



Microcytic	**Normocytic**	**Macrocytic**
MCV<80	MCV 80-95	MCV>95
Iron deficiency deficiency	Renal failure	Vit B12
Anemia of chronic Dx	Anemia of chronic Dx	Folate deficiency
Thalassemias	Hypothyroidism	Hypothyroidism
Sideroblastic anemia	Early nutritional deficiencies	Myelodysplasia
Lead poisoning	Acute blood loss	Alcoholic liver Dx
Hemoglobin E trait	Sickle cell anemia	Reticulocytosis

Anemia: An Overview

Iron deficiency anemia

Anemia of inflammation

Anemia of chronic kidney disease

B12 deficiency

Copper deficiency

Acquired Pure Red Cell Aplasia

Anemia of liver disease

Myelophthisic anemia

Anemia of malnutrition

Warm autoimmune hemolytic anemia

Cold autoimmune hemolytic anemia

Paroxysmal Cold Hemoglobinuria

Anemia secondary to HIV infection

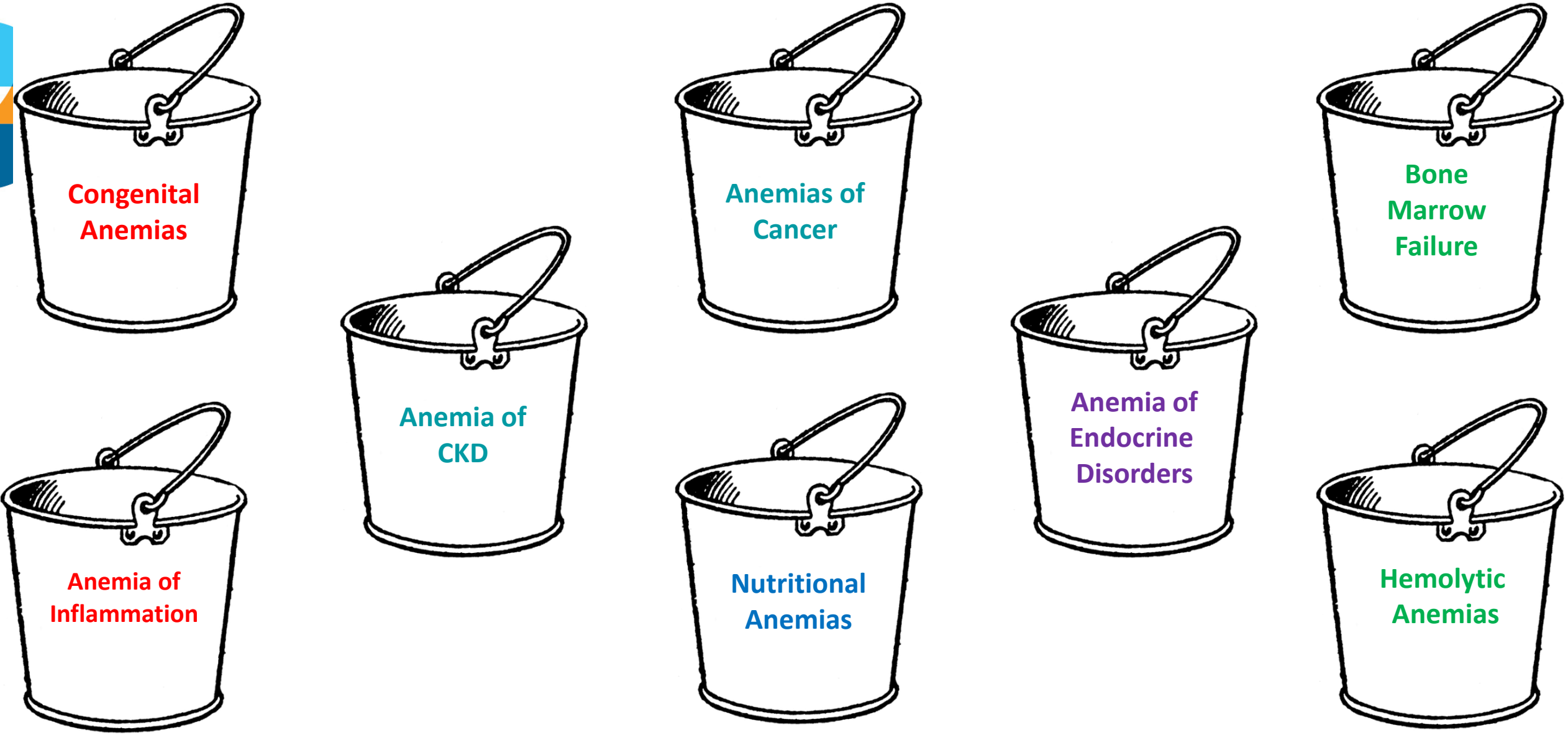
Beta thalassemia

Alpha thalassemia

Sickle cell anemia

G6PD Deficiency

March hemoglobinuria


Congenital Anemias
Anemias of Cancer
Bone Marrow Failure
Anemia of CKD
Anemia of Endocrine Disorders
Anemia of Inflammation
Nutritional Anemias
Hemolytic Anemias

Question 1

Mr. Curry is a 26 who is referred to hematology clinic for a macrocytic anemia with a Hb of 9.4g/dl and an MCV of 104. His WBC and platelet counts are also decreased. On neuro exam, he is noted to have a loss of vibratory sense. Work-up is notable for a decreased reticulocyte production index, B12: 288, folic acid: 24, normal LFTs, and normal thyroid studies. An SPEP with immunofixation is negative. He underwent a gastric bypass surgery 3 years ago and is currently on a proton pump inhibitor. What is the most appropriate next step in work-up?

A. Perform an ultrasound of the liver.
B. Check methylmalonic acid and homocysteine levels.
C. Check an H. pylori stool antigen.
D. Check a copper level.
E. Check a B6 level.

Question 1

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Vitamin B12 Deficiency

- B12 is necessary for purine and pyrimidine synthesis. A deficiency impairs erythropoiesis and myelin synthesis

- Most commonly results from pernicious anemia. Other causes include:
  - Gastric bypass surgery
  - Hypochlorhydria
  - Medication (e.g. PPIs)
  - Insufficient dietary intake

Clinical Challenge:

Vitamin B12 levels in isolation are neither sensitive nor specific for diagnosing B12 disorders:

- B12 results are highly variable
- A low B12 level does not indicate deficiency
- A normal B12 level does not always mean sufficient B12 is present

When in doubt, use your clinical sense and check homocysteine and methylmalonic acid

Green R. Vitamin B_{12} deficiency from the perspective of a practicing hematologist. Blood. 2017 May 11;129(19):2603-2611.
Thayabaran D, Burrage D. Nitrous oxide-induced neurotoxicity: A case report and literature review. Br J Clin Pharmacol. 2021 Sep;87(9):3622-3626..

Vitamin B12 Deficiency: Additional Pearls

- Dietary cobalamin deficiency develops slowly – over the course of years
- Hematologic findings are typically early in the course of illness, but patients may present with neurologic changes in the absence of cytopenias
- IM B12 treatment can cause intrinsic factor antibodies to be falsely positive. Wait at least a week after IM B12 treatment to check intrinsic factor antibodies
- Reticulocytes peak in the blood approximately 1 week after initiation of B12 therapy

ASH-SAP: American Society of Hematology Self-Assessment Program 7th Edition; Edited by Cuker A, Altman, JK, Gerds, AT, and Wun, T; American Society of Hematology;2019.
Green R. Vitamin B_{12} deficiency from the perspective of a practicing hematologist. Blood. 2017 May 11;129(19):2603-2611.

Question 2

Ms. Santiago is a 33YO, who is originally from the Dominican Republic, and presents to clinic for her first visit. She has no significant medical history and has two children. After the birth of her second child who is now 3 years old, she was told to take iron tablets twice daily. Aside from an oral contraceptive, iron is her only medication.

Laboratory studies reveal:

White blood cell count	4,600/mm^3	(4,000-10,000)
Hematocrit	35%	(36-48)
MCV	66 fL	(80-95)
Platelets	256,000/mm^3	(150,000-450,000)
Fe	150 μg/dL	(40-159)
TIBC	275 μg/dL	(250-400)
Ferritin	350 μg/dL	(20-150)

Question 2

The most appropriate next step in her care is:

A. Therapeutic phlebotomy for hereditary hemochromatosis

B. Send an ESR and CRP

C. Switch from oral iron sulfate to intravenous iron infusions

D. Discontinue iron therapy. Send hemoglobin electrophoresis

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Thalassemia

- Congenital disorder associated with defective synthesis of alpha or beta globin subunits of hemoglobin
- Confers immunity against malaria. High incidence (up to 25%) in individuals from the Mediterranean basin, the Middle East, tropical and subtropical regions of Africa, and Southeast Asia
- Results in a diverse clinical manifestations ranging from mild fatigue to fatal anemias in utero depending on the severity of the thalassemia

Pearls re: Thalassemia Minor

- Should be suspected in patients with low normal hemoglobin, microcytosis, a high normal or elevated RBC count, and normal iron studies
- Can be associated with mild fatigue
- Hemoglobin will worsen during pregnancy or times of bone marrow suppression
- Prenatal genetic testing of partners is important to understand risk of thalassemia in offspring
- Patients with thalassemia minor are at high risk of developing iron overload due to 1) increased iron absorption related to thalassemia and 2) inappropriate treatment of microcytosis with long term iron replacement

Question 3

Ms. Santiago is a 33YO, who is originally from the Dominican Republic, and presents to clinic for her first visit. She has no significant medical history and has two children. After the birth of her second child who is now 3 years old, she was told to take iron tablets twice daily. Aside from an oral contraceptive, iron is her only medication. Despite her oral contraceptive, she continues to have heavy periods. She notes fatigue and shortness of breath with exertion.

Laboratory studies reveal:

Hematocrit	35%	(36-48)
MCV	78 fL	(80-95)
Fe	50 μg/dL	(40-159)
TIBC	395 μg/dL	(250-400)
Ferritin	20 μg/dL	(20-150)

Question 3

The most appropriate next step in her care is:

A. Therapeutic phlebotomy for hereditary hemochromatosis

B. Send an ESR and CRP

C. Switch from oral iron sulfate to intravenous iron infusions

D. Discontinue iron therapy. Send ferritin and hemoglobin electrophoresis

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B. Send an ESR and CRP

C. Switch from oral iron sulfate to intravenous iron infusions

D. Discontinue iron therapy. Send ferritin and hemoglobin electrophoresis

Iron Deficiency

- For women worldwide, iron deficiency is the leading cause of years lived with disability burden
- Fatigue is the most common symptom of iron deficiency and results even in the absence of overt anemia
- The normal ferritin value listed in many EHRs is incorrect. A ferritin value less than 30 reflects exhausted iron stores even if no overt anemia is present
- In the setting of symptomatic iron deficiency that has not improved with oral iron replacement, please have a low threshold to give IV iron infusions

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- In the setting of symptomatic iron deficiency that has not improved with oral iron replacement, please have a low threshold to give IV iron infusions

Iron Deficiency

- Preferred IV iron formulations differ by location/health system
- In my practice, I favor the following:
  - Iron dextran (Infed): Covered by nearly all insurances, administration of 1000mg of iron in 1 hour, currently requires a test dose to minimize risk of allergic reactions
  - Ferumoxytol (Feraheme): Less frequently covered by insurance, administration of 510mg of iron in 20 minutes, does not require a test dose

** I rarely use Iron sucrose (venofer) as it is too little iron at a time and requires frequent visits to the infusion center

Question 4

Ms. Santiago is a 33YO, who is originally from the Dominican Republic, and presents to clinic for her first visit. After the birth of her second child who is now 3 years old, she developed new diffuse joint pains and rashes. She has started to see a rheumatologist who has diagnosed her with lupus. She notes fatigue and shortness of breath with exertion. She has not started any medications for her lupus.

Laboratory studies reveal:

Hematocrit	35%	(36-48)
MCV	78 fL	(80-95)
Fe	25 μg/dL	(40-159)
TIBC	195 μg/dL	(250-400)
Ferritin	350 μg/dL	(20-150)

Question 4

The most appropriate next step in her care is:

A. Therapeutic phlebotomy for hereditary hemochromatosis

B. Send an ESR and CRP

C. Switch from oral iron sulfate to intravenous iron infusions

D. Discontinue iron therapy. Send hemoglobin electrophoresis

Question 4

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D. Discontinue iron therapy. Send hemoglobin electrophoresis

Anemia of Inflammation

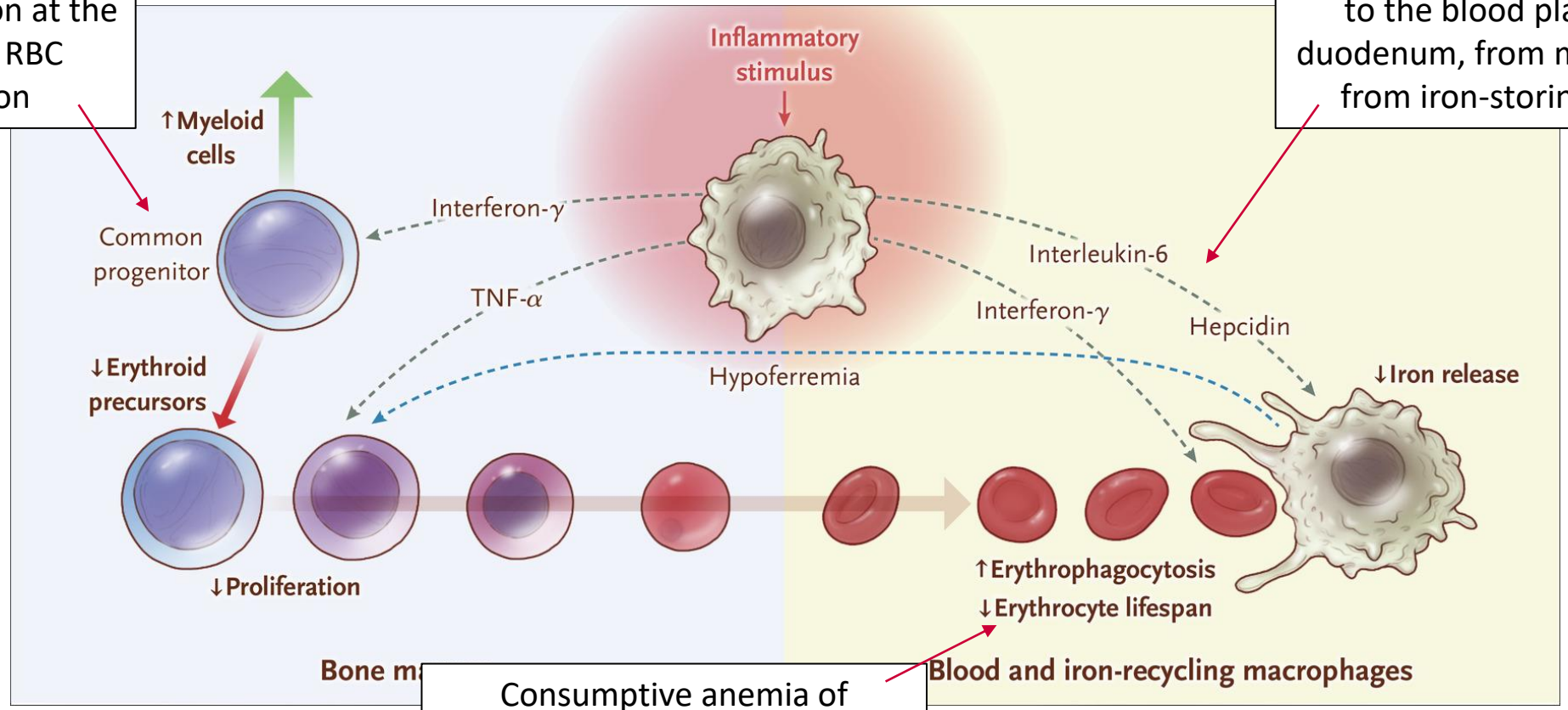
- Results in normal appearing red cells that become small and pale if iron deficiency is coexistent
- Can develop in as little as 1 week in critically ill patients. More frequently develops in weeks to months
- Goal is to limit non-transferrin-bound iron in the blood which acts as a potent stimulus to the pathogenicity of gram-negative bacteria
- Multifactorial process leading to decreased RBC production and decreased RBC lifespan

Ganz T. Anemia of Inflammation. N Engl J Med. 2019 Sep 19;381(12):1148-1157. doi: 10.1056/NEJMra1804281. PMID: 31532961.

Anemia of Inflammation

Inflammatory cytokines promote WBC production at the expense of RBC production

IL-6 increases hepcidin production leading to decreased transfer of iron to the blood plasma from the duodenum, from macrophages, and from iron-storing hepatocytes



Consumptive anemia of inflammation leads to 25% decrease in RBC lifespan

Ganz T. Anemia of Inflammation. N Engl J Med. 2019 Sep 19;381(12):1148-1157. doi: 10.1056/NEJMra1804281. PMID: 31532961.

Diagnosing Anemia of Inflammation

Table 1. Differences in Biomarkers of Iron Deficiency and Anemia of Inflammation.

Biomarker*	Iron Deficiency	Anemia of Inflammation
Mean corpuscular volume	Low	Normal
Mean corpuscular hemoglobin	Low	Normal
Reticulocyte hemoglobin content	Low	Normal
Percentage of hypochromic erythrocytes	High	Low
Serum transferrin	High	Low
Serum transferrin receptor	High	Normal
Serum ferritin	Low	High
Serum hepcidin	Low	High

* Intermediate biomarker values would be expected when both iron deficiency and anemia of inflammation are present.

Primary Clinical Challenge:

Patient with inflammation and iron deficiency that may be concurrent:

- Assess for signs/symptoms of bleeding
- If safe, trial IV iron infusion to assess for benefit

Ganz T. Anemia of Inflammation. N Engl J Med. 2019 Sep 19;381(12):1148-1157. doi: 10.1056/NEJMra1804281. PMID: 31532961.

Question 5

Ms. Jones is a 68YO with a history of heart failure with a systolic ejection fracture of 35%, hypertension, type 2 diabetes, hypothyroidism, and stage 3b chronic kidney disease. Her Cr is 1.87 with an eGFR of 38. She is referred by her primary care physician to hematology clinic for anemia. What percent of stable outpatients with stage 3 CKD will have a hemoglobin < 12 g/dl? What about < 10 g/dl?

A. 10% will be < 12 g/dl; 1% will be < 10 g/dl.
B. 23% will be < 12 g/dl; 1% will be < 10 g/dl.
C. 42% will be < 12 g/dl; 6% will be < 10 g/dl.
D. 75% will be < 12 g/dl; 6% will be < 10 g/dl.
E. 75% will be < 12 g/dl; 25% will be < 10 g/dl.

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D. 75% will be < 12 g/dl; 6% will be < 10 g/dl.
E. 75% will be < 12 g/dl; 25% will be < 10 g/dl.

Prevalence of Anemia in CKD

- Anemia in CKD is typically normocytic, normochromic, and hypoproliferative

- Multi-factorial process resulting from:
  - Relative erythropoietin (EPO) deficiency
  - Inflammation
  - Shortened RBC survival
  - Nutritional deficiencies
  - Blood loss

Frequency of Anemia by Stage of Kidney Disease:

Stage of Kidney Disease	Percent Hb < 12 g/dl	Percent Hb < 10 g/dl
1 (eGFR >90)	Uncommon	Uncommon
2 (eGFR 60-89)	Uncommon	Uncommon
3 (eGFR 30-59)	42%	6%
4 (eGFR 15-29)	54%	11%
5 non-dialysis (eGFR <15)	75%	50%
Dialysis-dependent	Nearly 100%	90% require an ESA

McClellan, William, et al. "The prevalence of anemia in patients with chronic kidney disease." *Current medical research and opinion* 20.9 (2004): 1501-1510.

Anemia of Chronic Kidney Disease

- Often accounts for mild anemia without an otherwise identifiable reason
- Anemic patients with diabetes mellitus and even modestly abnormal renal function are often erythropoietin deficient
- The normal range for erythropoietin values is for patients who are not anemic
- Anemia of any significant degree should lead to a rise in the erythropoietin level above the normal range

Question 6

Mr. O'Leary is a 73M who is referred to hematology clinic for a new anemia with a Hb of 10.8 g/dl. On history, he reports low grade fevers, vision changes, and pain when he combs his hair. His CRP and ESR are significant elevated. How long will it take for him to have a clinically significant hemoglobin increase once appropriate treatment for his underlying disorder is initiated.

A. 5 days.
B. 14 days.
C. 28 days.
D. 60 days.

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C. 28 days.
D. 60 days.

Weiss LM, Gonzalez E, Miller SB, Agudelo CA. Severe anemia as the presenting manifestation of giant cell arteritis. Arthritis Rheum 1995;38:434-436.

Treating Anemia of Inflammation

- Best treatment currently: Treating the underlying cause for the inflammation.
- With appropriate treatments, will have a clinically significant improvement in Hb:
  - 2 weeks for auto-immune disorders.
  - 4-8 weeks for tuberculosis.
- No clear efficacy to treatment with ESAs outside of CKD.

Table 2. Compounds under Development for the Treatment of Anemia of Inflammation.

Compound	Target*	Stage of Development (Study)
Heparin derivatives	BMPs that stimulate hepcidin synthesis	Preclinical stage (Poli et al.[57])
Soluble hemojuvelin	BMPs that stimulate hepcidin synthesis	Preclinical stage (Theurl et al.[58])
Engineered hepcidin binders	Hepcidin	Preclinical stage (Hohlbaum et al.[59]) and phase 1 (Boyce et al.[60])
Monoclonal antibodies	Ferroportin, blocking hepcidin access	Phase 1 (Sheetz et al.[61])
	BMP-6	Phase 1 (Sheetz et al.[61])
	Hepcidin	Phase 1 (Vadhan-Raj et al.[62]) and preclinical stage (Sasu et al.[63])
	Hemojuvelin	Preclinical stage (Kovac et al.[64])
Momelotinib	BMP receptor (ACVR1) and JAK1 and JAK2	Preclinical stage (Asshoff et al.[65]) and phase 3 (Mesa et al.[66])†
TP-0184	BMP receptor (ACVR1)	Phase 1 (Peterson et al.[67])
Prolyl hydroxylase inhibitors	HIF prolyl hydroxylases	Preclinical stage (Barrett et al.[68]) and phase 2 (Chen et al.[69])‡

* ACVR1 denotes activin A receptor 1, BMP bone morphogenetic protein, HIF hypoxia-inducible factor, and JAK1 and JAK2 Janus kinase 1 and 2, respectively.
† The phase 3 study involved patients with myelofibrosis.
‡ The phase 2 study involved patients with chronic kidney disease.

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Question 7

Ms. Adams is a 46F who is referred to hematology clinic due to concern for myelodysplastic syndrome. She reports recent fatigue and generalized weakness and on a routine CBC was found to have a Hb: 5.9 g/dl with an MCV of 107.9. Her WBC was 1.5 with an ANC of 200 and her platelet count was normal at 400. Her ferritin was elevated but her B12, MMA, homocysteine, folate, and Tsat were normal. Review of her peripheral smear showed mild anisopoikilocytosis with variable hypochromasia, microcytes, macrocytes, occasional dacrocytes, and pencil cells. Her WBCs and platelets had no significant qualitative changes. She has a history of bariatric surgery 30 months ago. What should be your next diagnostic step?

A. Check a copper level.
B. Send testing from the peripheral blood looking for genetic markers of MDS.
C. Perform a bone marrow biopsy.
D. Check flow cytometry for PNH.
E. Send SPEP with immunofixation.

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Copper Deficiency

- Rare syndrome that can mimic MDS.
- Has no specific MCV. Can cause an anemia that is microcytic, normocytic, or macrocytic.
- Can result from inadequate copper intake or impaired copper absorption.
- Most commonly follows gastric resection or bariatric surgery. May also result from zinc excess.
- Most patients also report neurologic deficits.

Oral copper replacement is the mainstay of treatment

Image from: https://creakyjoints.org/symptoms/copper-deficiency-rheumatoid-arthritis-emergency-care/

Thakral B, Saluja K, Eldibany M. Zinc-induced copper deficiency: a diagnostic pitfall of myelodysplastic syndrome. Pathology. 2014 Apr;46(3):246-8..

Question 8

Ms. Cruz is a 63F with a history of hypothyroidism who is referred to hematology clinic for subacute anemia. Two months ago, in the setting of fatigue, she was found to have hypothyroidism and a mild anemia (Hb: 9.8 g/dl). Iron studies at the time were notable for a ferritin: 30 and Tsat: 14%. She was started on thyroid replacement and oral iron and has been consistently taking both medicines every morning. Her TSH remains elevated and her Hb continues to be low (10.3 g/dl). Her iron studies have normalized. What would you recommend next for this patient?

A. Administer IV iron replacement.
B. Initiate an ESA.
C. Undergo a bone marrow biopsy.
D. Check ESR and CRP.
E. Stop oral iron and repeat a CBC in 1-2 months.

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Anemia of Primary Hypothyroidism

- One of the anemias associated with endocrine disorders. Others include:
  - Anemia secondary to hypogonadism.
  - Microcytic anemia in hyperthyroidism.
  - Dysfunction of the anterior lobe of the pituitary gland.
- Leads to a normocytic and normochromic anemia.
- Results from an absence of EPO-stimulated erythroid colony formation.

Clinical Pearls:

Anemia may take months to resolve after thyroid replacement is initiated.

Concurrent administration of levothyroxine and oral iron leads to impaired levothyroxine absorption.
(so consider IV rather than PO iron administration).

ASH-SAP: American Society of Hematology Self-Assessment Program 7th Edition; Edited by Cuker A, Altman, JK, Gerds, AT, and Wun, T; American Society of Hematology;2019.

Question 9

A 54 year-old man of Greek ancestry is seen for follow-up 3 days after completing a course of trimethoprim/sulfamethoxazole for an upper respiratory tract infection. While his his cough has improved, he now feels more shortness of breath with exertion and fatigue. In addition, he notes that his eyes have become yellow.

Laboratory studies reveal:

• White blood cell count	5,860/mm^3	(4,000-10,000)
• Hematocrit	28%	(36-48)
• Reticulocyte count	11%	(1-1.5%)
• MCV	101 fL	(80-95)
• Platelets	175,000/mm^3	(150,00-450,000)

Question 9

The most appropriate course of action at this time is:

A. Obtain folate and vitamin B12 levels

B. Observation, return visit in a few weeks for further laboratory studies

C. Test for glucose-6-phosphate dehydrogenase deficiency

D. Bone marrow aspirate and biopsy

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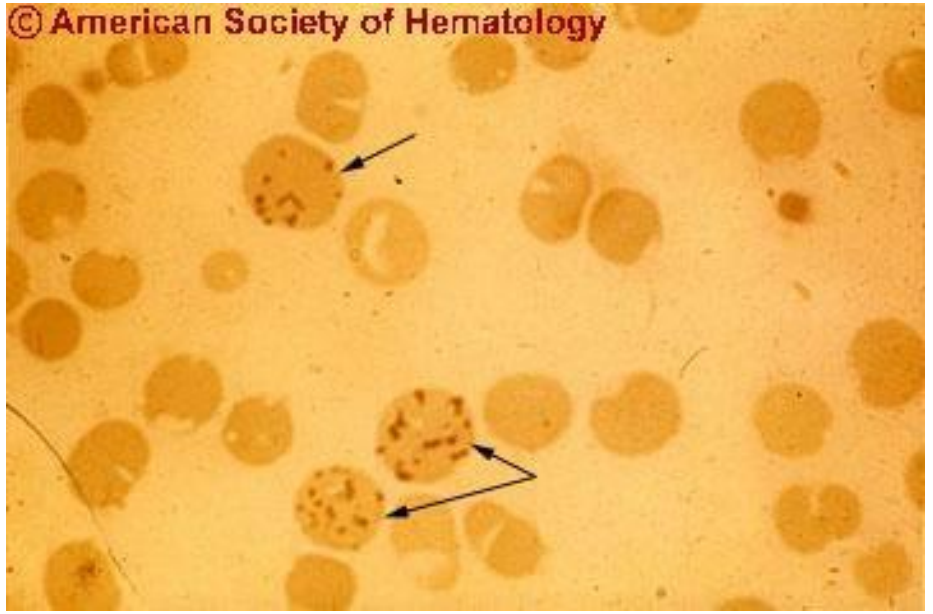
G6PD Deficiency

Two Isoforms:

1. A-isoform
   - G6PD activity declines due to enzyme instability during the red cell life-span
   - Present in 10% of African-American males
   - G6PD levels in reticulocytes are normal
   - May require Heinz Body identification to diagnose during acute hemolytic episode

2. Mediterranean Isoform
   - Essentially no G6PD activity in RBC = more severe
   - Present in 5% of individuals from the Mediterranean
   - Can always be diagnosed (even during hemolysis)



Heinz bodies: oxidized, denatured precipitates of hemoglobin

Oxidant Stressors in G6PD Deficiency

Antibacterials

- Dapsone
- Nalidixic acid
- Nitrofurantoin
- Sulfamethoxasole
- Sulfapyridine

Antimalarials

- Primaquine
- Pamaquine

Miscellaneous

- Doxorubicin
- Methylene blue
- Phenazopyridine (PYRIDIUM)
- Phenylhydrazine
- Probenacid

Environmental/Food

- Fava beans
- Naphthalene (moth balls)
- Toluene blue

Question 10

A 35 year-old woman comes to the emergency room with shortness of breath on exertion over the past several days. Her past medical history is unremarkable. She takes no medications and notes no systemic symptoms. She is afebrile and her vital signs are stable. Physical examination is remarkable for a few small ecchymoses on the upper and lower extremities, mild scleral icterus, and a grade I/VI holosystolic murmur.

Question 10

Laboratory studies reveal:

White blood cell count	9,600/mm^3	(4,000-10,000)
Hematocrit	23%	(36-48)
Platelets	36,000/mm^3	(150,000-450,000)
PT	12 s	(11-13)
PTT	26 s	(22-34)
Fibrinogen	450 mg/dL	(200-400)
Creatinine	0.8 mg/dL	(0.7-1.3)
LDH	1535	(107-231)

Peripheral blood smear reveals decreased platelets and moderate schistocytes.

Question 10

Which of the following is the appropriate next step:

A. Send serum toxicology panel and stool studies for E. coli 0157:H7

B. Initiate therapeutic plasma exchange as soon as possible

C. Observation for now, initiate plasma exchange if the platelet count < 20,000/mm^3

D. Observation for now, initiate plasma exchange if the patient becomes febrile or the creatinine rises

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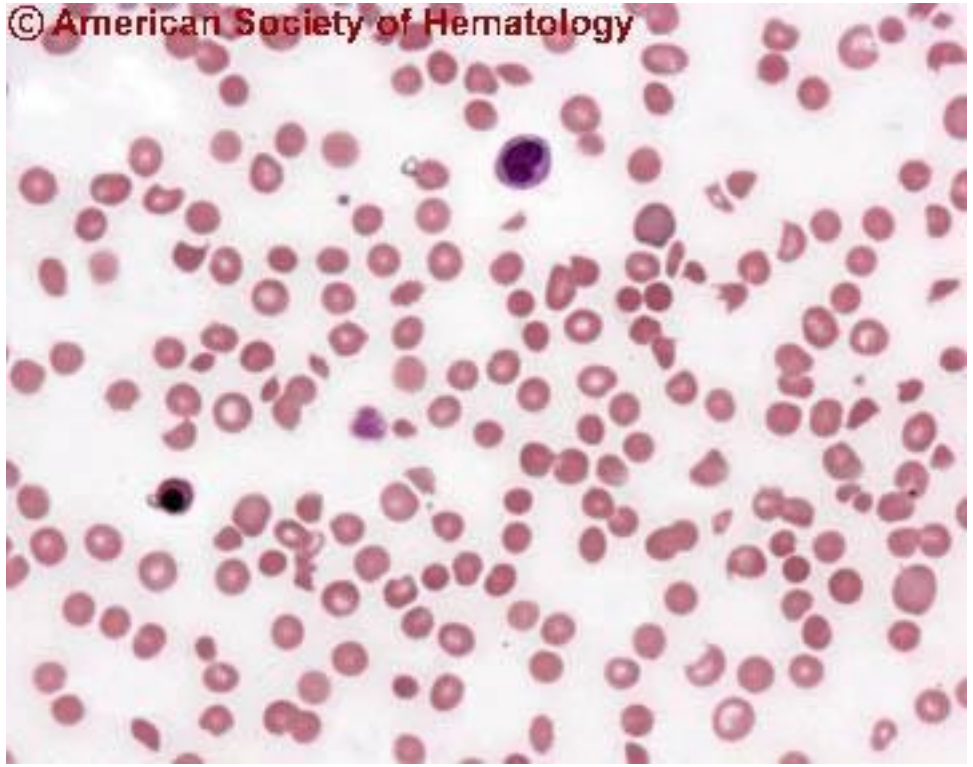
D. Observation for now, initiate plasma exchange if the patient becomes febrile or the creatinine rises

TTP Smear: Schistocytes



Diagnosis of TTP

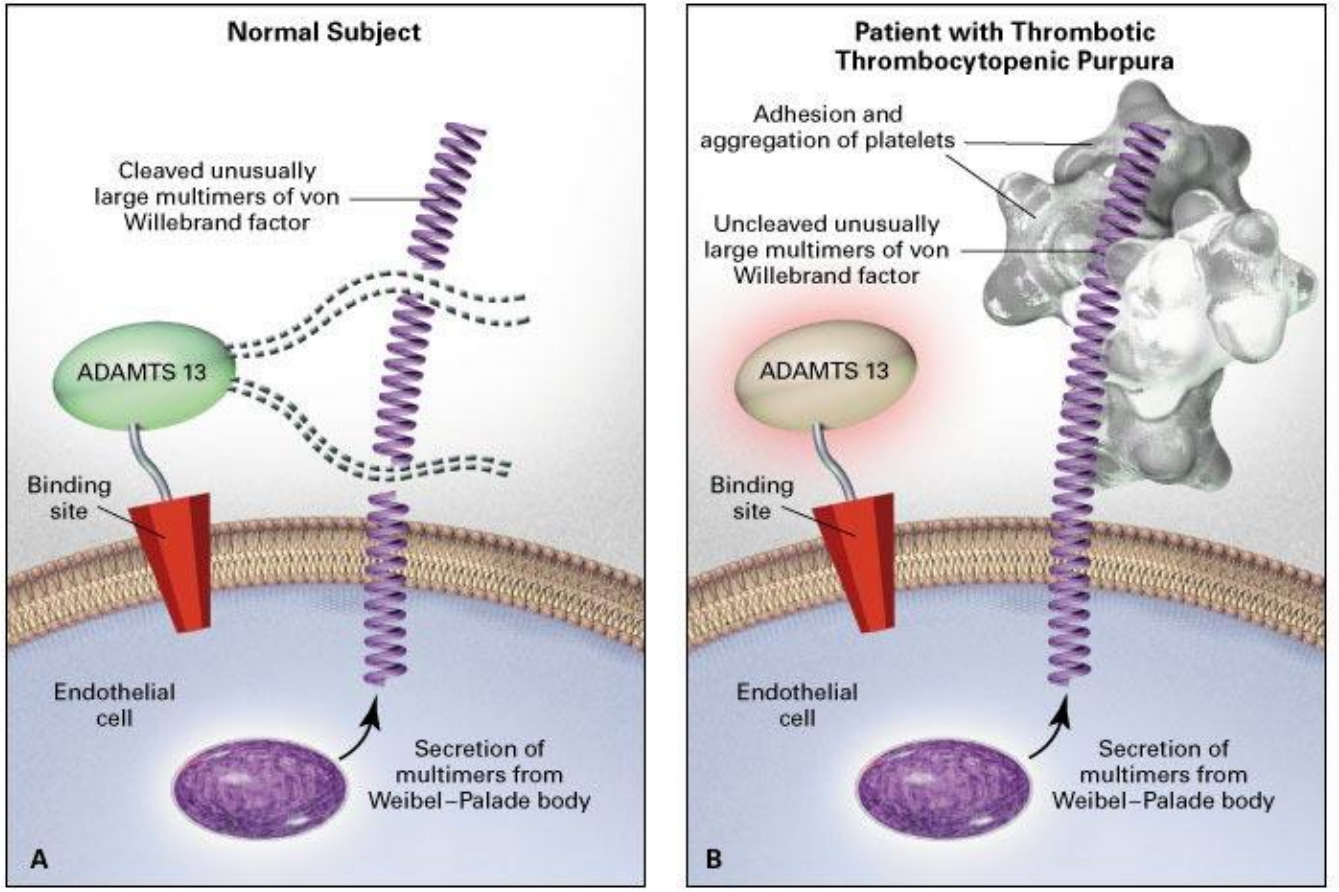
Two major characteristics of the classic pentad are enough to diagnose TTP:

- Microangiopathic hemolytic anemia
- Thrombocytopenia

Others manifestations may or not be present

- Fever
- Neurologic symptoms
- Renal Insufficiency/Failure

Pathophysiology of TTP



Moake, J. L. N Engl J Med 2002;347:589-600

Course of TTP

- About 90% of cases of TTP improve with plasma exchange.
- However, given that 30% of patients after plasma exchange, rituximab is now commonly used along with plasma exchange as first line therapy.
- Additional therapies to consider include cytotoxic agents, caplacizumab (blocks VWF-PLT binding)

Question 11

Mr. Thompson is a 52M with a known history of HIV infection and severe alcohol use disorder who has had limited access to food. He presented to the ED last night and was found to have a leukopenia (WBC: 2.4) and anemia (Hb 8.4) with a normal platelet count. His red cells were both normocytic and normochromic. He has been compliant with his HIV therapies but appears cachectic on exam. To assess the cause of his leukopenia and anemia, he underwent a bone marrow biopsy that demonstrated complete replacement of the marrow by hyaluronic acid extracellular matrix material. Testing for parvovirus is negative. As the heme consult attending, what treatment would you recommend for the patient?

A. Initiation of IV iron infusions.
B. Nutrition and social work consults with focus on alcohol use disorder and addressing his food insecurity.
C. Initiation of testosterone replacement.
D. Initiation of high dose steroids.
E. Initiation of an ESA.

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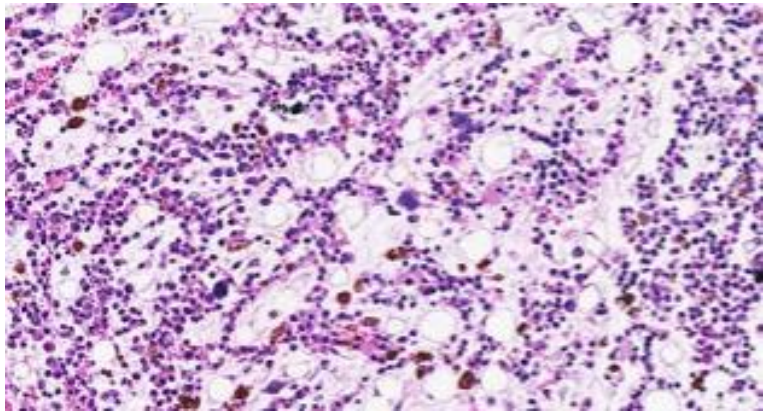
Anemia from Malnutrition

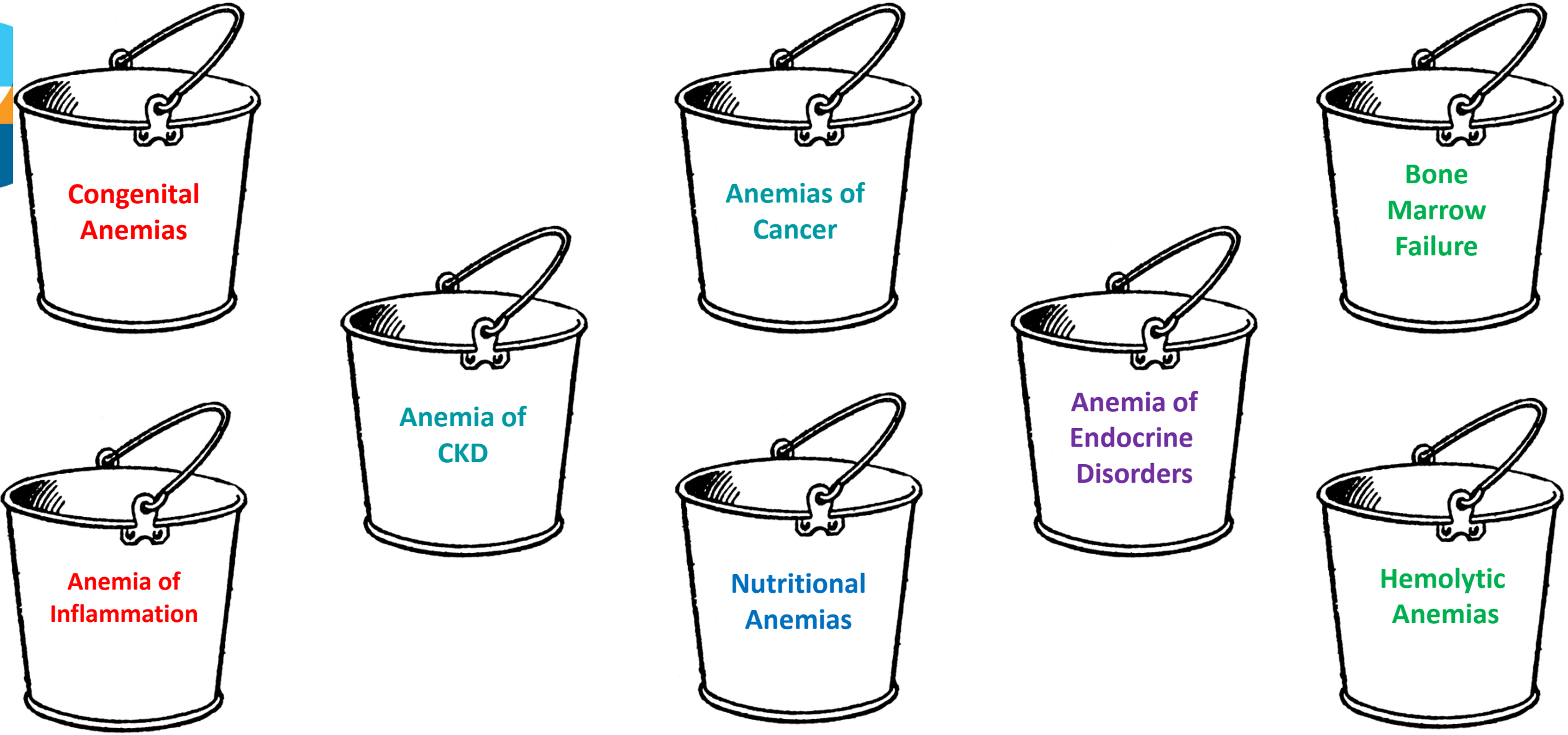
- A normocytic, normochromic anemia can develop in the setting of severe malnutrition.
- Anemia and neutropenia are more common than thrombocytopenia.
- Disorders leading to malnutrition include:
  - Anorexia.
  - Alcohol use disorder.
  - Cachexia secondary to cancer or chronic infection.
- Rarely, patients develop gelatinous transformation of their bone marrow as described in this case stem.



Bone Marrow with Severe Hypoplasia and Gelatinous Material in the Interstices

Barbin FF, Oliveira CC. Gelatinous transformation of bone marrow. Autops Case Rep. 2017 Jun 30;7(2):5-8..

De Filippo E, Marra M, Alfinito F, Di Guglielmo ML, Majorano P, Cerciello G, De Caprio C, Contaldo F, Pasanisi F. Hematological complications in anorexia nervosa. Eur J Clin Nutr. 2016 Nov;70(11):1305-1308.


Congenital Anemias
Anemias of Cancer
Bone Marrow Failure
Anemia of CKD
Anemia of Endocrine Disorders
Anemia of Inflammation
Nutritional Anemias
Hemolytic Anemias

Thank You!!

MOC REFLECTIVE STATEMENT (BRIEF TAKE HOME NOTES FOR REFERENCE)

- Vitamin B12 levels in isolation are neither sensitive nor specific for diagnosing B12 disorders
- Thalassemia should be suspected in patients with low normal hemoglobin, microcytosis, a high normal or elevated RBC count, and normal iron studies
- Fatigue is the most common symptom of iron deficiency and results even in the absence of overt anemia and a ferritin level <30 indicates low iron stores regardless of Hgb level
- Patients may have anemia of inflammation and concurrent iron deficiency
- Hematologists tend to be nice people who are always happy to answer questions so please reach out to your local **(or even not local)** friendly hematologist with questions!

Resource for Providers

Blood Journal: How I Treat Series –

Excellent series of case-based articles on work-up and treatment of common hematology topics

TREATMENT OF VENOUS THROMBOTIC DISORDERS | JANUARY 30, 2020

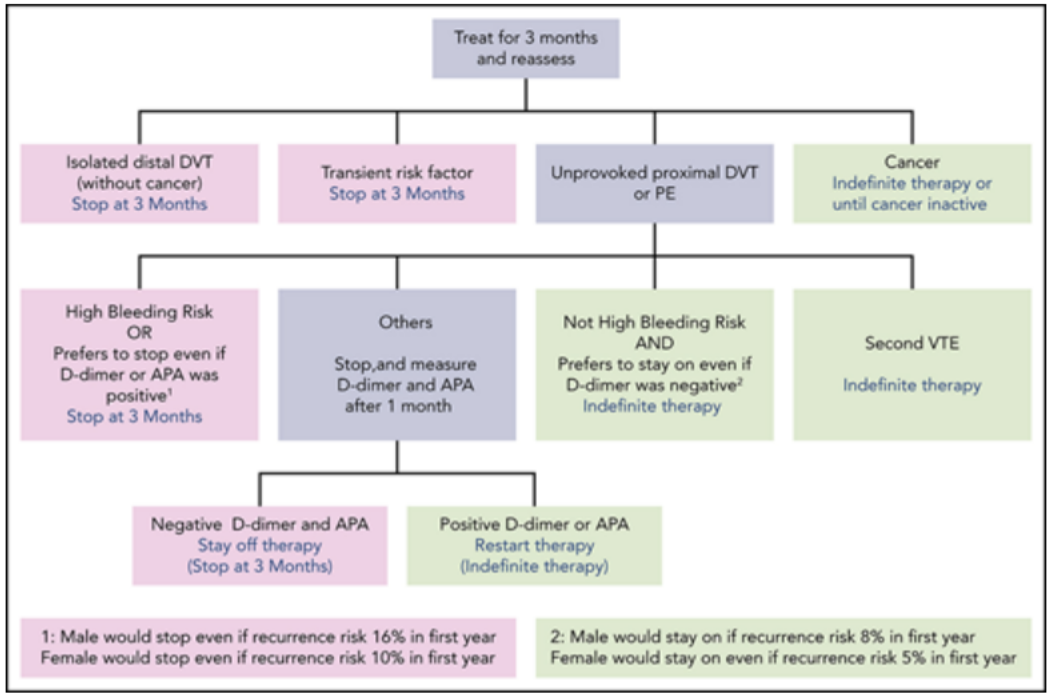
Long-term treatment of venous thromboembolism

Clinical Trials & Observations

Clive Kearon, Susan R. Kahn

Check for updates

Blood (2020) 135 (5): 317–325.



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4. Kidney Disease: Improving Global Outcomes (KDIGO). KDIGO clinical practice guideline for anemia in chronic kidney disease. Kidney Int Suppl. 2012;2(4):282-335.
5. Parfrey P. Hypoxia-Inducible Factor Prolyl Hydroxylase Inhibitors for Anemia in CKD. N Engl J Med. 2021 Dec 16;385(25):2390-2391.