Hematology - Part 1

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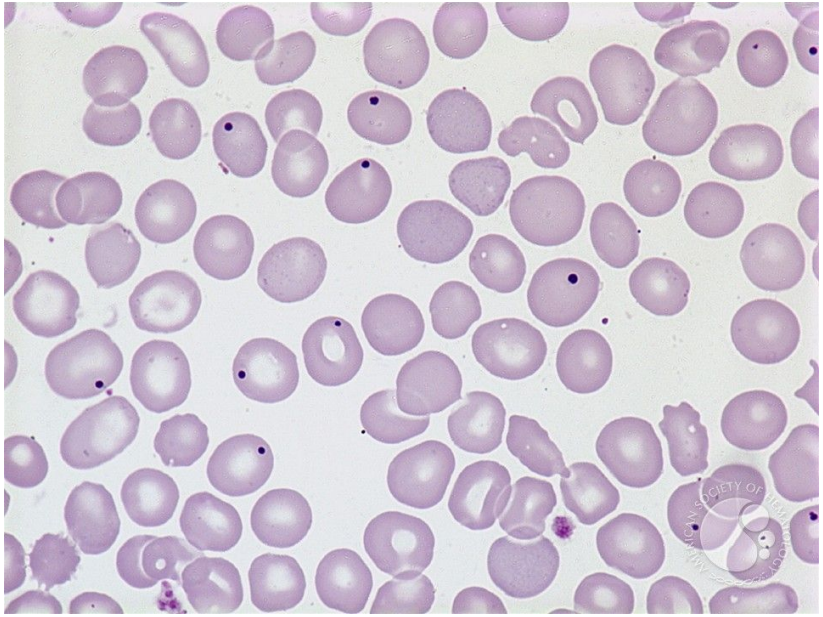

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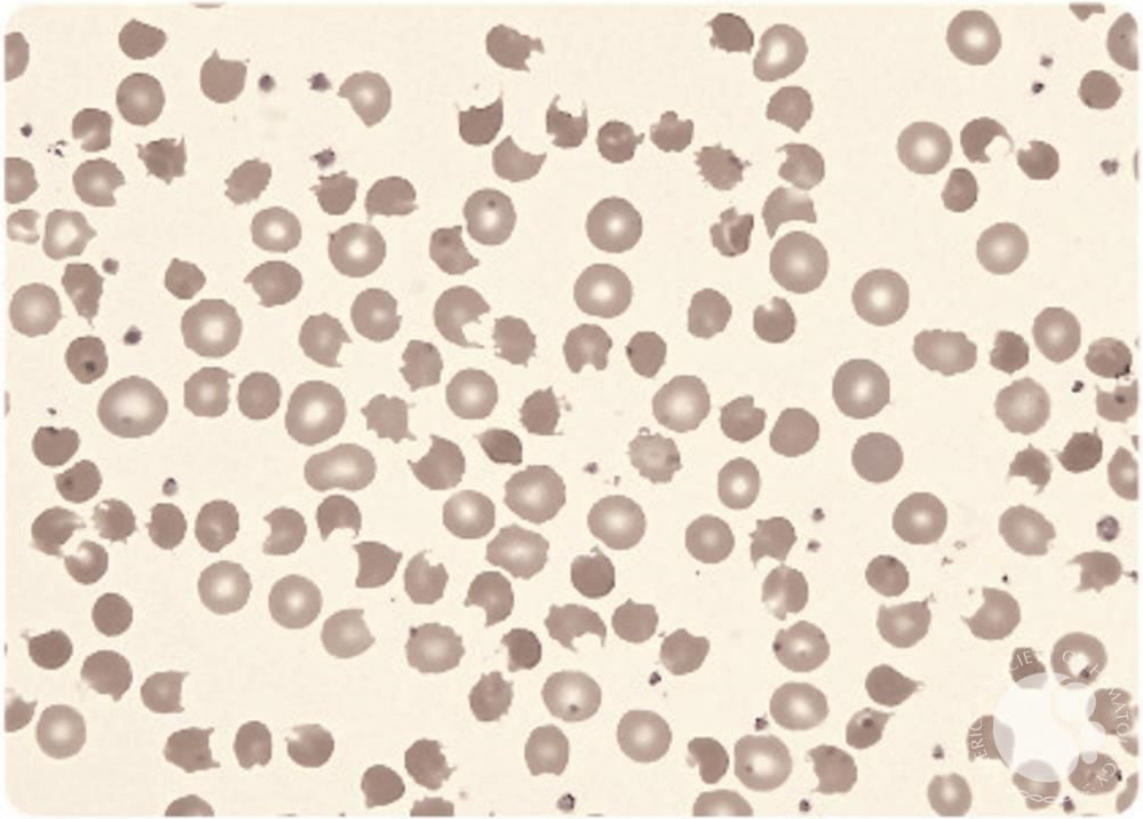

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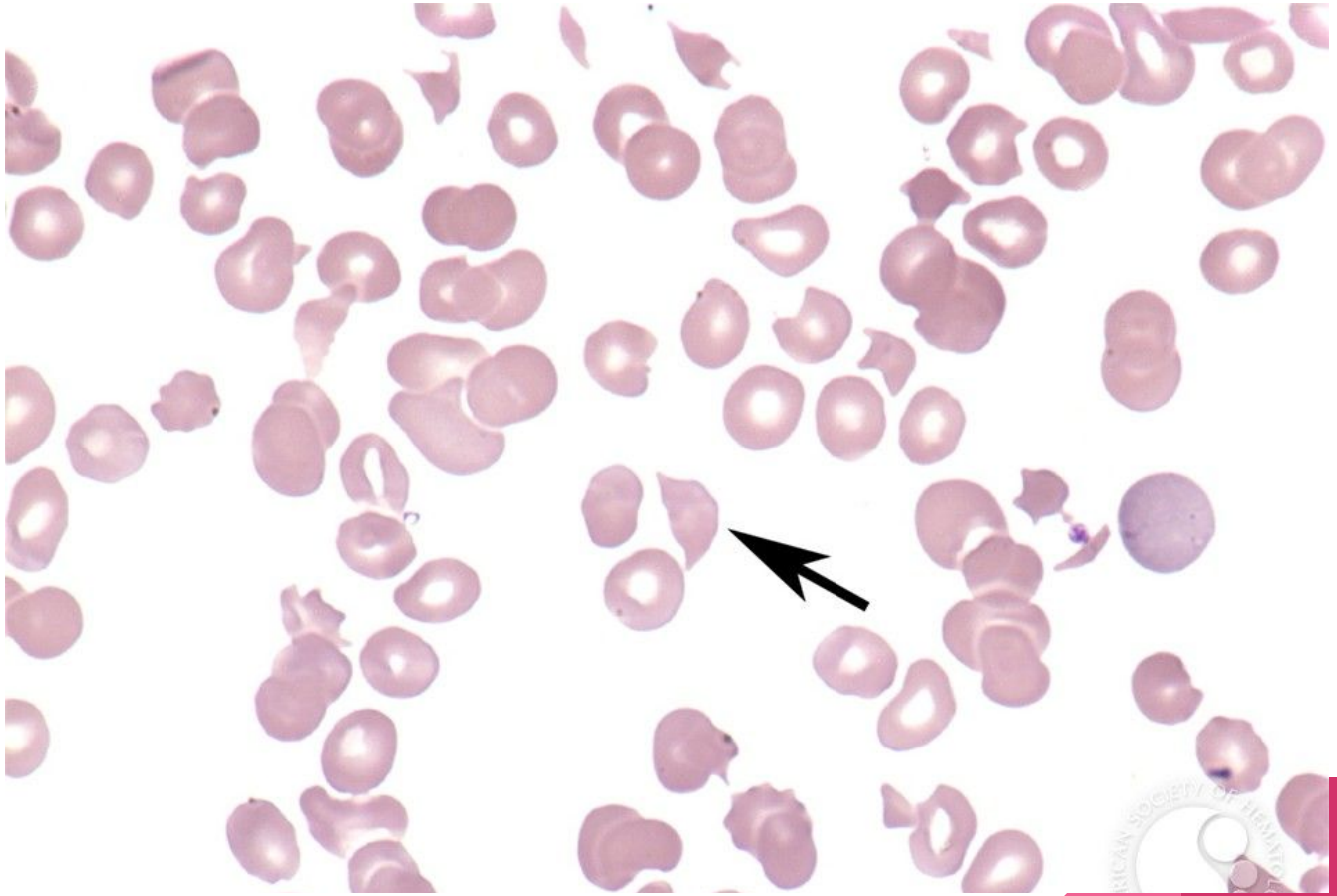

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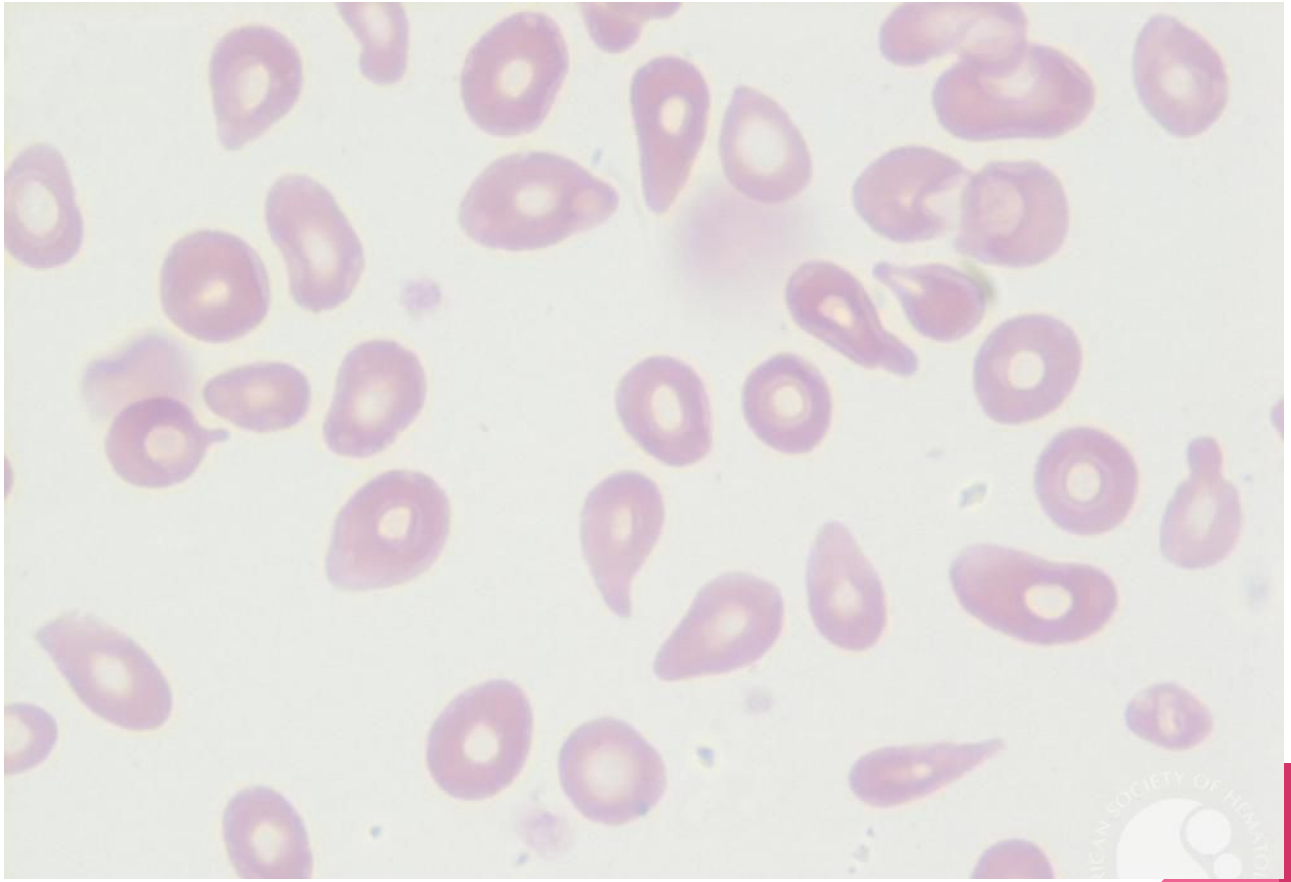

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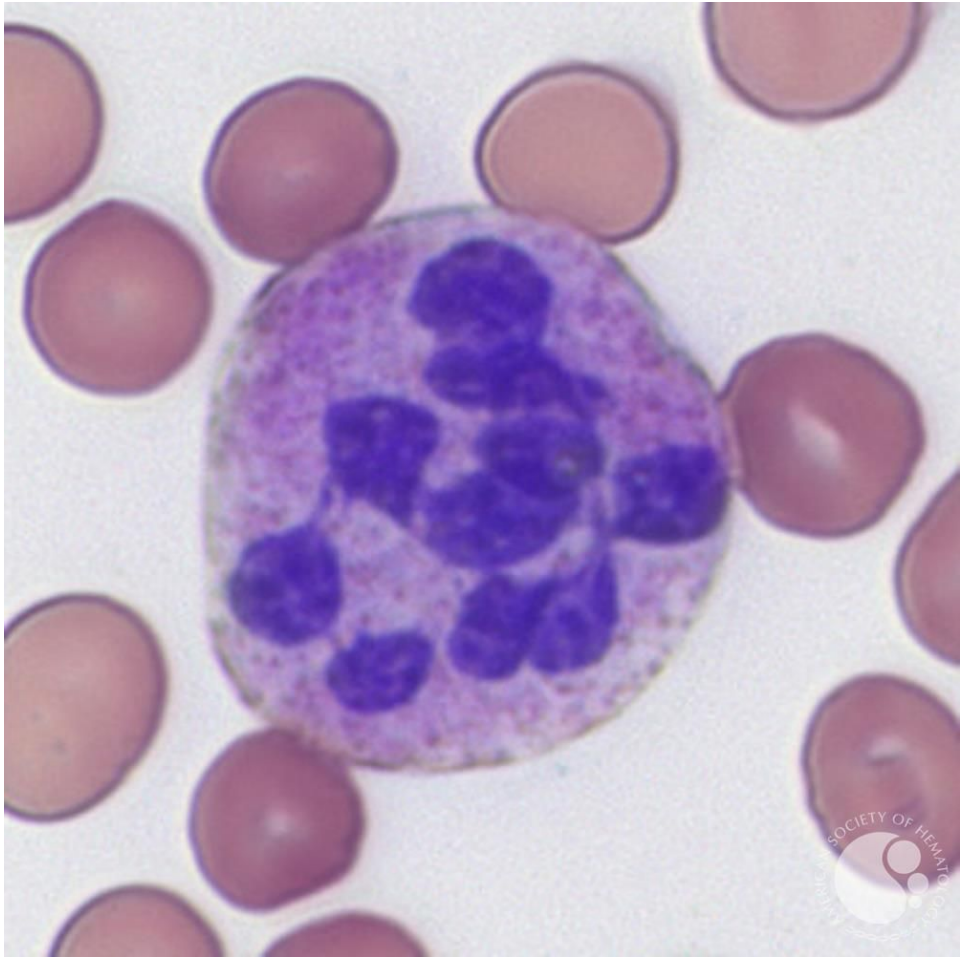

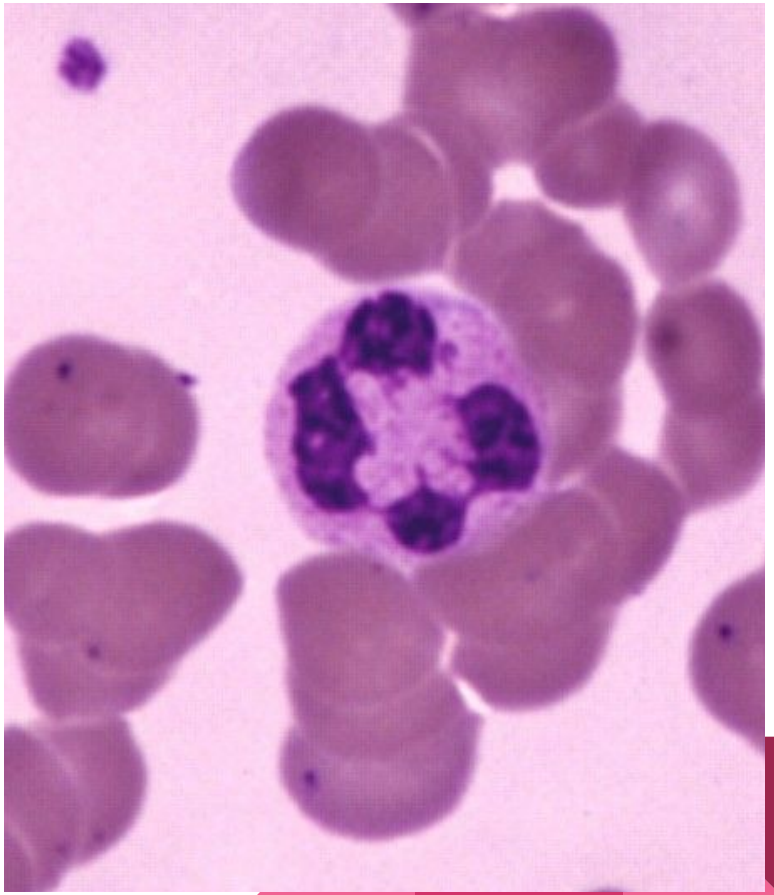

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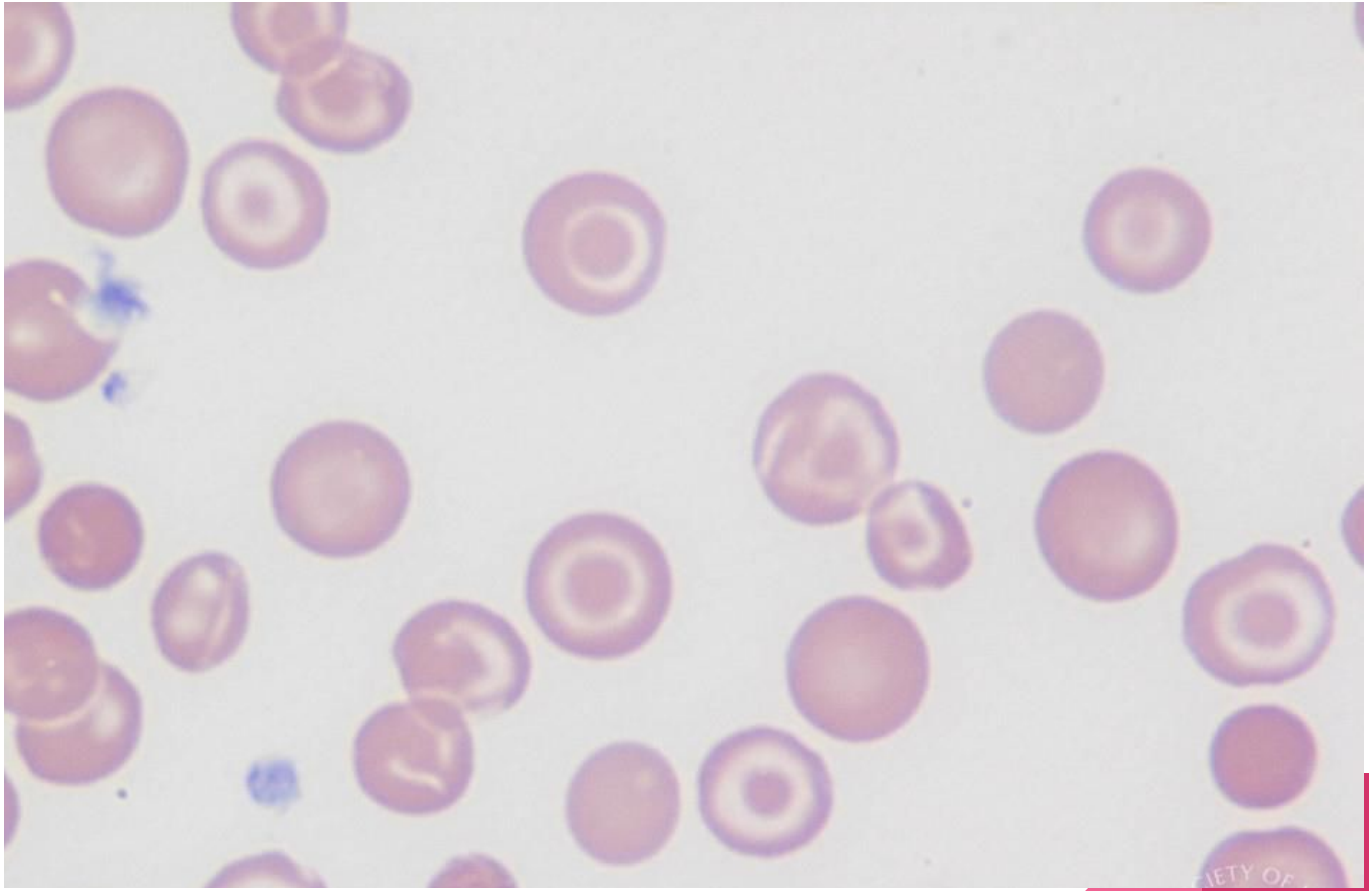

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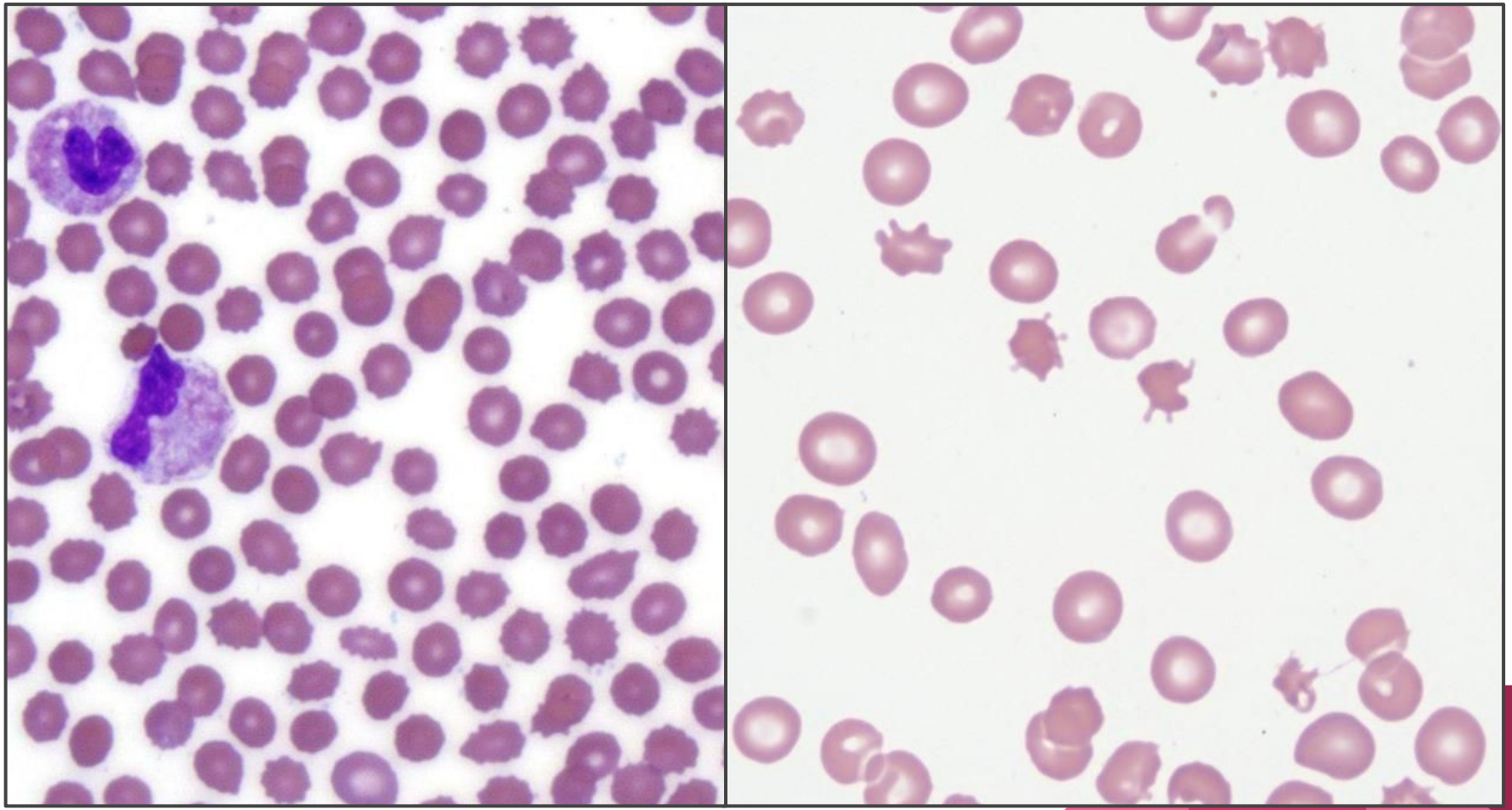

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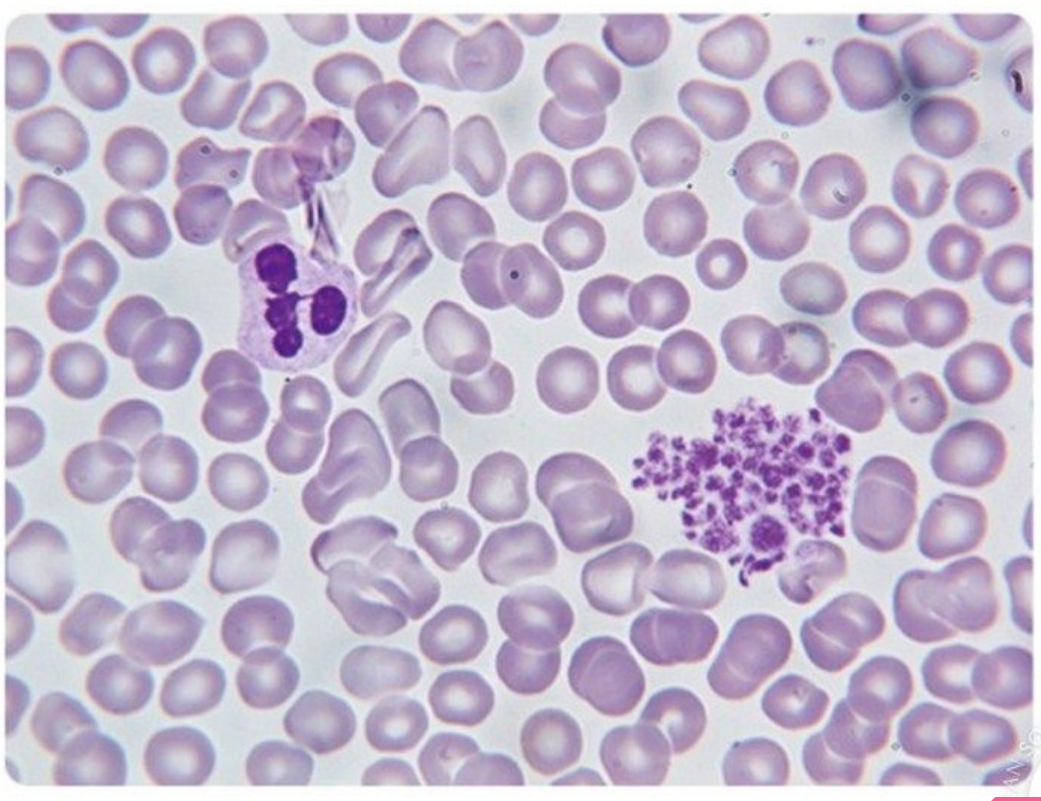

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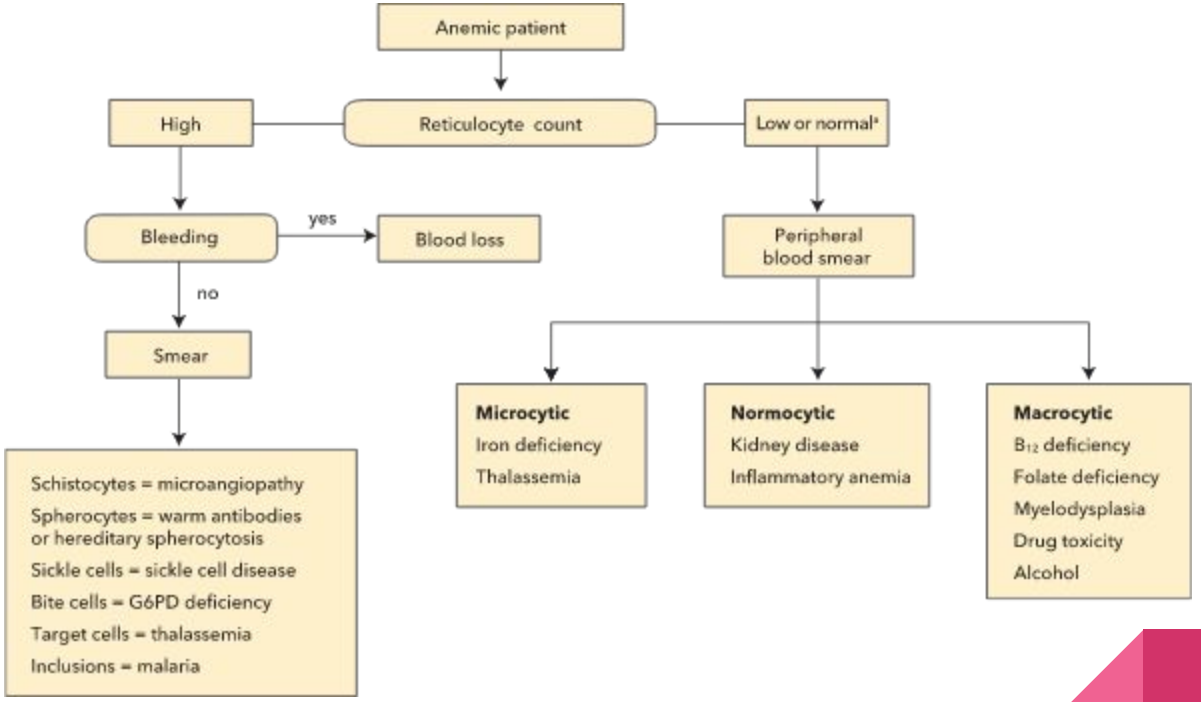
Anemia


Anemic patient
Reticulocyte count
High
Low or normal[a]
Bleeding
yes
Blood loss
no
Smear
Schistocytes = microangiopathy
Spherocytes = warm antibodies or hereditary spherocytosis
Sickle cells = sickle cell disease
Bite cells = G6PD deficiency
Target cells = thalassemia
Inclusions = malaria
Peripheral blood smear
Microcytic
Iron deficiency
Thalassemia
Normocytic
Kidney disease
Inflammatory anemia
Macrocytic
B_{12} deficiency
Folate deficiency
Myelodysplasia
Drug toxicity
Alcohol

MKSAP 24

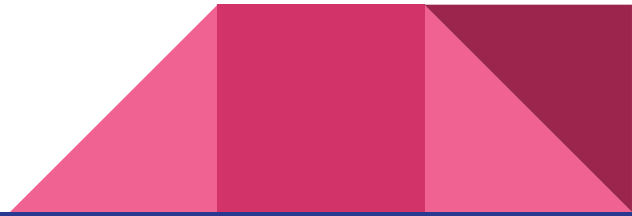
A 28-year-old woman is evaluated for decreased exercise tolerance and ice cravings for the past several weeks. Medical history is notable for Crohn colitis diagnosed 6 years ago. Her symptoms flared 3 months ago with increased abdominal pain and diarrhea, and she began therapy with azathioprine and infliximab. Her only other medication is ferrous sulfate tablets, 325 mg once daily, which she has been taking for 6 weeks after being diagnosed with iron deficiency anemia; her hemoglobin level at that time was 8.2 g/dL.

On physical examination, vital signs are normal. She is thin, with pale conjunctivae and nail beds. Cardiac exam reveals a grade 2/6 systolic flow murmur. The remainder of the examination is unremarkable.

Laboratory studies show a hemoglobin level of 7.5 g/dL and a serum ferritin level of 1 ng/mL .

Which of the following is the most appropriate treatment?

A. Intravenous iron preparation
B. Oral iron in a liquid preparation
C. Oral iron tablets three times daily
D. Sustained-release iron preparation



Iron Deficiency Anemia

Causes

Blood Loss

Decreased absorption

- After gastric surgeries
- Celiac disease
- H. pylori
- AI atrophic gastritis

Increased requirements

Physical Exam

Pallor

Pica

Glossitis

Stomatitis

Koilonychia

Treatment

IV Iron if absorption is a concern

Hgb usually increases ~ few weeks

Continue treatment 3 -6 months after Hgb normalizes

Inflammatory Anemia & Anemia of Kidney Disease

Condition	MCV	Serum Fe	% sat	TIBC	Ferritin
Fe Deficiency	Low	Low	Low	Elevated	Low
AOCD	Low/ Normal	Low	Normal	Low/Normal	Normal/ Elevated

- Treatment of AoCD: treat underlying disease
- AoKD: treat if Hgb <10
- Burr Cells
- Complications of ESAs: worsening HTN, volume overload, thrombotic complications

MKSAP 56

A 56-year-old man is brought to the ER after being found lying unresponsive in the local train station. Medical history is significant for chronic alcohol dependence. He is homeless. The patient is a frequent visitor to the ER for minor trauma and ailments; his last visit was 6 months ago. Until that time, the patient lived in various shelters and received at least one nutritious meal per day. His whereabouts and living circumstances since that time are unknown. His medical history is otherwise not significant, and at his last visit to the ER, he was taking no medications.

On exam, vital signs are normal. The patient is disheveled, cachectic, and malodorous. He moans in response to painful stimuli and moves all extremities. He has poor dentition. Hepatomegaly is noted.

Hypersegmented neutrophils are seen on the peripheral blood smear.

Hgb	7.4 g/dL
WBC	4200 /µL
MCV	110 fL
Platelet	97,000
Reticulocyte count	1% of erythrocytes
Blood alcohol level	500 mg/dL

MKSAP 58

Which of the following is the most likely cause of this patient's anemia?

A. Cobalamin deficiency
B. Folate deficiency
C. Inflammatory anemia
D. Iron deficiency

Folate and Vitamin B12 Deficiency

Causes of Folate Deficiency

- Dietary
- EtOH use
- Decreased absorption
- Medications
  - Phenytoin
  - Methotrexate
- Increased Need/Increased Cell Turnover
  - Pregnancy
  - Hemolysis
  - Psoriasis

Causes of Vit B12 Deficiency

- Dietary
- Malabsorption
  - IBD
  - Pancreatic insufficiency
  - SIBO
  - Pernicious anemia
- Medications
  - PPIs
  - Metformin
  - Nitrous oxide

Folate and Vitamin B12 Deficiency

- Homocysteine, MMA
  - Elevated in vitamin B12 deficiency, MMA normal in folate deficiency
- Intrinsic Factor Abs, Parietal Cells Abs
- Treatment for Vitamin B12 Deficiency
  - Oral 1000-2000 µg daily
  - Can see increased reticulocytes and decreased LDH/Bili in a few days
  - Hypersegmented PMNs disappear ~2 weeks
  - Pancytopenia improves ~2-4 weeks
  - Hgb increases 1 g/week
- Treatment for Folate Deficiency
  - Exclude vitamin B12 deficiency
  - Folate 1-5 mg PO qDay

MKSAP 43

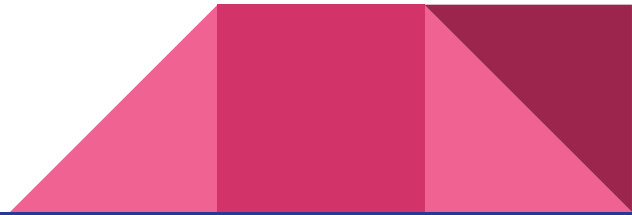
A 22-year-old woman undergoes routine evaluation for chronic anemia, which was diagnosed 6 years ago. Medical history is otherwise unremarkable, but a maternal aunt also has anemia. Her only medication is a combination oral contraceptive pill. On physical examination, vital signs are normal. No hepatosplenomegaly is noted.

Hemoglobin electrophoresis reveals a normal pattern of migration of hemoglobin A and normal levels of hemoglobin A_2 and hemoglobin F.

Hgb	10 g/dL
MCV	67 fL
Ferritin	200 ng/mL
Iron	150 µg/dL
TIBC	340 µg/dL

Which of the following is the most likely diagnosis?

A. Inflammatory anemia
B. Iron Deficiency
C. α - thalassemia silent carrier
D. α - thalassemia trait
E. β - thalassemia minor



Thalassemias

- Disruption in the normal alpha globin and beta globin production
- Alpha-Thal: African and SE Asian Descent
- Beta - Thal: Mediterranean countries, SE Asian, Indian, Pakistan
- Think Thalassemia when Iron overload + Microcytosis
- Low MCV/Microcytosis, normal RDW
- PBS will show microcytosis, nucleated RBCs, target cells
- Will need folate supplementation
- Avoid iron supplementation

Alpha Thalassemias

α-Thal minima/ silent carrier
(SIngle Gene Deletion)

- normal clinically
- Normal electrophoresis/labs
- no treatment

α-Thal minor/trait
(Two Deletions)

- Mild anemia
- Normal electrophoresis
- Folate
- Genetic counseling

Hemoglobin H Disease
(Three Deletions)

- severe anemia
- Abnormal electrophoresis (hgb H)
- At risk for iron overload

Hydrops Fetalis
(4 Deletions)

- In utero/neonatal demise

Beta Thalassemias

β-Thal major/ Transfusion Dependent

- Symptoms ~6 mos. of age
- Organomegaly
- Bony abnormalities
- Iron Overload
- HbA2 (5% or more); HbF (up to 95%); no HbA

β-Thal intermedia/ Non transfusion dependent

- Symptoms ~ 2-4 y.o
- Varied clinical presentation
- HbA2 (4% or more); HbF (up to 50%)

β-Thal Minor

- Mild anemia
- Usually asymptomatic
- HbA2 (4% or more); HbF (up to 5%)

MKSAP 21

A 52-year-old man is evaluated in the ER for decreased exercise tolerance and yellowing of the eyes for the past 3 days. He was diagnosed with leprosy 6 days ago and began antibacterial therapy 4 days ago. His CBC at that time was normal. He is a Haitian immigrant. Medications are dapsone, rifampicin, and clofazimine.

On exam, temperature is 36.7 °C, BP is 125/75 mm Hg, HR is 100/min, and RR is 18/min. He has icteric sclerae. Cardiac exam reveals a grade 2/6 systolic flow murmur. Multiple raised erythematous papules with decreased sensation are noted on the back and hands. No organomegaly is observed.

Examination of the peripheral blood smear shows bite cells. The direct antiglobulin (Coombs) test is negative.

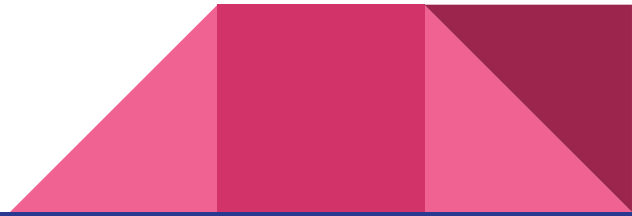
Haptoglobin	Undetected
Hgb	5.6 g/dL
WBC	5,600/μL
Platelet	223,000
Retic Count	12%

Which of the following is the most appropriate immediate management?

A. Administer prednisone
B. Administer rituximab
C. Discontinue dapsone
D. Measure ADAMTS13 activity
E. Measure glucose-6-phosphate dehydrogenase level

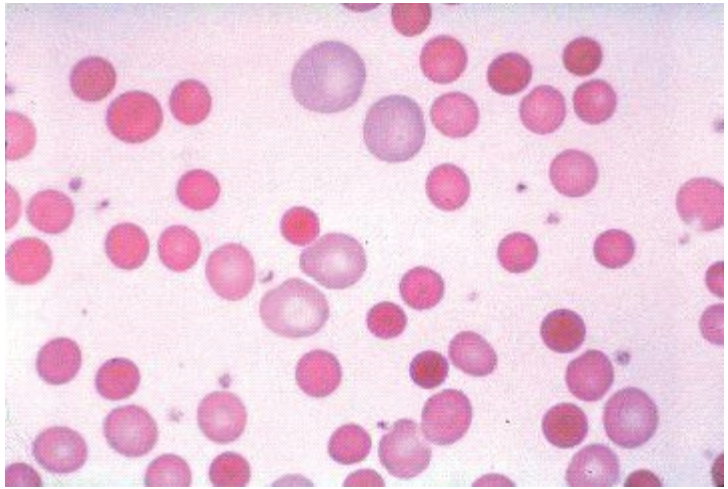
G6PD Deficiency

- Hemolysis occurs 2-3 days after triggering event/exposure
- Medications
  - Dapsone
  - Primaquine
  - Methylene blue
  - Nitrofurantoin
  - Pyridium
  - Rasburicase
- Foods
  - Fava beans
- Chemicals
  - Naphthalene (mothballs)
- Infections
- Only transfuse if severely symptomatic
- Test 3 months after inciting event



Hereditary Spherocytosis

- Affected patients usually well compensated until triggering event (ex: infection, nutritional deficiencies)
  - Ex: Parvovirus
- Elevated MCHC
- May see splenomegaly, pigment gallstones
- Test: Osmotic Fragility Test, Flow Cytometry
- If severe, will need splenectomy
  - Give all the required immunizations!



Sickle Cell Anemia

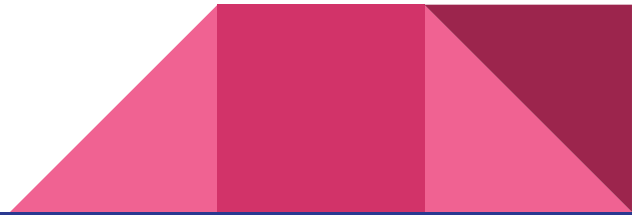
Evidence-Based Management of Sickle Cell Disease: Expert Panel Report, 2014

Sickle Cell Anemia

- Rapid initiation of opioids for vaso-occlusive crisis
- Use of incentive spirometry in hospitalized patients
- Use of analgesics and physical therapy for treatment of avascular necrosis
- Use of ACE inhibitors in patients with microalbuminuria
- Regular ophthalmologic examinations and referral for laser photocoagulation for retinopathy
- Use of echocardiography to evaluate signs of pulmonary hypertension
- **Hydroxyurea** for patients with more than 3 vaso-occlusive crises per year, for those with pain or chronic anemia interfering with daily activities, or those with recurrent acute chest syndrome
- Preoperative transfusion to serum hemoglobin level of 10 g/dL for surgeries requiring general anesthesia
- Assess for iron overload and begin oral iron chelation if necessary

Sickle Cell Disease - Vaso-occlusive Crisis

- Opiates are preferred analgesic (avoid meperidine)
- Incentive spirometry every 2-4 hours, encourage ambulation
- Keep O2 sat >95%
- Hydration
- Oral L-Glutamine and crizanlizumab are also used to prevent pain crisis

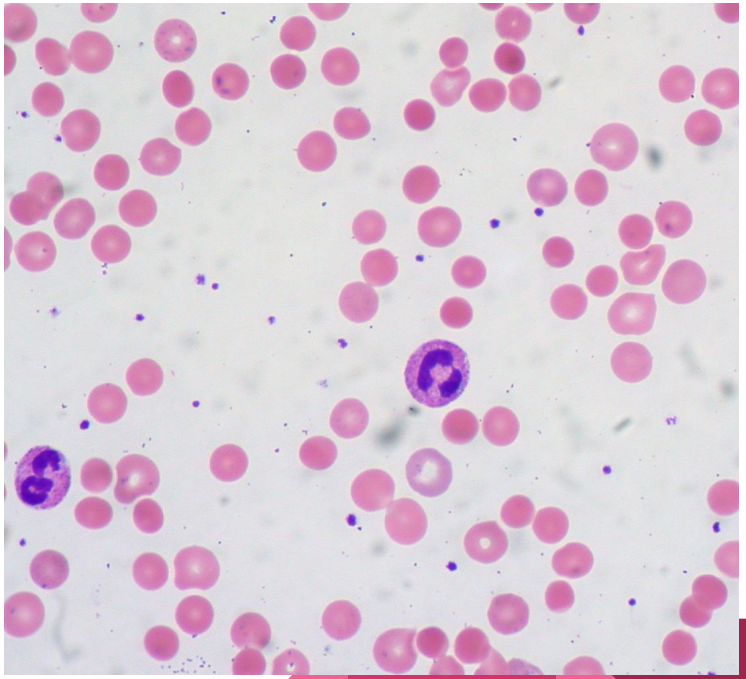


Sickle Cell Anemia - Acute Chest Syndrome

- ACS: fever, tachypnea, hypoxia, SOB, pulmonary infiltrate
- Can be caused by infections, VTE/thrombosis, fat embolism
- Increased frequency in patients with SCD + asthma, or with prior ACS events
- Oxygen therapy, bronchodilators (goal O2 sat >95%)
- Antibiotics if infection present (IV cephalosporin, oral macrolide)
- pRBC transfusion
- Exchange transfusion
    - Other indications: acute stroke, acute retinal artery occlusion

Warm Autoimmune Hemolytic Anemia

- Causes
  - Idiopathic
  - Infections: HIV, HCV
  - AI disorders: SLE, RA
  - Malignancy: CLL, MM
  - Medications: Penicillin, cephalosporin, methyldopa
- Coombs test: positive for IgG
- Treatment:
  - Steroids
  - IVIG
  - Rituximab
  - Splenectomy
- ~30% can have thromboembolic disease



E. Uthman, MD - https://www.flickr.com/photos/euthman/2989437967

MKSAP

A 32-year-old woman is hospitalized with progressive exertional dyspnea. She has noted dark urine for the last week and yellowing of her skin for several days. Medical history is unremarkable, and she takes no medications.

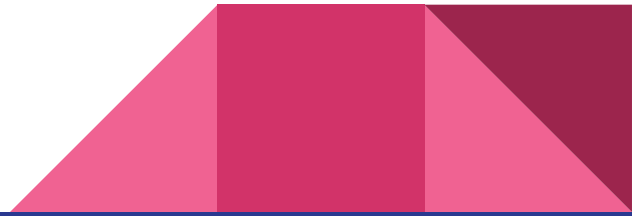
On exam, temperature is 36.7 °C, blood pressure is 100/70 mm Hg, pulse rate is 100/min, and respiration rate is 18/min. Icteric sclera and skin are noted. Cardiac exam reveals a grade 2/6 systolic flow murmur. No lymphadenopathy or hepatosplenomegaly is present.

A peripheral blood smear shows erythrocyte agglutination. A direct antiglobulin (Coombs) test is positive for C3. Diagnostic testing for *Mycoplasma* and Epstein-Barr virus is negative.

Haptoglobin	Undetectable
Hemoglobin	4.8 g/dL
WBC	8200/μL
MCV	134 fL
Platelet	230,000
Reticulocyte count	12% of erythrocytes
Total Bilirubin	6.7 mg/dL
Direct Bilirubin	1.2 mg/dL
LDH	660 U/L
Urinalysis	Dipstick positive for 4+ blood; 0-1 leukocytes/hpf, and 0 erythrocytes/hpf

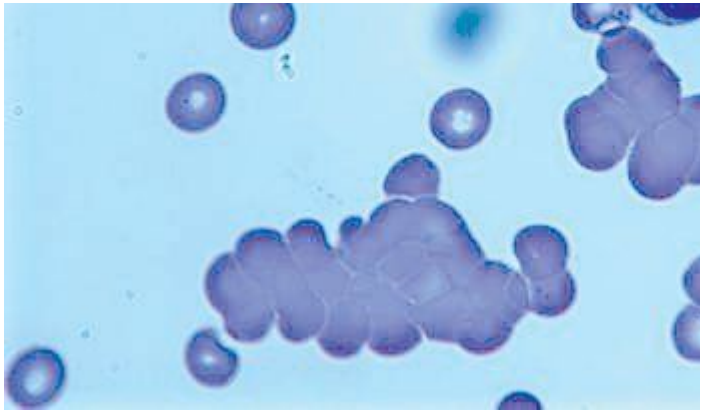
Which of the following is the most appropriate treatment?

A. Intravenous immune globulin
B. Prednisone
C. Rituximab
D. Splenectomy



Cold Agglutinin Disease

- Causes
  - Infections: Mycoplasma, EBV
  - Malignancy: Lymphomas
- Coombs test: + C3
- Treatment
  - Avoid cold temperatures
  - Rituximab, fludarabine
  - Steroids, IVIG, splenectomy NOT helpful



Paroxysmal Nocturnal Hemoglobinuria (PNH)

- Characterized by episodic hemolysis, pancytopenia, thrombosis (esp in atypical locations)
- Other symptoms: abdominal pain, discolored urine
- Patients with PNH are at higher risk for leukemia or myelodysplasia
- Diagnosis with flow cytometry (test for CD55, CD59)
- Treatment: folate, steroids, eculizumab
    - Will need meningococcal vaccination

MKSAP (16) 56

A 35 year-old woman is evaluated for new-onset thrombocytopenia. She is gravida 1 at 36 weeks' gestation. Her pregnancy has been otherwise uncomplicated. She takes only a prenatal vitamin.

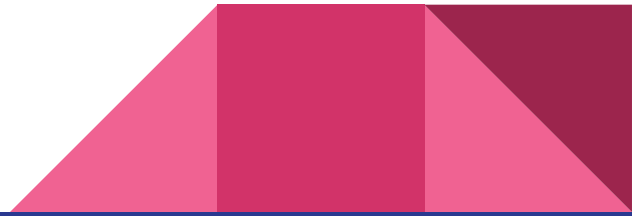
On exam, temperature is normal, BP is 110/65 mmHg, pulse is 100/min, and respiration rate is 22/min. There are no ecchymoses or petechiae. Abdominal exam discloses no right upper quadrant pain. She has a gravid uterus. Neurologic exam is normal, and there is no peripheral edema.

No schistocytes or platelet clumping is seen on the peripheral blood smear.

Hemoglobin	11.0 g/dL
Leukocyte count	9500/μL
MCV	85 fL
Platelet count	95,000/μL
Fibrinogen	350 mg/dL
ALT	Normal
AST	Normal
Urinalysis	Normal

Which of the following is the most appropriate management?

A. Corticosteroids
B. Emergent delivery of the fetus
C. Intravenous immune globulin
D. Plasma exchange
E. Repat CBC in 1-2 weeks



Thrombocytopenia

Decreased Production
Examples:

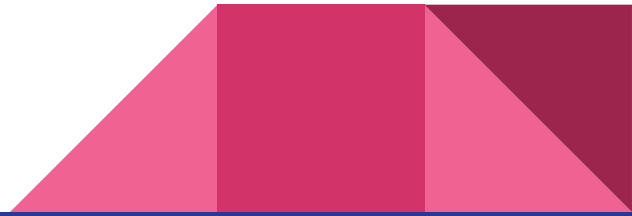
- Aplastic anemia
- Myelodysplasia
- Nutritional deficiencies
- Metastatic tumors
- Infections
- Toxins

Increased Consumption
Examples:

- ITP
- TTP
- aHUS
- HIT
- DIC
- Mechanical destruction

Sequestration
Examples:

- Splenomegaly



Immune-Mediated Thrombocytopenia

- Always rule out pseudothrombocytopenia
- Associated Conditions
  - Autoimmune (SLE, RA)
  - Infections: HIV, HCV, H. Pylori,
  - Malignancy: CLL, lymphoma
- Test for HIV, HCV
- Antiplatelet antibody testing is not recommended because of low sensitivity
- Treatment if bleeding or if counts <30,000 with steroids vs IVIG
- Treatment
  - First line: Steroids, IVIG
  - Second line: splenectomy, rituximab
  - Other agents: Eltrombopag, romiplostim

Heparin-Induced Thrombocytopenia

- Type 1: non-immune mediated, occurs within first few days of exposure
- Type 2: occurs 5-10 days after exposure 2/2 Abs against platelet factor 4
- Signs: thrombosis/VTEs, arterial thrombosis, skin necrosis at site of injection
- 4T scoring system
- Screening test & Confirmatory test
- If on differential/high 4T score, stop heparin
- Alternative anticoagulants: argatroban, bivalirudin, fondaparinux
- Transition to warfarin (Can also consider DOAC)
- Patients should be instructed to avoid heparin for life

MKSAP 51

A 42-year-old man is admitted to the hospital with an acute change in mental status and fever of 2 days' duration. Medical history is noncontributory, and he takes no medications.

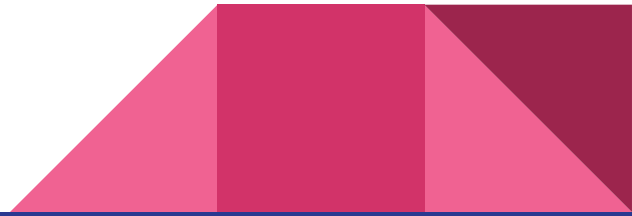
On physical examination, temperature is 38.2 °C, blood pressure is 108/70 mm Hg, pulse rate is 104/min, and respiration rate is 18/min. Oxygen saturation is 96% breathing ambient air. He is agitated and disoriented to place and time. Petechiae are noted on his shins. The remainder of the examination is normal.

The direct antiglobulin (Coombs) test is negative.

Haptoglobin	20 mg/dL
Hemoglobin	10.2 g/dL
WBC	9800/μL
Platelets	44,000/μL
Reticuloycte Count	6.8% of erythrocytes
Creatinine	1.4 mg/dL
LDH	1600 U/L

Therapy should be immediately initiated pending results of which of the following studies?

A. ADAMTS13 activity
B. Coagulation studies
C. Peripheral blood smear
D. Stool culture and testing



Thrombotic Thrombocytopenic Purpura

- MAHA + thrombocytopenia
- Mild renal failure
- nausea/vomiting, abdominal pain; Fevers, neuro symptoms
- Inherited or acquired deficiency in ADAMTS13
  - Acquired: cyclosporine, gemcitabine, bevacizumab, quinine, ecstasy, cocaine
- ADAMTS13 level < 10% = TTP
- Do not wait for levels to come back before starting treatment
- Treatment
  - Plasma exchange
  - Steroids
  - Rituximab if refractory

Hemolytic Uremic Syndrome

- Renal failure, MAHA, thrombocytopenia
- Classic: after acute diarrheal illness (Shigella, O157:H7 E Coli)
  Complement Mediated: w/o diarrhea, complement-mediated
  - Associated with medications, AI disorders (ex: SLE), Infections (ex: HIV, influenza, S. pneumoniae)
- Treatment
  - HUS: Plasma Exchange
  - Complement mediated: Eculizumab

MKSAP 2

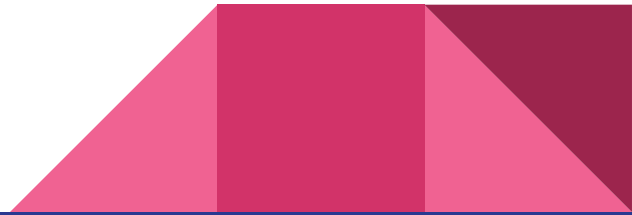
A 68-year-old man is evaluated for epistaxis, gum bleeding, and easy bruising of 3 months' duration. Medical history is notable for anxiety, depression, and hyperlipidemia. Medications are atorvastatin, citalopram, a multivitamin, and ginkgo biloba.

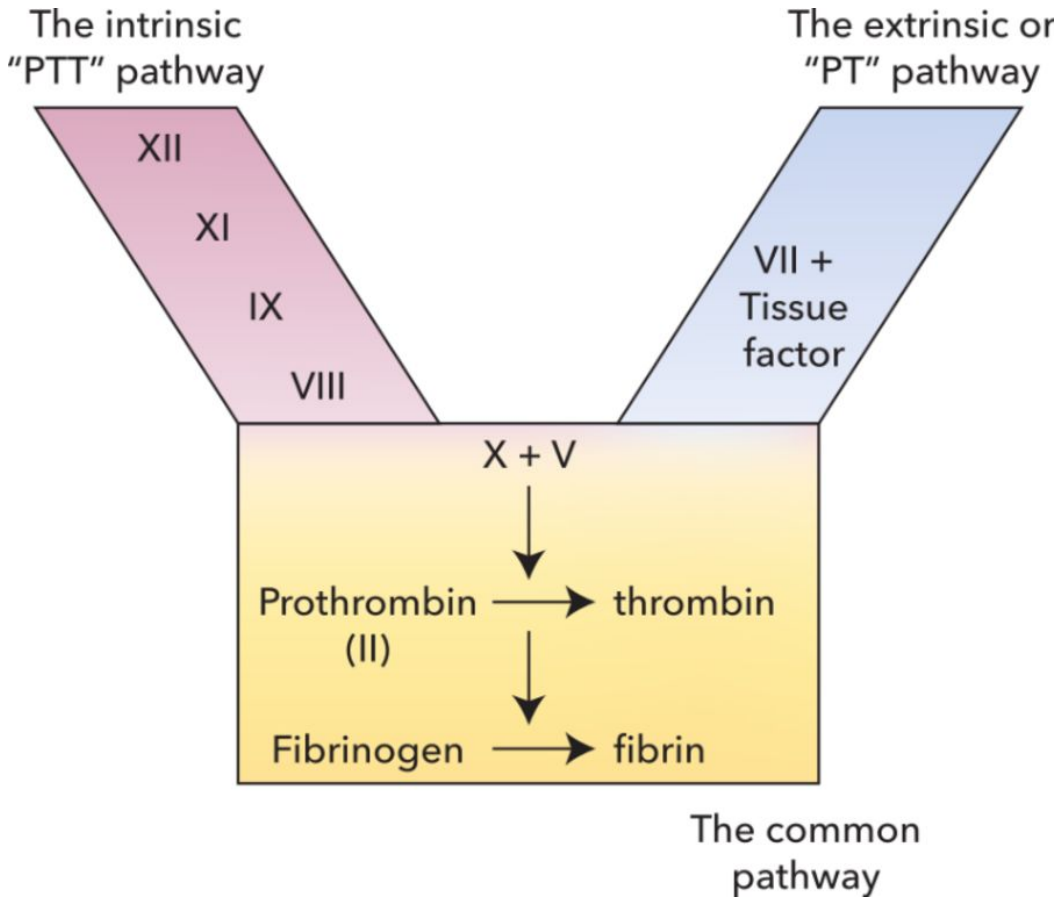
On physical examination, vital signs are normal; BMI is 21. Scattered petechiae and several small ecchymoses are visible on the anterior thigh. The examination is otherwise normal.

aPTT	Normal
Hemoglobin	14.8 g/dL
WBC	4200/μL
Platelet	245,000/μL
PT	Normal
Thrombin time	Normal

Which of the following is the most appropriate diagnostic test to perform next?

A. Fibrinogen level
B. Mixing studies for PT and aPTT
C. Peripheral blood smear review
D. Platelet Function Analyzer-100
E. Serum protein electrophoresis





PT/INR - sensitive to II, VII, X

PTT - sensitive to VIII, IX, XI, XII

Thrombin time - fibrinogen to fibrin clot conversion

Platelet Function Analyzer-100 - platelet function

MKSAP 71

A 64-year-old woman is evaluated in the emergency department for large ecchymoses, bleeding gums, and a hematoma extending from her upper thigh to her knee. Medical history is significant for chronic lymphocytic leukemia, which has been asymptomatic and managed expectantly. She has experienced no previous bleeding symptoms and has no family history of bleeding disorders. She takes no medications.

On physical exam, other than a pulse rate of 104/min, vital signs are normal. Ecchymoses are present on her arms and legs. Small cervical and axillary lymph nodes are palpable. Other examination findings are normal.

aPTT	88 s
aPTT + mixing study	64 s
Hemoglobin	10.8 g/dL
WBC	65,000/μL
Platelet	215,000/μL
PT	11.5 s
Factor VIII	1%

Administration of which of the following is the most appropriate management?

A. Activated factor VII
B. Cryoprecipitate
C. Desmopressin
D. Fresh frozen plasma

Congenital Hemophilia

- Hemophilia A (VIII), Hemophilia B (IX)
- Congenital: X-linked
- Mild (5-40%), Moderate (1-5%), severe (<1%)
- Symptoms: hemarthrosis, bleeding into deep muscles, excessive/delayed bleeding after trauma
- Normal PT, prolonged PTT that corrects with mixing study
- Treatment
  - Inactivated factor concentrates
  - Antifibrinolytic agents: Tranexamic acid, ε-aminocaproic acid
  - Mild hemophilia A: desmopressin

Congenital Hemophilia

Deficiency	Inheritance	Labs affected	Treatment
VII	Autosomal	+PT	FFP/PCC
X	Autosomal	+/- PTT +/- PT	FFP/PCC
XI (aka Hem C)	Autosomal	+PTT	FFP, factor XI
XII	Autosomal	+PTT	No risk for bleeding
XIII	Autosomal	+/- Thrombin time	cryo/FactorXIII

Acquired Hemophilia

- 2/2 antibodies to clotting factors, most common factor VIII
- Associated with:
  - pregnancy/postpartum state
  - Malignancy
  - AI disorders: SLE, RA
  - Medications: PCNs, IFNs, etc
- Normal PTT, prolonged PTT that does not correct with mixing study
- Bethesda assay to quantify inhibitor
- Management
  - Do NOT give factor VIII
  - Activated factor VII
  - Immunosuppression: steroids, cyclophosphamide

Von Willebrand Disease

- Both genetic and acquired cases
  - Acquired: valvular heart dz, ECMO, LVADs
- Symptoms: bleeding gums, epistaxis, menorrhagia, easy bruising
- 3 types
  - Type I: Most common, mucocutaneous bleeding
  - Type II: 2/2 dysfunctional vWF
  - Type III: most severe (jt and deep muscle bleeding)
- Labs: normal coagulation factors*, prolonged closure time on PFA-100
  - Prolonged PTT can be seen in severe deficiency
- Management
  - Type 1: Desmopressin
  - Type 2 &3: vWF concentrates
  - Can give antifibrinolytic agents after surgery

MKSAP 73

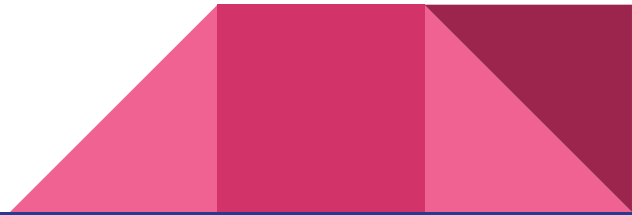
A 26-year-old man undergoes follow-up evaluation after hospitalization for deep venous thrombosis last week. He reports no recent travel, surgery, or immobilization. He has a sister who was diagnosed with an unprovoked deep venous thrombosis 1 year ago at 35 years of age. Medical history is otherwise unremarkable. His only medication is rivaroxaban.

On physical examination, vital signs are normal. The examination is otherwise unremarkable.

The possibility of an inherited thrombophilia is discussed with the patient. After reviewing the risks and benefits of additional testing, he would like to be further evaluated for a possible thrombophilia.

Which of the following is the most appropriate testing strategy?

A. Test now
B. Test in 3-4 weeks
C. Test a saved blood sample obtained during hospitalization but before anticoagulation
D. Temporarily stop rivaroxaban after 3 months of treatment and test 2 weeks later



Thrombophilia Testing

Who to test

- Recurrent idiopathic thrombosis
- < 45 yo with unprovoked thrombosis
- Thrombosis at unusual site
- Warfarin-induced skin necrosis
- Family hx in first degree relative

Inherited Disorders

- Factor V Leiden
- Prothrombin G20210A gene mutation
- Protein C deficiency
- Protein S deficiency
- Antithrombin deficiency

Antiphospholipid Antibody Syndrome

- Primary or associated with AI disease (ex: SLE)
- Diagnosis: Clinical + Lab findings
  - Clinical: Thrombosis (venous or arterial) OR Pregnancy morbidity
  - Lab: Presence of one or more aPL Ab x 2 (and 12 weeks apart): Anticardiolipin IgG/IgM, B2 Glycoprotein IgG/IgM, or Lupus Anticoagulant
- Prolonged PTT that does not correct with mixing
- Treatment: Lifelong anticoagulation (use warfarin)
- Catastrophic APS: widespread thrombotic disease with multiorgan failure
  - Treatment: anticoagulation, steroids, PEX/IVIG

<u>Diff Dx for Arterial + Venous Clots</u>

- Antiphospholipid Antibody Syndrome
- HIT
- Myeloproliferative neoplasms
- PNH
- IBD

MKSAP 27

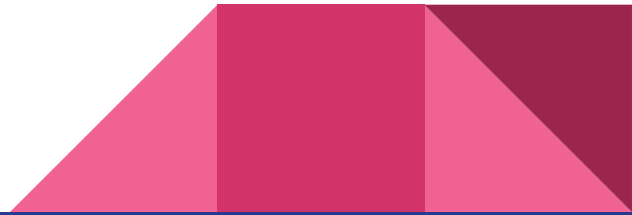
A 45-year-old man is evaluated in the hospital for worsening pain and progressive swelling of the left lower extremity that began abruptly approximately 12 hours ago. Medical history is otherwise noncontributory, and he takes no other medications.

On physical examination, pulse rate is 112/min; other vital signs are normal. He has erythema and marked edema of the entire left lower extremity. The left foot appears cyanotic, with decreased sensation, absent arterial pulses, and delayed capillary refill. The physical examination is otherwise unremarkable.

Doppler ultrasonography of the left lower extremity shows extensive ileofemoral deep venous thrombosis.

Which of the following is the most appropriate management?

A. Alteplase
B. Argatroban
C. Rivaroxaban
D. Unfractionated heparin
E. Unfractionated heparin plus inferior vena cava filter insertion



DVT and Pulmonary Embolism

- Patients at very low risk do not need further work up
  - <50 yo, HR <100, O2 sat >94%, no unilateral leg swelling, no hemoptysis, no surgery/trauma <4 weeks, no hx of VTE, no estrogen use
- Outpatient treatment if: <80 yo, no significant comorbidities, stable vital signs
- Thrombolysis indicated: massive PE and submassive PE with poor prognostic features (ex: elevated BNP, troponin), DVTs leading to limb ischemia
- Upper extremity DVTs
  - tx : 3 months of anticoagulation (or as long as catheter is in place)
- Distal DVTs do not require treatment
  - Can treat if higher risk: elevated D-dimer, proximity to proximal veins, active cancer, hx of VTE, etc
- Superficial vein thrombosis
  - Usually no treatment unless >5 cm in length or close to deep venous system, cancer, hx of VTE, etc

	Dabigatran	**Rivaroxaban**	**Apixaban**	**Edoxaban**	**Betrixaban**
Class	Direct factor IIa inhibitor	Direct factor Xa inhibitor	Direct factor Xa inhibitor	Direct factor Xa inhibitor	Direct factor Xa inhibitor
FDA-approved indications	A-fib VTE treatment	A-fib VTE treatment VTE prevention	A-fib VTE treatment VTE prevention	A-fib VTE treatment	VTE prophylaxis
	-Requires bridging -normal Thrombin Time = not working -Increased GI bleeding		-approved for ESRD/dialysis patients	Requires bridging	

Anticoagulation Pearls

- LMWH, heparin: can use protamine for severe bleeding
- Fondaparinux: protamine and HD ineffective. Can use PCC and FFP for severe bleeding
- DOACs
  - Activated charcoal if <2-8 hours
  - Tranexamic acid, ε-aminocaproic acid
  - PCCs, rFVIIa
  - Andexanet alfa for rivaroxaban, apixaban
  - Idarucizumab for dabigatran
    - HD

Anticoagulation: Warfarin

Clinical Scenario	Management
INR < 4.5, no bleeding	Hold dose
INR 4.5-10, no bleeding	Hold dose *Consider low dose vitamin K if greater risk for bleeding
INR >10, no bleeding	Hold dose Low dose PO vitamin K
Any serious bleeding	Hold dose IV Vitamin K 4-factor PCC

MKSAP 16(3)

A 32-year-old woman undergoes preoperative evaluation prior to a complex spinal surgery for repair of severe scoliosis. Her expected blood loss is 2.5 liters. She had a severe anaphylactic reaction during a prior erythrocyte transfusion she received for postpartum hemorrhage at age 25 years.

On exam, temperature is 36.8C, blood pressure is 132/76 mmHg, and pulse rate is 78/min.

Lab studies indicates a hemoglobin level of 13.6 g/dL, WBC of 7800/µL, and a platelet count of 186,000/µL. Previous lab studies indicate an IgG level of 868 mg/dL, an IgA level <5 mg/dL, and an IgM level of 64 mg/dL. No monoclonal spike is found on serum protein electrophoresis.

Which of the following is the most appropriate erythrocyte product for this patient?

A. Cytomegalovirus negative
B. γ- Irradiated
C. Leukoreduced
D. Washed

Modification in pRBC/platelet products	Effect
Leukocyte Reduced (decreases # of WBCs present)	Reduces febrile nonhemolytic transfusion reactions Reduces class I HLA alloantibody production and subsequent platelet transfusion refractoriness
Irradiated (prevents replication of WBCs and circulating stem cells)	Prevents GVHD in patients with heme malignancies, severe immunodeficiencies or receiving immunosuppression, high grade sarcomas, etc
Washed (removes plasma proteins)	Used in patients with a history of severe/recurrent allergic reactions, IgA deficiency

Transfusion Complications	
Acute hemolytic transfusion reaction	2/2 ABO mismatch Fever, flank pain, hypotension, DIC, hemoglobinuria Stop transfusion, notify blood bank Supportive care (pressors, fluids, etc)
Anaphylaxis	Hypotension, angioedema, wheezing, stridor Antihistamines, epi, IVFs, bronchodilators Check for IgA deficiency
Delayed Hemolytic transfusion reaction	2/2 Abs to minor antigens Low grade fever, worsening anemia 1-2 weeks after transfusion Notify blood bank
Febrile nonhemolytic transfusion reaction	2/2 proinflammatory cytokines Occurs within 4 hours after transfusion

Transfusion Complications (Cont.)	
TACO	RFs: older age, CV/kidney disease, rapid infusion rate SOB within 6 hours, + fluid overload, elevated BNP, pulm edema on CXR Tx: diuretics, slow rate of infusion
TRALI	Noncardiogenic pulm edema within 6 hrs 2/2 Donor plasma Abs to HLA/PMN Fever, hypotension Tx: supportive
Infections	Bacteria (Skin flora, gram neg, Babesia) Viruses, Prions, Parasites (chagas) Send donor blood for culture/analysis
t.a.Graft vs Host disease	At risk: HSCT, hematologic malignancies, immunocompromised patients receiving chemotherapy Rash, Diarrhea, Pancytopenia, LFT abnormalities prevent with irradiated products

Transfusion Complications (Cont.)	
Massive Transfusion	8-10 units of blood/24 hours Transfuse platelets (dilutional coagulopathy) Electrolyte abnormalities: hypocalcemia, metabolic alkalosis, hyperkalemia/hypokalemia

MKSAP 28

A 68-year-old man is evaluated in the ER for fatigue and exertional dyspnea. He has a 5-year history of chronic lymphocytic leukemia, which has not required therapy. He takes no medications.

On exam, temp is 37 °C, BP is 123/82 mm Hg, pulse rate is 108/min, and respiration rate is 18/min. O2 sat is 95% breathing ambient air. Cervical, axillary, and inguinal lymphadenopathy and splenomegaly are present.

A direct antiglobulin test result is positive for IgG and C3. The patient is group A-positive and crossmatch incompatible with 5 units of group A-positive blood.

Glucocorticoid therapy is started.

Hemoglobin	5 g/dL
WBC	35,000/µL, Lymphocyte predominant
Platelet count	180,000/µL
Reticulocyte count	10% of erythrocytes

In addition to glucocorticoid therapy, which of the following is the most appropriate initial treatment?

A. Intravenous immune globulin
B. Plasmapheresis
C. Delay transfusion until compatible erythrocytes are available
D. Transfuse crossmatch-incompatible blood
E. Transfuse O-negative uncrossmatched blood