Hematology Board Review

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September 2016

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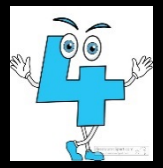

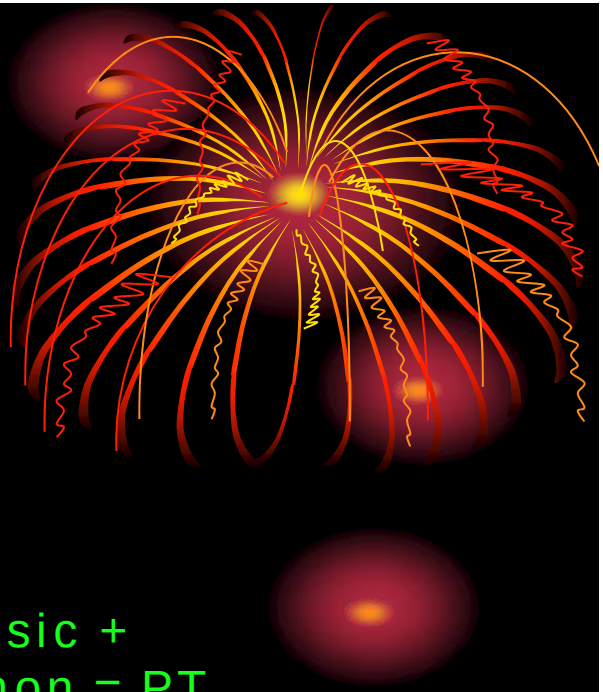

Intrinsic + Common = aPTT

Extrinsic + Common = PT

10

5

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Question 1.

- C; Aplastic Anemia

Diagnose Aplastic Anemia

Acquired

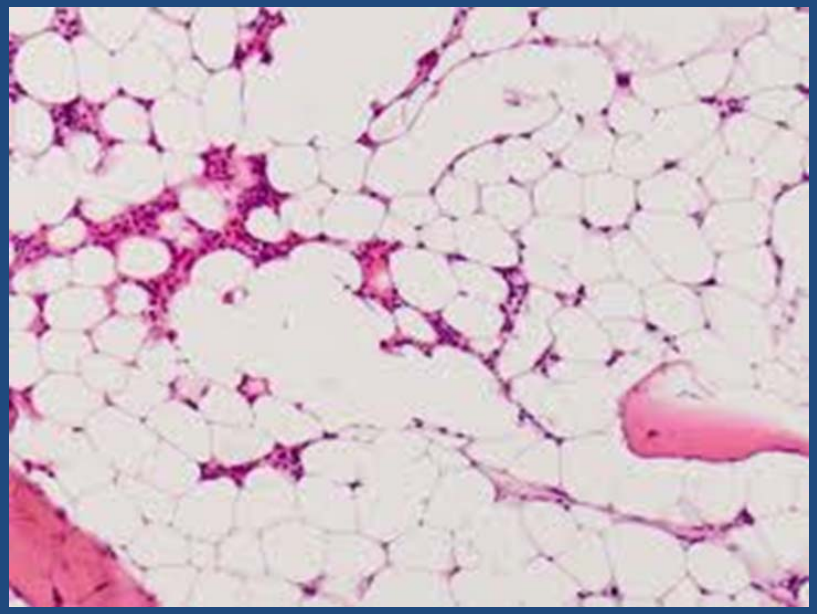
- **Drugs**
  - Chloramphenicol, sulfonamide, carbamezapine, indomethacin
- **Infections**
  - ParvoB19, HIV, Hepatitis, EBV, Herpes viruses
- **Toxins**
  - Radiation, Benzene, Glue
- **Hematologic**
  - Hypocellular MDS
  - B12 deficiency
  - Paroxysmal Nocturnal Hemoglobinuria
- ***Autoimmune**

Congenital/Genetic

- Fanconi anemia, autosomal recessive or X-linked

Treatment of Aplastic Anemia

- Immunosuppression
  - Antithymocyte globulin
  - Cyclosporin
  - 60-85% long term survival with relapse in 1/3
- Supportive care



Treatment of severe aplastic anemia:

- Two or more:
  - ANC 200-500/uL
  - Platelet <20,000/uL
  - Absolute retic ct <40,000/uL
- Allogeneic bone marrow transplant
  - Age <40
  - Minimal comorbidities
  - HLA compatible sibling
  - 75-90% cure

Question 2.

- D; JAK2 V617F mutation analysis

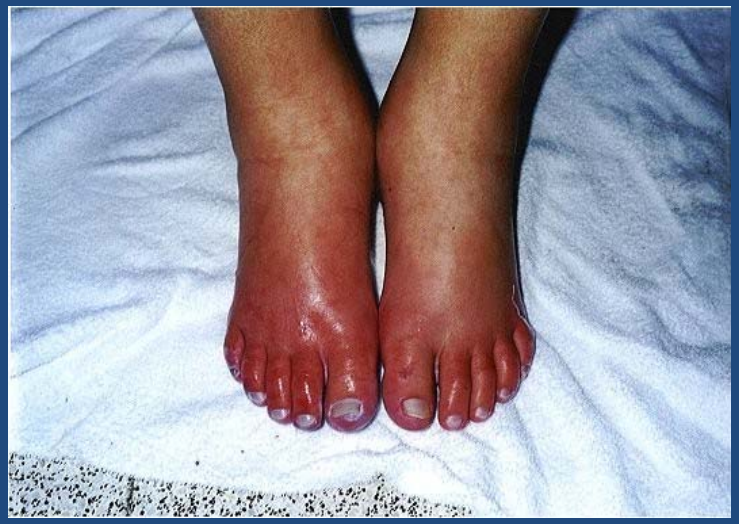
Diagnose Polycythemia Vera

Pathophysiology:

- Neoplastic disorder of a pluripotent stem cell

Epidemiology:

- Age 50-75
- 5% < 40



Clinical presentation:

- Asymptomatic
- Pruritis (hot shower) 30-40%
- Erythromelalgia
- Thrombosis: venous (portal vein, splenic or mesenteric vein) and arterial (20%)
- Gastritis and PUD
- Gout

Diagnose Polycythemia Vera

Diagnostic Criteria:

- Men Hgb >18.5 g/dL
- Women Hgb >16.5 g/dL
- O2 saturation ≥ 92%
- Palpable spleen
- Platelet > 400,000/uL
- WBC >12,000/uL
- B12 > 900

Confirming the Diagnosis:

- JAK2 V617F mutation (97%)
- Low or undetectable erythropoietin

Complications:

- Thrombosis
- Myelofibrosis
- Myelodysplastic syndromes
- Acute myelogenous leukemia

Treatment:

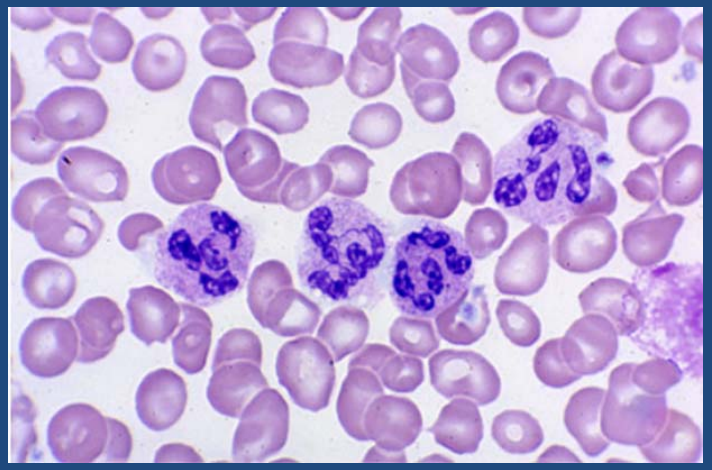
- Low dose aspirin
- Phlebotomy to induce iron deficiency
- Hydroxyurea age > 60 or previous thrombosis

Question 3.

- D; Methylmalonic acid level measurement

Diagnose Cobalamin Deficiency

- Laboratory findings:
  - Macroovalocytes, hypersegmented neutrophils, leukopenia and thrombocytopenia
  - Increased indirect bilirubin
  - Increased LDH and decreased haptoglobin consistent with hemolysis (ineffective hematopoiesis in the bone marrow)
  - Inappropriately low reticulocyte index
  - Increased homocysteine and methylmalonic acid
- Symptoms:
  - Anemia
  - Parasthesia, numbness, neuropsychiatric changes
- Diagnosis:
  - Serum B12 level < 200 pg/mL (specificity 95+%)
  - Serum B12 level > 300 pg/mL (1-5% still may have deficiency)
  - Between 200-300 check MMA and homocysteine
  - MMA and Homocysteine ↑= B12 def
  - Homocysteine only ↑= folate def

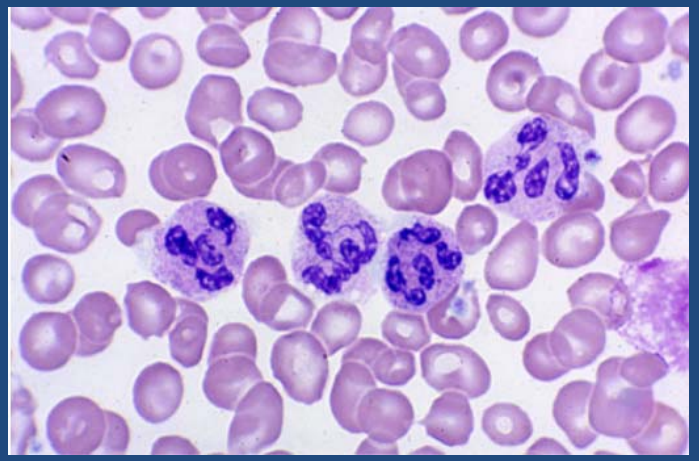


Diagnose Cobalamin Deficiency

- Find REASON for B12 deficiency:
  - 3 partner dance:
  - Protein + B12 enters stomach→acid
  - R Factor + B12 enters duodenum→pancreatic proteases
  - Intrinsic factor (IF) + B12→ileum absorption

- Etiologies:
  - Chronic atrophic gastritis (↓ acid)
  - PPIs (↓ acid)
  - H. Pylori (achlorhydria)
  - Pancreatic exocrine failure (no pancreatic proteases)
  - Metformin (interferes with ileal absorption)
  - Bacterial overgrowth (interferes with B12 attachment to IF)
  - Pernicious anemia (IF antibody)
  - Bariatric surgery/gastrectomy (no IF)

- Treatment/Replacement:
  - 1000 mcg SQ or IM q day x 1 week, then q week x 1 month then once a month for life
  - High dose oral or nasal formulations



Question 4.

- B; Delayed hyperhemolytic transfusion reaction

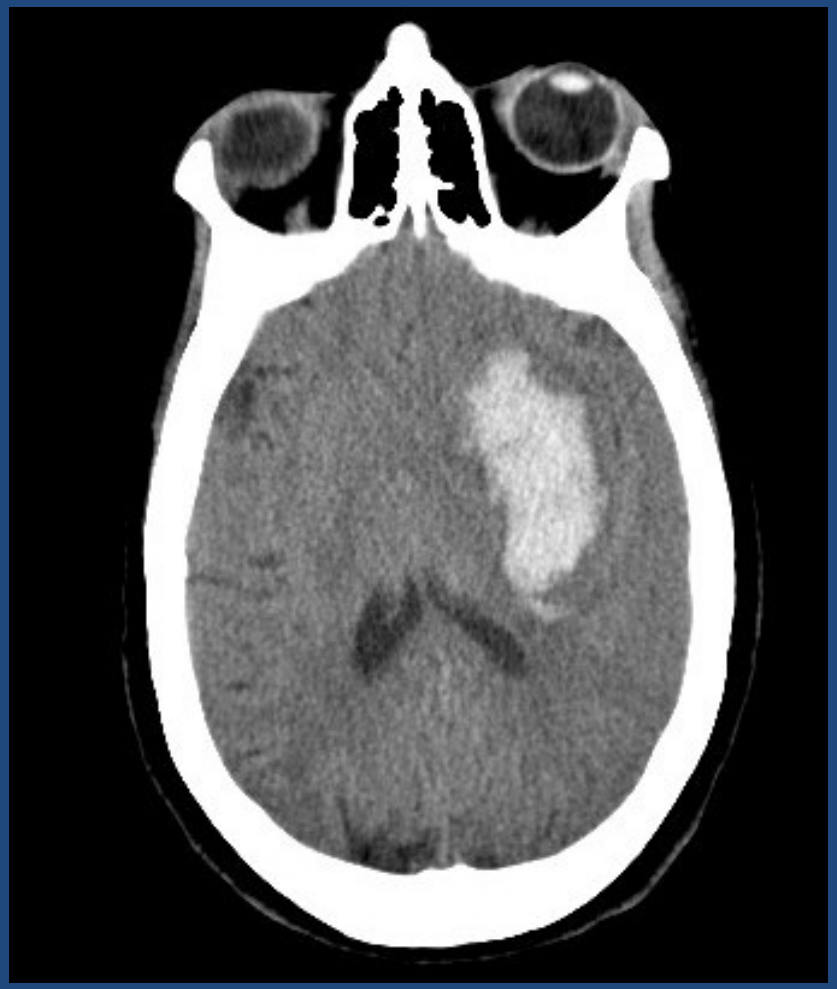
Diagnose delayed hyperhemolytic transfusion reaction

Transfusion Reaction	Mechanism
Acute Hemolytic Reaction	ABO incompatibility
Delayed Hemolytic Reaction	Alloimmunization
Febrile Non-hemolytic Reaction	Release of cytokines from donor WBC (not leukopore filtered)
TACO	Large volume/poor pump
Transfusion-related Sepsis	Bacterial contamination
TRALI	Recipient neutrophils activated in the lungs
Anaphylaxis Transfusion Reaction	IgA deficient patients
Urticarial Transfusion Reaction	Donor serum proteins and antibody-allergen interactions

Question 5.

- A; 4-Factor prothrombin complex concentrate

Treat a patient with life-threatening bleeding who takes warfarin



- Anti-coagulation Associated Intracerebral Hemorrhage (AAICH) is a medical emergency
- 90% of warfarin-related deaths are due to AAICH
- 30-day mortality rate:
  - Unconscious on admission **96%**
  - Unconscious before treatment starts **80%**
  - Treatment with warfarin reversal agents while still conscious 28%

Treat a patient with life-threatening bleeding who takes warfarin

OPTIONS to REVERSE AC:

1. **Vitamin K**
   - Takes **12-24 hours** for effect
   - 10 mg IV by SLOW INFUSION
2. **Fresh Frozen Plasma**
   - May take up to 8 units to reverse (2 liters volume)
   - Transfusion associated circulatory overload (TACO)
   - Takes time to cross match and thaw
3. **Unactivated Prothrombin Complex Concentrates (30 minutes)**
   - Four factor alone (available in Canada, Europe)
   - Three factor + factor VIIa or FFP in the United States
   - MUST GIVE VITAMIN K in addition to PCC or there will be a delayed secondary rise in INR

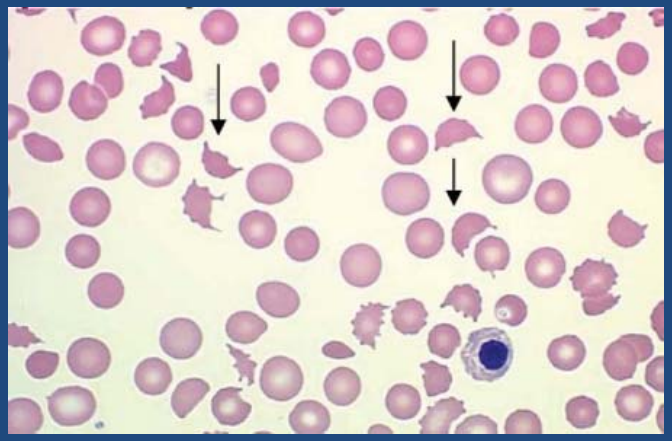
Question 6.

- C; Peripheral blood smear

Diagnose a patient with thrombotic thrombocytopenic purpura

Definition of TTP:

- Initiation of intravascular platelet aggregation and coagulation/fibrin strands within the microcirculation
- Deficiency of ADAMTS 13
- Cannot break down von Willebrand multimers



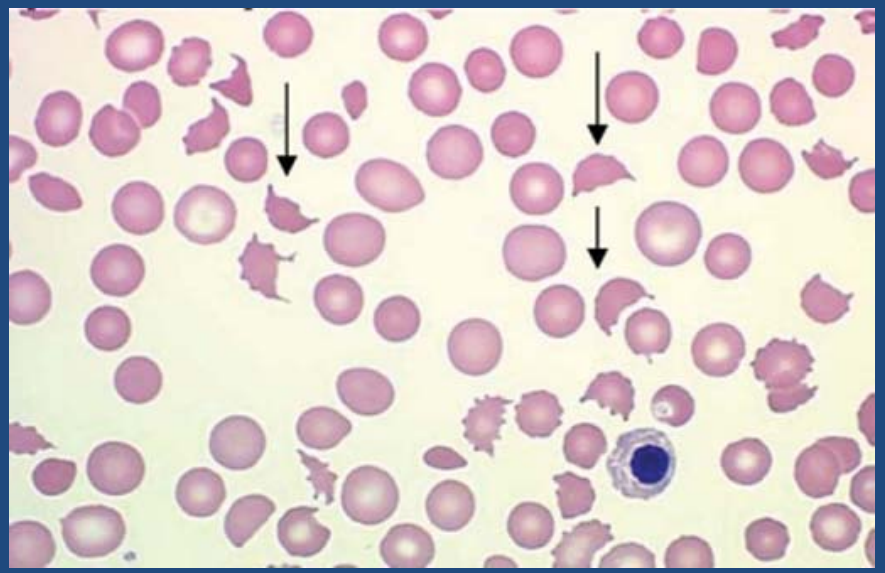
Clinical Diagnosis: Pentad of TTP:

1. *Thrombocytopenia
2. *Microangiopathic hemolytic anemia (schistocytes)
3. Neurologic Deficits
4. Kidney Impairment
5. Fever

(Diagnosis needs only these 2 major criteria without another clinically apparent cause to initiate therapy)

Diagnose a patient with thrombotic thrombocytopenic purpura

- Associated Conditions:
  - Drug-induced
    - Quinine, clopidogrel, chemotherapy, immunosuppressive agents
  - Pregnancy related
  - Following bloody diarrhea (shiga toxin producing E.coli)
  - Idiopathic (ADAMTS13)
  - Autoimmune (lupus)
  - Hereditary



Question 7.

- B; Low-molecular-weight heparin

Treat a patient with a deep venous thrombosis and cancer

CLOT trial; NEJM 2003

- Dalteparin versus coumarin for 6 months following dx of DVT in patient with cancer

Annual event rates of recurrent venous thromboembolism

DURATION OF FOLLOW-UP	PROVOKED BY SURGERY	PROVOKED BY NONSURGICAL FACTOR	UNPROVOKED (IDIOPATHIC)
12 months	1%	5.8%	7.9%
24 months	0.7%	4.2%	7.4%

DATA FROM IORIO A, KEARON C, FILIPPUCCI E, ET AL. RISK OF RECURRENCE AFTER A FIRST EPISODE OF SYMPTOMATIC VENOUS THROMBOEMBOLISM PROVOKED BY A TRANSIENT RISK FACTOR: A SYSTEMATIC REVIEW. ARCH INTERN MED 2010; 170:1710–1716.

Cancer-related VTE recurrence at 12 months is *three times* that of unprovoked VTE at *21%*

CLOT trial, NEJM 2003

- Mortality at 6 months: not significant
  - LMWH 39%
  - Vit K 41%
- Major bleeding: not significant
  - LMWH 6%
  - Vit K: 4%
- Recurrent VTE: significant!
  - P= <0.0002
  - LMWH: 9%
  - Vit K 17%

Treat a patient with a deep venous thrombosis and cancer

- <u>RULES and RECOMMENDATIONS CHEST 2012 GUIDELINES:</u>

- Avoid anticoagulating people with active bleeding, recent surgery, platelets <50K, coagulopathy; may use filter

- Treatment should begin with LMWH for 3 months; continue anticoagulation *after* 3 months if risk of bleeding is low (1B recommendation) *and* continue anticoagulation after 3 months if risk of bleeding is high (2B recommendation)

- Continuously re-evaluate risk/benefit ratio for optimal patient care depending on risk of bleeding and life expectancy

Table 10 Clinical characteristics comprising the HAS-BLED bleeding risk score

Letter	Clinical characteristic[a]	Points awarded
H	Hypertension	1
A	Abnormal renal and liver function (1 point each)	1 or 2
S	Stroke	1
B	Bleeding	1
L	Labile INRs	1
E	Elderly (e.g. age >65 years)	1
D	Drugs or alcohol (1 point each)	1 or 2
		Maximum 9 points

[a]'Hypertension' is defined as systolic blood pressure >160 mmHg. 'Abnormal kidney function' is defined as the presence of chronic dialysis or renal transplantation or serum creatinine ≥200 μmol/L. 'Abnormal liver function' is defined as chronic hepatic disease (e.g. cirrhosis) or biochemical evidence of significant hepatic derangement (e.g. bilirubin >2 x upper limit of normal, in association with aspartate aminotransferase/alanine aminotransferase/alkaline phosphatase >3 x upper limit normal, etc.). 'Bleeding' refers to previous bleeding history and/or predisposition to bleeding, e.g. bleeding diathesis, anaemia, etc. 'Labile INRs' refers to unstable/high INRs or poor time in therapeutic range (e.g. <60%). Drugs/alcohol use refers to concomitant use of drugs, such as antiplatelet agents, non-steroidal anti-inflammatory drugs, or alcohol abuse, etc. INR = international normalized ratio. Adapted from Pisters *et al.*[60]

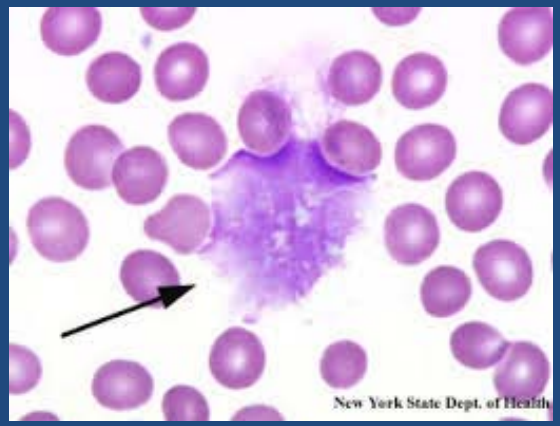
≥ 3 is considered too high risk for AC

Question 8.

- A; Hematopoietic stem cell transplant

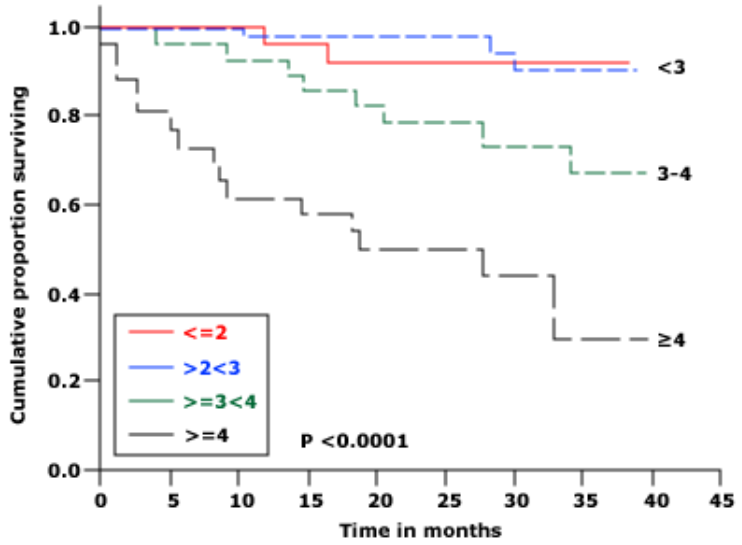
Evaluate a patient with newly diagnosed chronic lymphocytic leukemia

- Epidemiology:
  - Most common lymphoid malignancy of all the hematologic neoplasms
  - 30% of all leukemias of adults in US
  - Incidence increases with age (median age 70)
- Clinical presentation:
  - Asymptomatic (25%)
  - "B" symptoms
  - Lymphadenopathy
  - Hepatosplenomegaly
  - Infections/Autoimmune Hemolytic Anemia
- Diagnosis:
  - Absolute B lymphocyte count ≥ 5000
  - Demonstration of clonal population by **flow cytometry** of peripheral blood
- Stage/Risk Assess:
  - Rai and Binet
  - Other prognostic molecular features
  - B2 microglobulin



Evaluate a patient with newly diagnosed chronic lymphocytic leukemia

Survival of patients with chronic lymphocytic leukemia stratified by beta-2 microglobulin levels



This graph illustrates overall survival (Kaplan-Meier method) in 153 patients with chronic lymphocytic leukemia, stratified according to their serum levels of beta-2 microglobulin. The numbers to the right of each graph refer to the beta-2 microglobulin concentration in milligrams per liter.
Data from Fayad, L, et al. Blood 2001; 97:256.

Question 9.

- C; Serum free light chain testing

Diagnose and manage a patient with monoclonal gammopathy of undetermined significance (MGUS)

Diagnostic Criteria for MGUS:
(All 3 must be met)

1. Serum monoclonal protein
< 3gm/dL
2. Bone Marrow Plasma Cells
< 10%
3. NO end organ damage

1% per YEAR will become myeloma:

**Follow labs 6 mos/yearly and sooner if symptoms develop*

Risk for Progression to Multiple Myeloma:

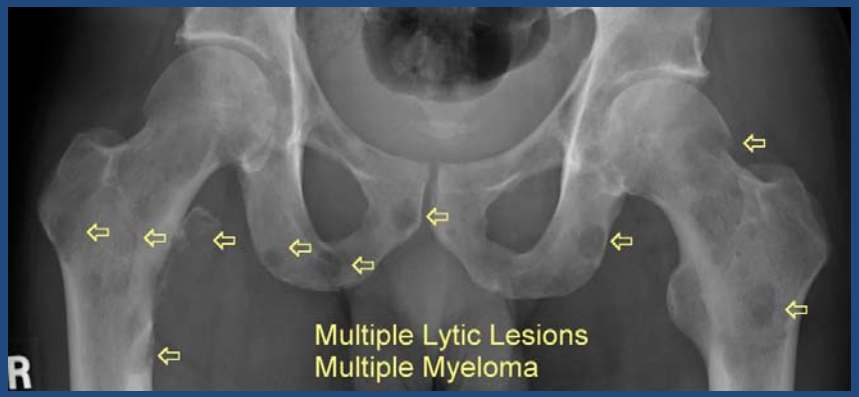
1. A non-IgG M protein
2. M protein level of at least 1.5 g/dL
3. Abnormal serum free light chain ratio (FLC)

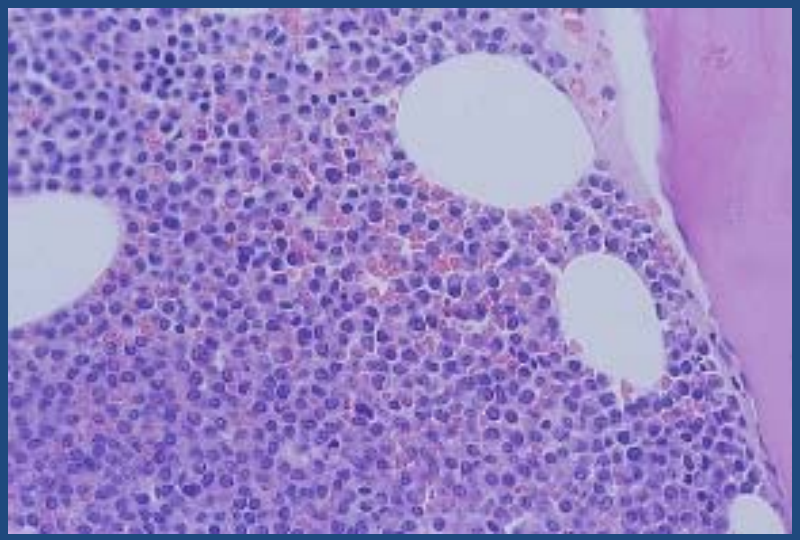
Diagnose and manage a patient with monoclonal gammopathy of undetermined significance (MGUS)

Diagnostic Criteria for Multiple Myeloma

(All 3 must be met):

1. Presence of a serum or urine monoclonal protein
2. Presence of ≥ 10% clonal plasma cells in the bone marrow or a plasmacytoma
3. Presence of end-organ damage felt to be due to the plasma cell dyscrasia such as:
   - Hypercalcemia
   - Lytic bone lesions
   - Anemia or
   - Renal failure





Question 10.

- C; Factor IX deficiency

Diagnose Factor IX deficiency (hemophilia B)

Bleeding patient due to **primary** hemostasis problem:

- Platelet dysfunction and vonWillebrand diseases
  - Epistaxis/Gingiva
  - Menorrhagia
- Petechiae/superficial ecchymosis

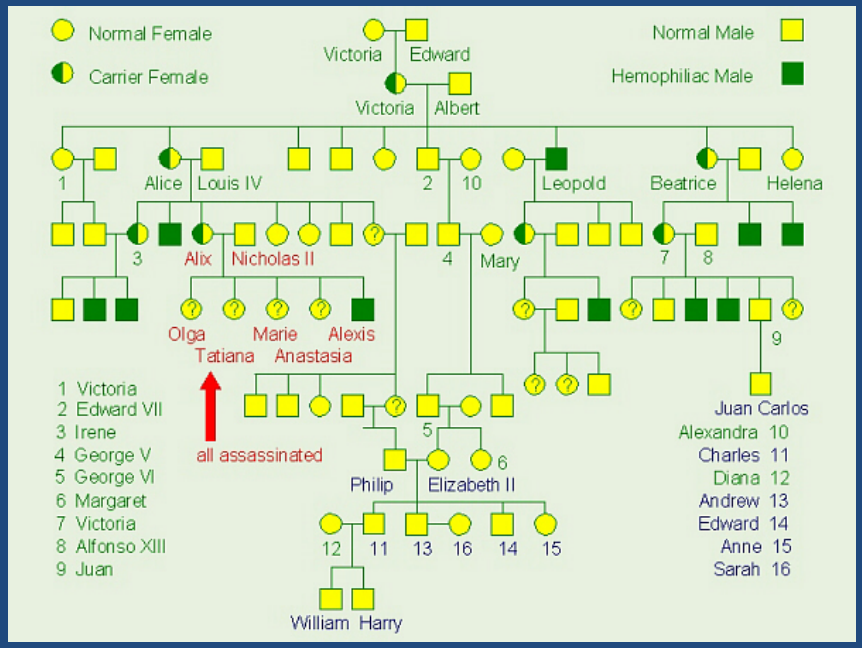
Bleeding patient due to **secondary** hemostasis problem:

- Coagulation factor deficiencies and inhibitors
  - Hemarthroses
- Deep soft tissue hematomas
- Delayed bleeding after surgery
- Normal platelet number
- Normal prothrombin time (PT)
- Prolonged activated partial thromboplastin time (aPTT)

Diagnose Factor IX deficiency (hemophilia B)

- A MIXING STUDY determines whether the patient has a factor DEFICIENCY or an INHIBITOR!

- aPTT corrects to normal with mixing= deficiency
- aPTT does NOT correct to normal with mixing= inhibitor



No male to male transmission: x-linked hemophilia

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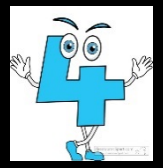

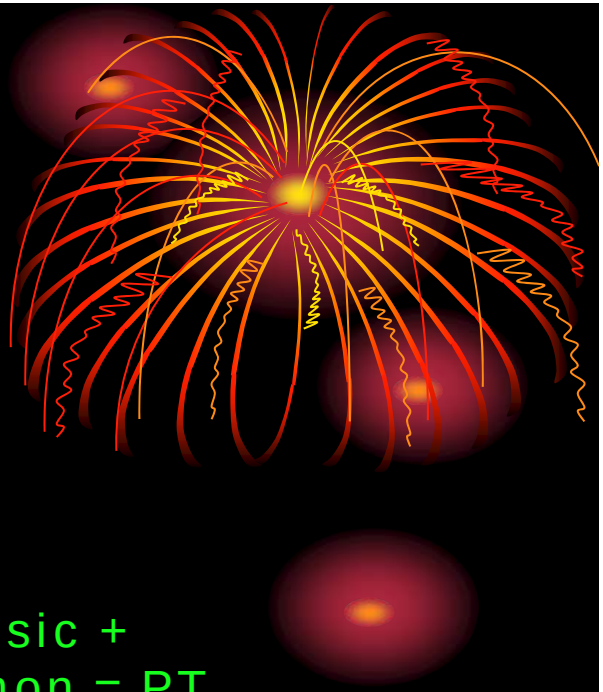

Intrinsic + Common = aPTT

Extrinsic + Common = PT

10

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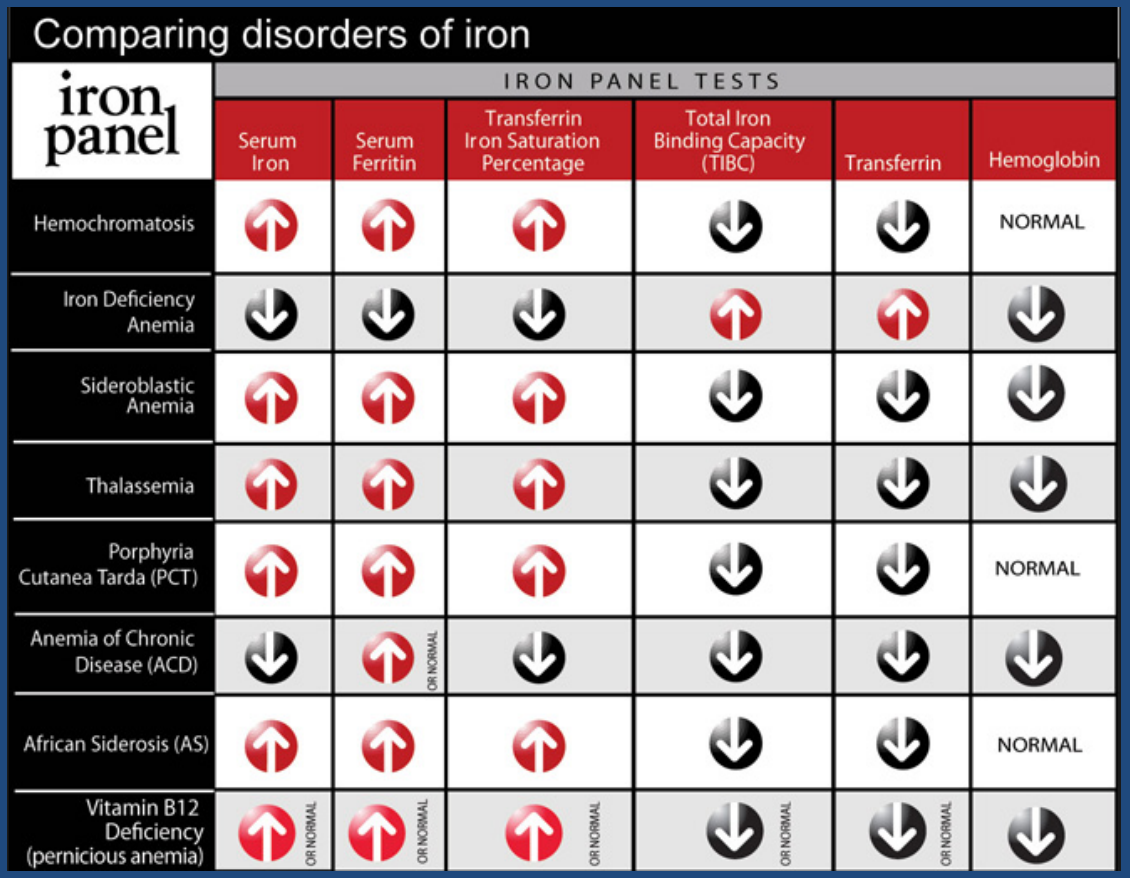
1

Question 11.

- D; Continue current management

Diagnose Inflammatory Anemia (Anemia of Chronic Disease)

- Best test to diagnose iron deficiency = FERRITIN < 30
- Ferritin > 100, statistically *unlikely* to be iron deficient
- Transferrin LOW indicates ACD

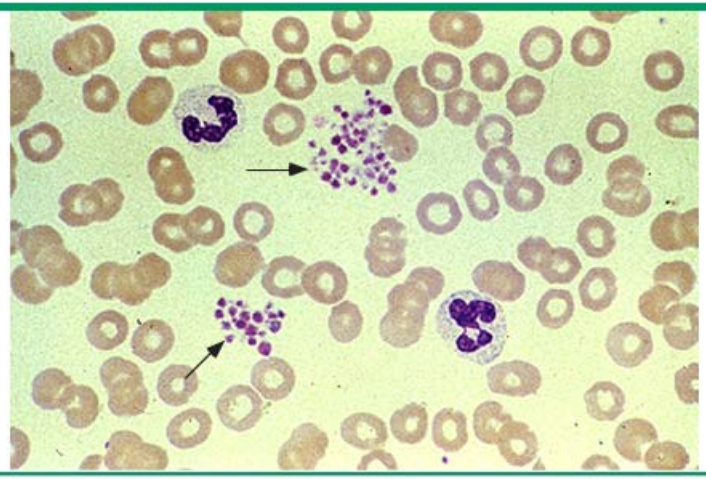


Question 12.

- D; Repeat complete blood count with a citrated tube (EDTA-free)

Diagnose Pseudothrombocytopenia

Pseudothrombocytopenia due to platelet clumping in EDTA

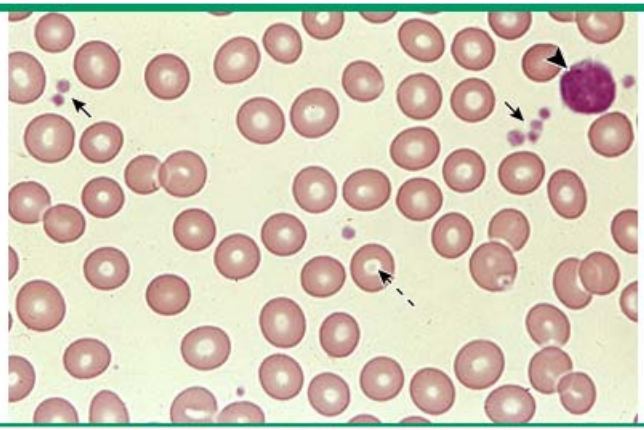


This peripheral blood smear shows platelet clumping (arrows) in an EDTA-anticoagulated blood sample. This patient had an EDTA-dependent platelet agglutinin which caused in vitro platelet clumping, resulting in an artifactually low platelet count (ie, "pseudothrombocytopenia"). No platelet clumping was seen, and the platelet count was normal, in a blood sample from this patient anticoagulated with sodium citrate.

Reproduced with permission from Beutler, E, Lichtman, MA, Coller, BS, et al, Hematology, 5th ed, McGraw-Hill, New York, 1995.

Graphic 68949 Version 2.0

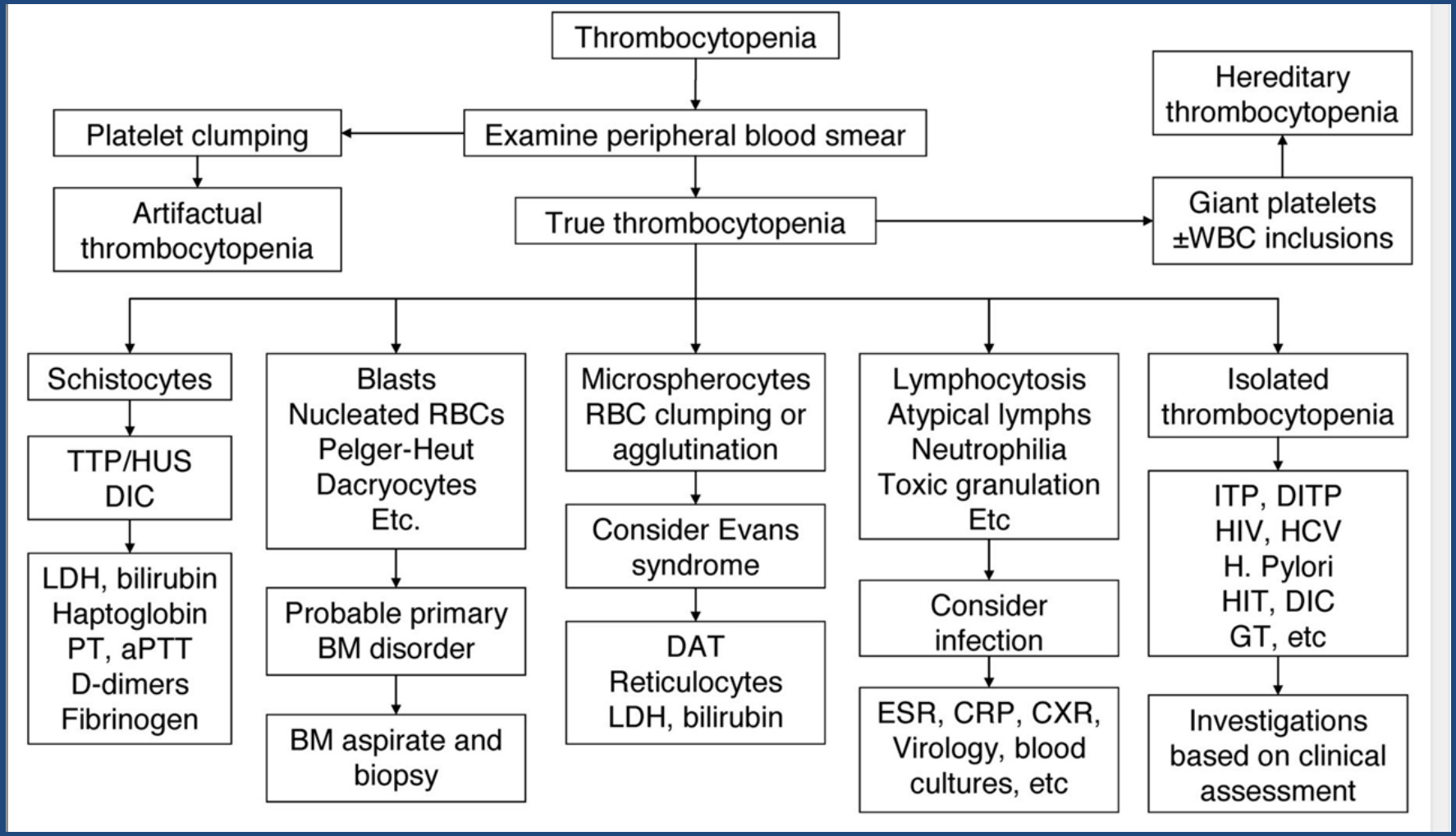
Normal peripheral blood smear



High-power view of a normal peripheral blood smear. Several platelets (arrows) and a normal lymphocyte (arrowhead) can also be seen. The red cells are of relatively uniform size and shape. The diameter of the normal red cell should approximate that of the nucleus of the small lymphocyte; central pallor (dashed arrow) should equal one-third of its diameter.

Courtesy of Carola von Kapff, SH (ASCP).

Graphic 59683 Version 4.0


Thrombocytopenia
Examine peripheral blood smear
Platelet clumping
Artifactual thrombocytopenia
True thrombocytopenia
Hereditary thrombocytopenia
Giant platelets ±WBC inclusions
Schistocytes
TTP/HUS DIC
LDH, bilirubin Haptoglobin PT, aPTT D-dimers Fibrinogen
Blasts Nucleated RBCs Pelger-Heut Dacryocytes Etc.
Probable primary BM disorder
BM aspirate and biopsy
Microspherocytes RBC clumping or agglutination
Consider Evans syndrome
DAT Reticulocytes LDH, bilirubin
Lymphocytosis Atypical lymphs Neutrophilia Toxic granulation Etc
Consider infection
ESR, CRP, CXR, Virology, blood cultures, etc
Isolated thrombocytopenia
ITP, DITP HIV, HCV H. Pylori HIT, DIC GT, etc
Investigations based on clinical assessment

Question 13.

- E; von Willebrand's disease

Diagnose probable von Willebrand's disease in a person with abnormal bleeding

Problem List:

- 19 year-old woman
- Menorrhagia
- Bleeding with tooth extraction
- Family history of mother and sister with menorrhagia

- Hemoglobin 8 g/dL
- aPTT 25 seconds

vWD Subtypes

Type	Inheritance	Deficiency
Type 1	Autosomal dominant	Quantitative
Type 2	Autosomal dominant	Qualitative
Type 3	Autosomal recessive	Severe/absent

Terminology - von Willebrand factor

Designation	Function	Assay
Von Willebrand factor (VWF)	Multimeric glycoprotein that promotes platelet adhesion and aggregation and is a carrier for factor VIII in plasma	See below
Von Willebrand factor activity		
1 - von Willebrand factor: ristocetin cofactor (VWF:RCo)	Ability of VWF to bind to normal platelets in the presence of ristocetin with consequent agglutination	Quantitate platelet agglutination/aggregation after addition of ristocetin and VWF (patient plasma)
2 - von Willebrand factor: collagen binding (VWF:CB)	Ability of VWF to bind to collagen	Quantitate binding of VWF (patient plasma) to collagen-coated plates
Von Willebrand factor antigen (VWF:Ag)	VWF protein as measured by immunologic assays; does not imply functional ability	Immunologic assay such as ELISA, RIA, or Laurell electroimmunoassay

Question 14.

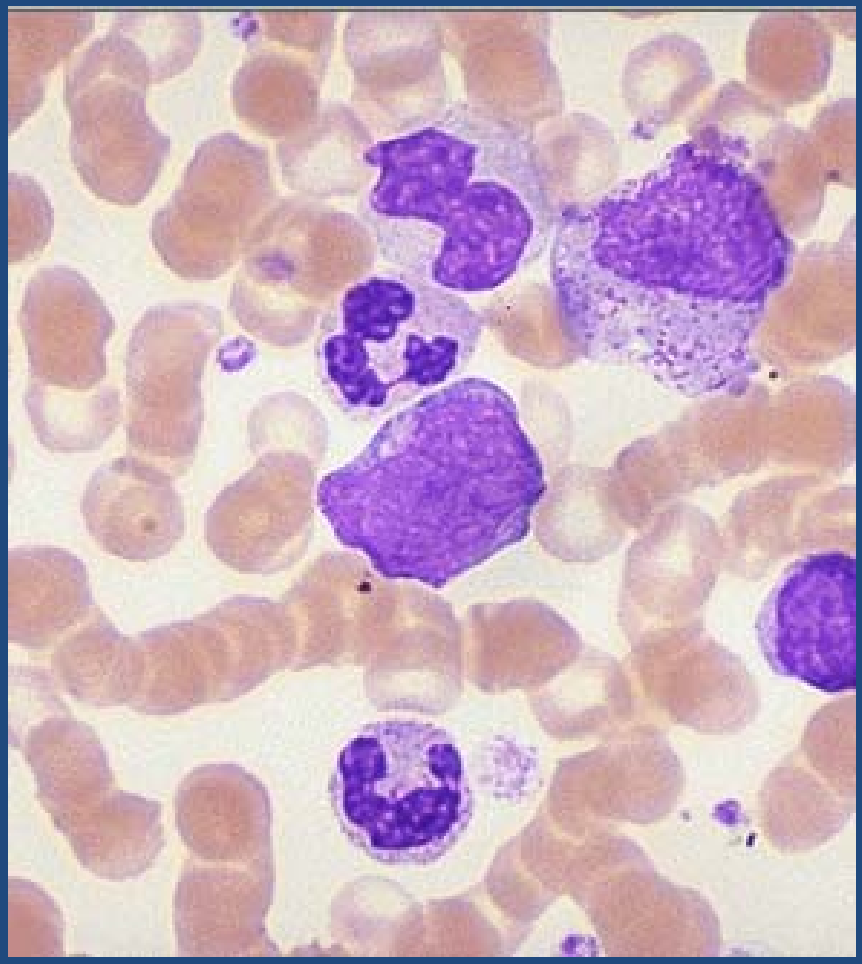
- B; Fluorescence in situ hybridization assay for t(9;22)

Diagnose
chronic myelogenous leukemia (CML)

Problem List:

- 46 year-old woman
- Fatigue, night sweats
- Early satiety, 10 lb wt loss
- Symptoms x 5 months
- Big spleen
- No lymphadenopathy or hepatomegaly

- Hemoglobin 11.6 g/dL
- WBC 56,000/uL
- Platelets 385 K/uL



Diagnose
chronic myelogenous leukemia (CML)

Risk factors:

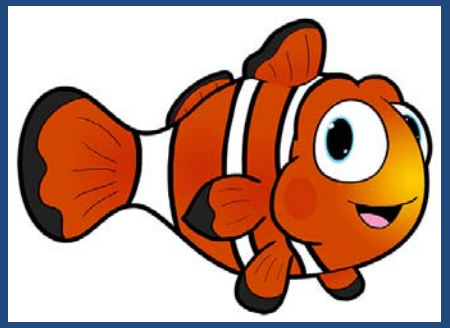
- Age
- Male
- Radiation

Differential diagnosis:

- Leukemoid reaction

Diagnostic testing:

- FISH for the 9;22 translocation in peripheral blood
- PCR for the 9;22 translocation in peripheral blood



Question 15.

- C; Initiate argatroban

Treat a patient with heparin-induced thrombocytopenia

The 4 T's

- Thrombocytopenia (2 pts)
- Timing (2 pts)
- Thrombosis (0 pts)
- oTher (2 pts)

Pre-test Probability

- 6-8 points: high (80%)
- 4-5 points: intermediate
- ≤ 3 points: low (< 5%)

"4 T's"

	2 points	1 point
Thrombocytopenia	>50% drop nadir > 20K	30–50% drop nadir 10–19K
Timing	5–10 days < 1d + prior hep < 30ds	? 5–10 d >10 d <1d + prior hep 30–100d)
Thrombosis	New Clot anaphylaxis, skin necrosis	Suspected progressive or recurrent clot
alTernative dx	none	possible

"4 T's"

Score	HIT risk	Action:
1–3 points	< 1%	Don't test
4–5 points	10%	Test (SRA?)
6–9 points	50%	Test (HIT ELISA?)

Pretest Probability of HIT by 4T score*	ELISA test result (OD)	Reasonable clinical action:
Low (0–3 points) *<1% chance patient has HIT*	>2.00	Order SRA**
	1.50 – 1.99	
	0.60 – 1.49	HIT ruled out***
	< 0.6	
Intermediate (4–5 points) *~10% chance patient has HIT*	>2.00	Treat HIT
	1.50 – 1.99	Order SRA**
	0.60 – 1.49	
	< 0.6	HIT ruled out***
High (6–8 points) *~50% chance patient has HIT*	>2.00	Treat HIT
	1.50 – 1.99	
	0.60 – 1.49	Order SRA**
	< 0.60	

Treat a patient with heparin-induced thrombocytopenia

TREATMENT PRINCIPLES WHEN HIT IS STRONGLY SUSPECTED (OR CONFIRMED)

1. Discontinue and avoid all heparin.
2. Give a nonheparin alternative anticoagulant. (Argatroban or lepirudin)
3. Postpone warfarin pending substantial platelet count recovery (give vitamin K if warfarin has already been started).
4. Test for HIT antibodies.
5. Investigate for lower-limb deep-vein thrombosis.
6. Avoid prophylactic platelet transfusions.

Question 16.

- A; Antiphospholipid syndrome testing

Diagnose Antiphospholipid Antibody Syndrome

Problem List

- 32 year-old woman
- Unprovoked PE
- Raynaud's phenomenon
- Four early miscarriages
- aPTT is 56 seconds

- How do you treat the PE?

Box 1: Revised classification criteria for APS

APS is present if at least one of the clinical criteria and one of the laboratory criteria that follow are met:

Clinical criteria:

1. Vascular thrombosis
   One or more clinical episodes of arterial, venous, or small-vessel thrombosis, occurring in any tissue or organ. Thrombosis must be confirmed by objective validated criteria (ie, by appropriate imaging studies or histopathology). Histopathologically, thrombosis should be present without significant evidence of inflammation in the vessel wall.
2. Pregnancy morbidity
   (a) One or more unexplained deaths of morphologically normal fetuses at or after the 10th week of gestation, with normal fetal morphology documented by ultrasound or by direct examination of the fetus, or
   (b) One or more premature births of morphologically normal neonates before the 34th week of gestation because of (i) eclampsia or severe preeclampsia defined according to standard definitions or (ii) recognized features of placental insufficiency; or
   (c) Three or more unexplained consecutive spontaneous abortions before the 10th week of gestation, with maternal anatomic or hormonal abnormalities and paternal and maternal chromosomal causes excluded.

Laboratory Criteria :

1. Lupus anticoagulant present in plasma*
2. aCL of IgG and/or IgM isotype in serum or plasma, present in medium or high titer*
3. Anti–β-2-GP I IgG and/or IgM isotype in serum or plasma*

*on two or more occasions at least 12 weeks apart.

Question 17.

- D; Plasma exchange

Diagnose and Treat Thrombotic Thrombocytopenic Purpura

Clinical Diagnosis: Pentad of TTP:

1. *Thrombocytopenia
2. *Microangiopathic hemolytic anemia (schistocytes)
3. Neurologic Deficits
4. Kidney Impairment
5. Fever

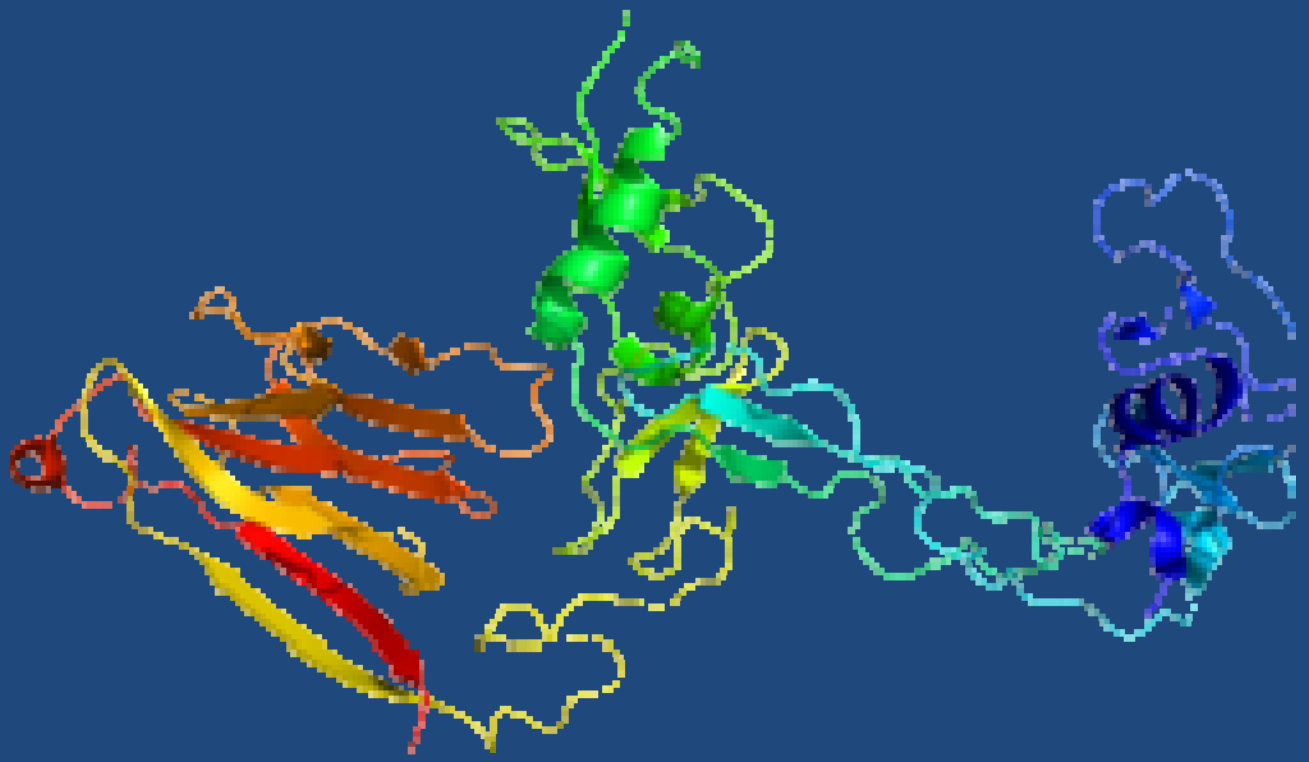
(Diagnosis needs only these 2 major criteria without another clinically apparent cause to initiate therapy)

Definition of TTP:

- Initiation of intravascular platelet aggregation and coagulation/fibrin strands within the microcirculation
- ***Deficiency of ADAMTS 13***
- Cannot break down von Willebrand multimers

Treatment:

- Plasma exchange
- Fresh frozen plasma
- Steroids



ADAMSTS 13:

- Cleaves von Willebrand multimers turning off platelet activation/clotting
- Deficiency causes TTP
- Treatment is to remove plasma of patient which contains antibodies to ADAMSTS 13, and replace with plasma that contains the metalloproteinase.

Question 18.

- D; Diagnose B-thalassemia

Diagnose B-thalassemia

The thalassemias: Genetic, clinical, and laboratory findings

Disorder	Genotype	MCV	Anemia	Hemoglobin electrophoresis
Alpha thalassemia				
Silent carrier	α α / α -	NL	None	Normal <3% Hb Barts at birth
Minor	α α / - - or α - / α -	Low	Mild	Normal 3 to 8% Hb Barts at birth
Hb H disease (deletional)	α - / - -	Low	Moderate	5 to 30% HbH present in adults 20 to 40% Hb Barts at birth
Major (fetal hydrops)	- - / - -	Low	Fatal	Hb Barts, Hb Portland, and HbH present HbA, HbF, and HbA_2 are absent
Beta thalassemia				
Minor (trait)	β / β° or β / $β^+$	Low	Mild	HbA_2 normal or increased (up to 7 to 8%) HbF increased in approximately half of patients
Intermedia	$β^+$ / $β^+$ and others*	Low	Moderate	
Major	β° / β°	Low	Severe	HbA absent Only HbA_2 and HbF are present

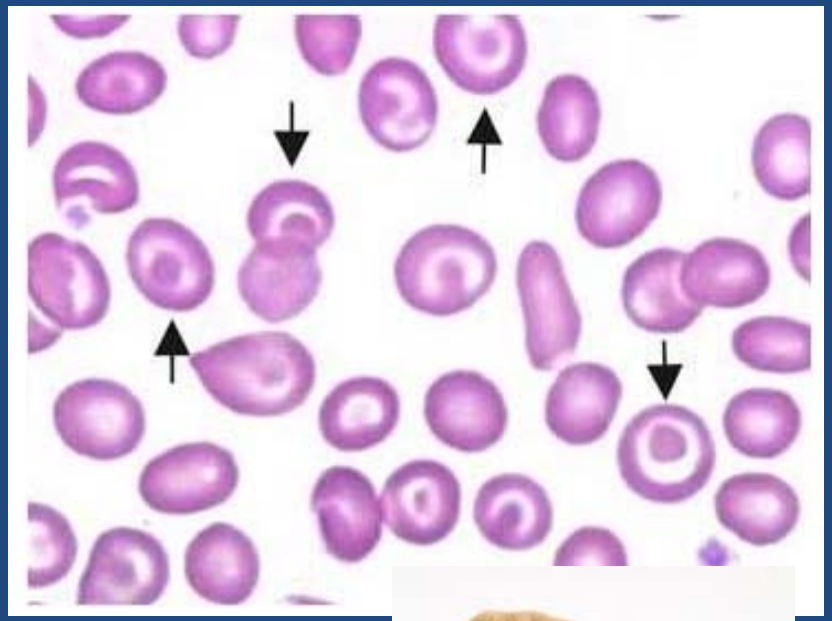
Refer to UpToDate content on thalassemia genetics and diagnosis for additional information on clinical manifestations and laboratory testing.

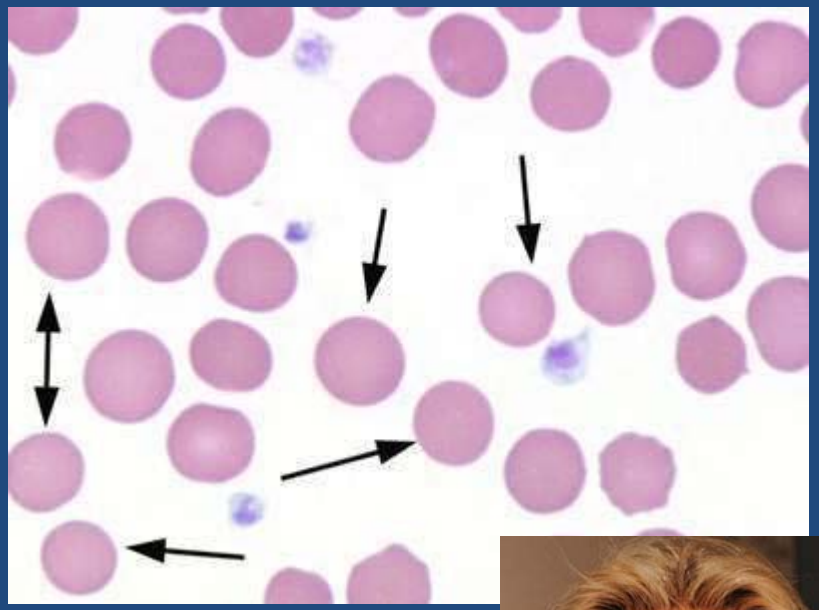
MCV: mean corpuscular volume; Hb: hemoglobin; $β^+$: beta globin allele producing some β chain; β°: beta globin allele producing no β chain.
* Refer to UpToDate content on beta thalassemia for multiple other possible genotypes.

Courtesy of Stephen A Landaw, MD, PhD.

Graphic 50393 Version 8.0

Target Cells:
The Opposite of Spherocytes





Surface Area

Volume

Surface Area

Volume

Question 19.

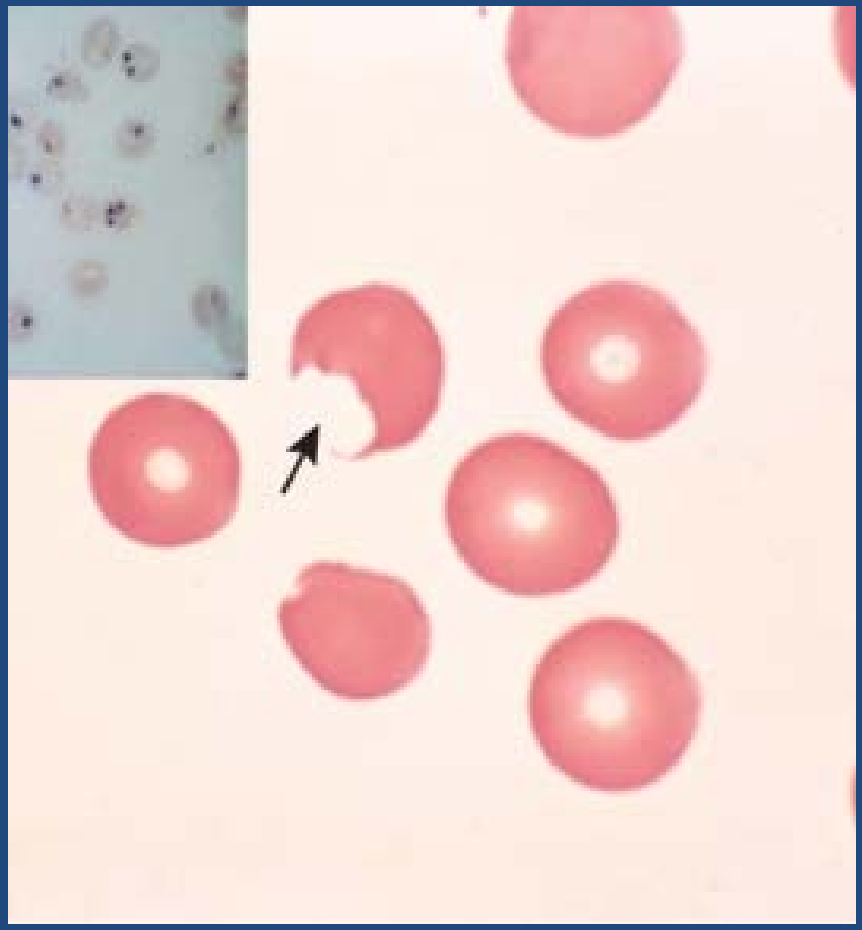
- B; Glucose- 6-phosphate dehydrogenase deficiency

Diagnose Glucose-6-Phosphate Dehydrogenase Deficiency

Problem List:

- 25 year-old black man
- Fatigue, brown urine, and short of breath x 1 day
- Recent TMP-SMX for UTI

- Hematocrit 21%
- LDH 350 U/L
- Reticulocyte count 10%



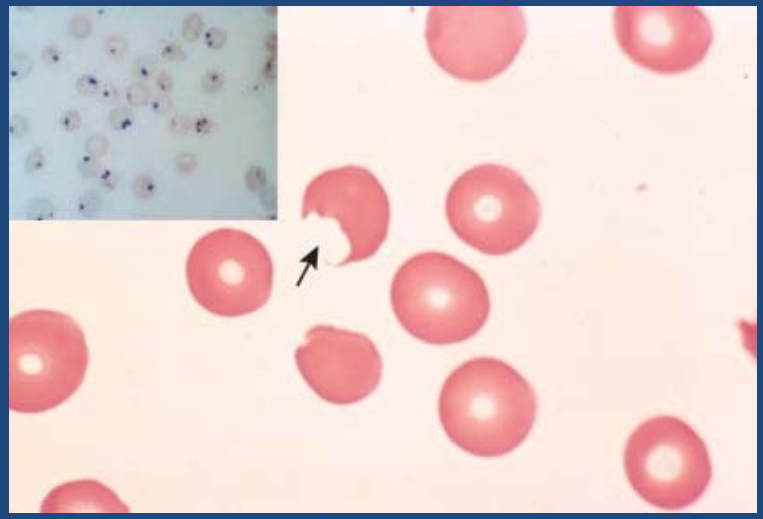
Diagnose Glucose-6-Phosphate Dehydrogenase Deficiency

- X-linked recessive
- Mediterranean, 10% of American black population
- Deficiency of G6PD results in hemolysis due to certain triggers

- Hemolytic anemia
- Increased LDH/ decreased haptoglobin
- Coomb's negative
- Hyperproliferative (increased retic index)
- Bite cells, Heinz bodies on peripheral smear

<u>Triggers:</u>

- Medications
  - TMP/SMX, nitrofurantoin, dapsone, isoniazid
- Infections
  - Viral hepatitis (vaccinate)
- Foods
  - Broad beans (fava beans)



Question 20.

- D; No thrombophilia testing

Perform thrombophilic screening in a patient with idiopathic venous thromboembolism

Who should NOT be tested?

- Recent major surgery, trauma, or immobilization
- Active malignancy
- Lupus
- Inflammatory bowel disease
- Myeloproliferative disorders
- HITT with thrombosis
- Preeclampsia at term
- Retinal vein thrombosis
- Upper limb venous thrombosis

Who SHOULD be tested?

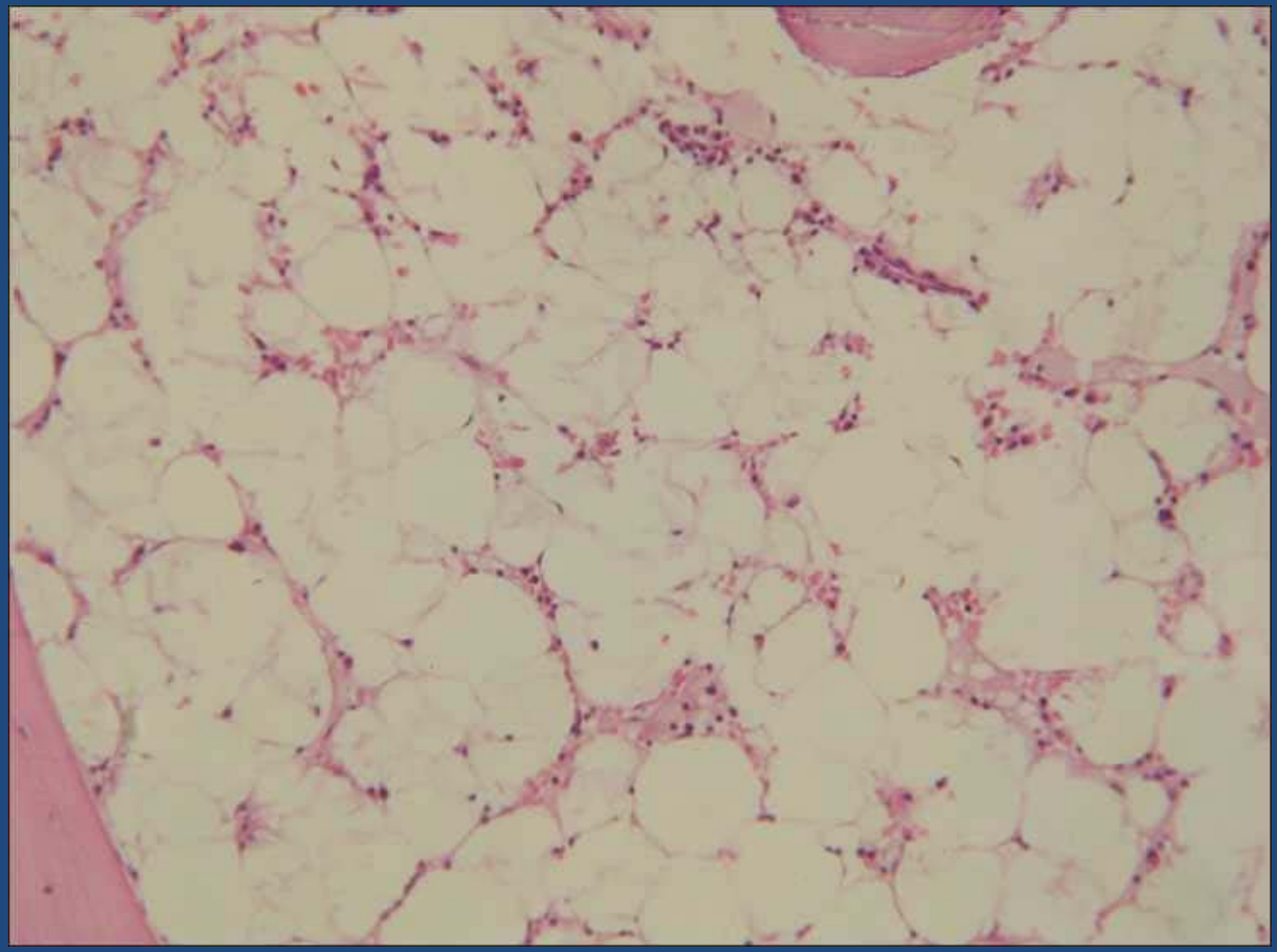
- Initial thrombosis before age 50
- Strong family history of thrombosis
- Recurrent thrombosis
- Associated with contraceptive use or pregnancy
- Unusual location of clot (hepatic, portal, mesenteric, cerebral)
- History of warfarin skin necrosis

Clinical settings which may interfere with testing for thrombophilia

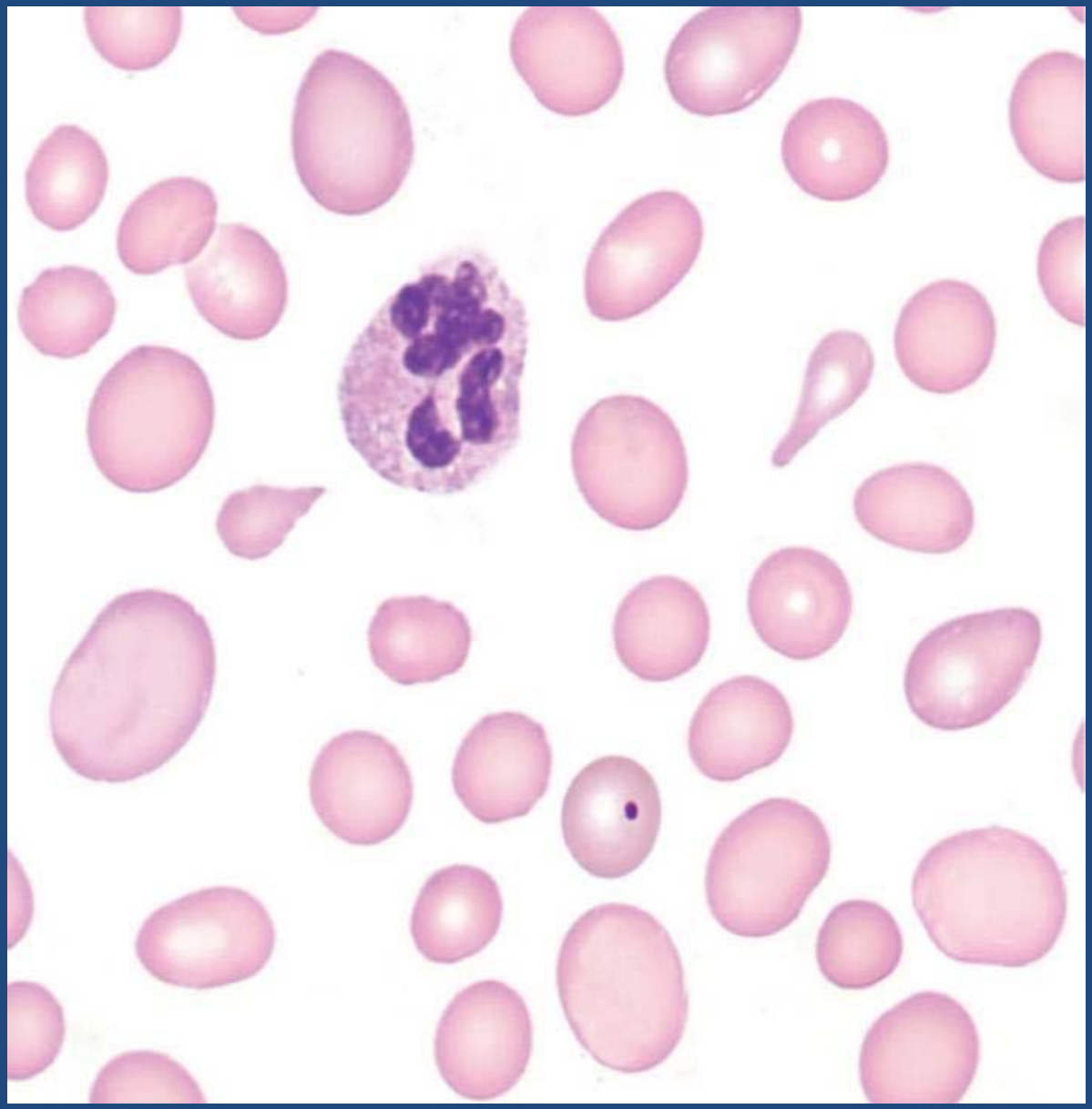
Hypercoagulable disorder for testing	Confounding Factors		
	Acute thrombosis	Heparin therapy	Warfarin therapy
Antithrombin (deficiency)	Can be lowered*	Lowered	NC; Rarely increased
Antiphospholipid antibodies	NC	NC	NC
Factor V Leiden	NC	NC	NC
Factor VIII level	Acute phase reactant. Do not test while inflammation is still present.		
Lupus anticoagulant	NC	Cannot measure	False positives possible
Protein C (deficiency)	Can be lowered*	NC	Cannot measure•
Protein S (deficiency)	Can be lowered*	NC	Cannot measure•
Prothrombin gene mutation	NC	NC	NC
Acquired AT deficiency:			
neonatal period, pregnancy, liver disease, DIC, nephrotic syndrome, major surgery, acute thrombosis, treatment with L-asparaginase, heparin, or estrogens			
Acquired Protein C deficiency:			
neonatal period, liver disease, DIC, chemotherapy (CMF), inflammation, acute thrombosis, treatment with warfarin or L-asparaginase			
Acquired Protein S deficiency:			
neonatal period, pregnancy, liver disease, DIC, acute thrombosis, treatment with warfarin, L-asparaginase, or estrogens			

NC: not changed; LMW heparin: low molecular weight heparin; AT: antithrombin; DIC: disseminated intravascular coagulation; CMF: cyclophosphamide, methotrexate, 5-fluorouracil.
* Results can be affected by acute thrombosis; it is most cost effective to avoid testing for these deficiencies during the initial presentation. However, if plasma levels are well within the normal range at presentation, deficiency of these proteins is essentially excluded. Common causes for an acquired deficiency of Antithrombin (AT), Protein C, or Protein S are listed below:
• If it is important to measure for these deficiencies while the patient is still anticoagulated, switch the treatment to full dose heparin or LMW heparin and discontinue coumadin for at least two weeks before measurement. Comparing protein S or C levels with prothrombin antigen in stably anticoagulated patients is not reliable, as accurate measurement of prothrombin antigen levels is a research assay which is not generally available.

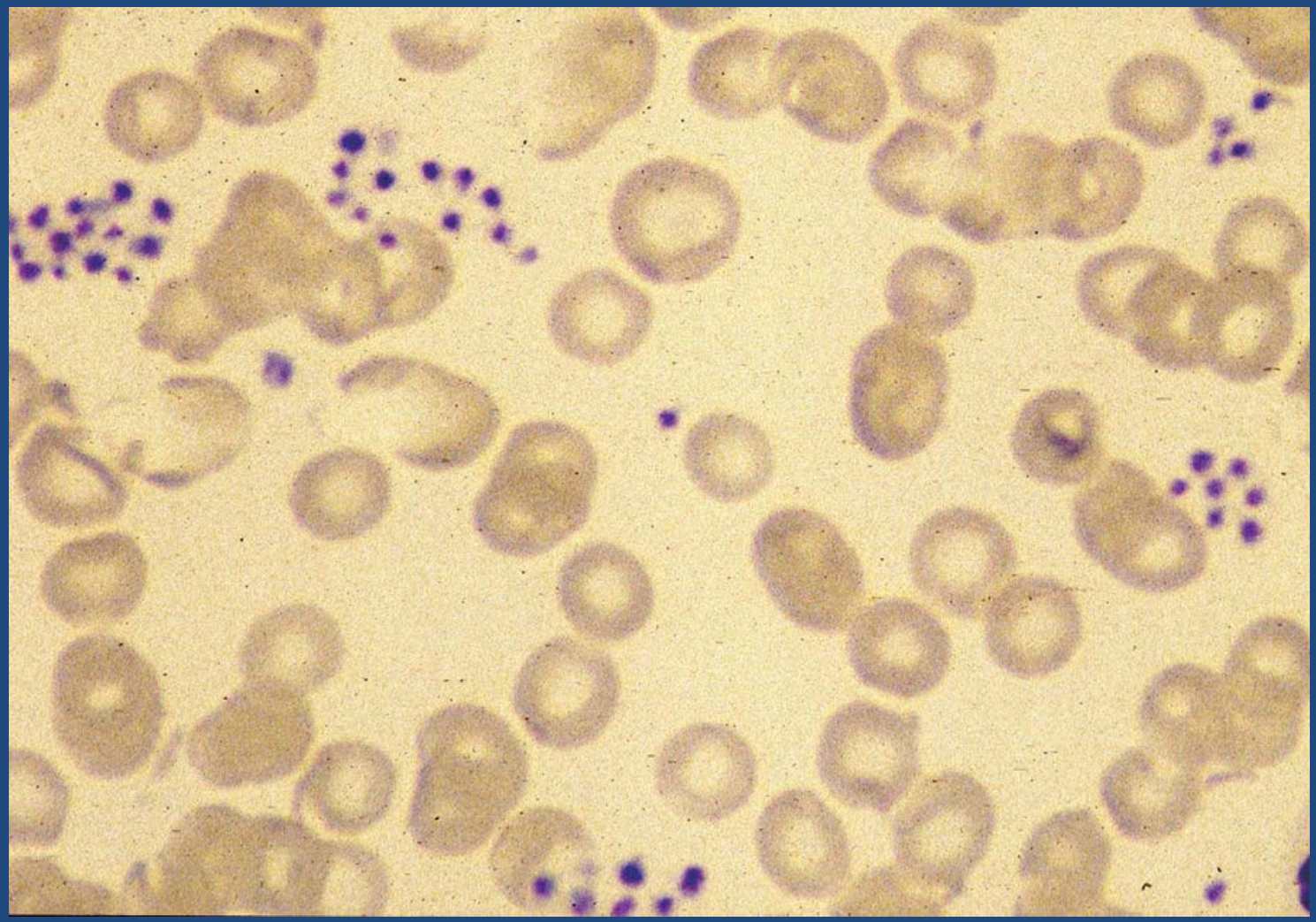
Question 1. (Figure 1)



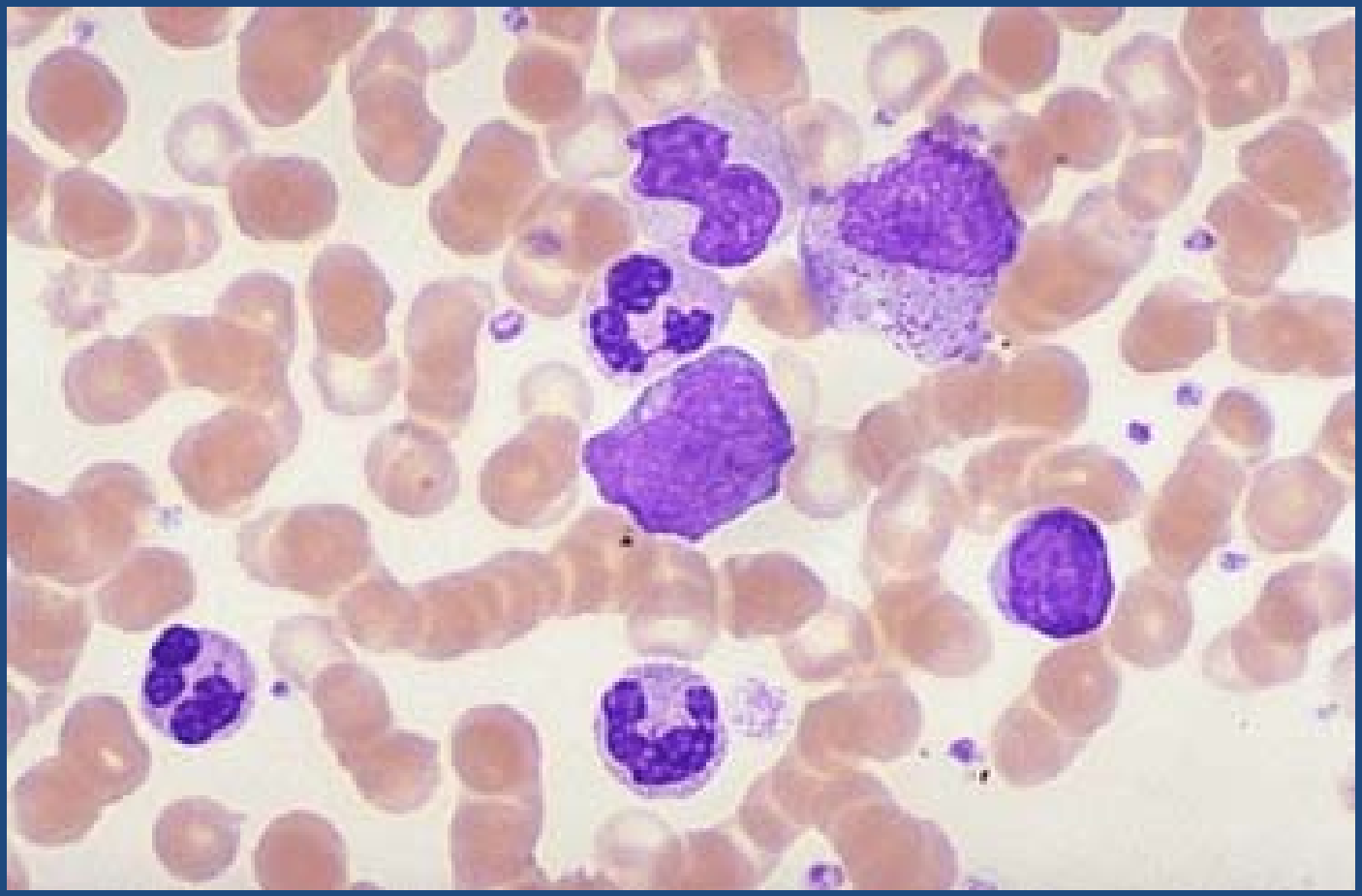
Question 3 (Figure 2)



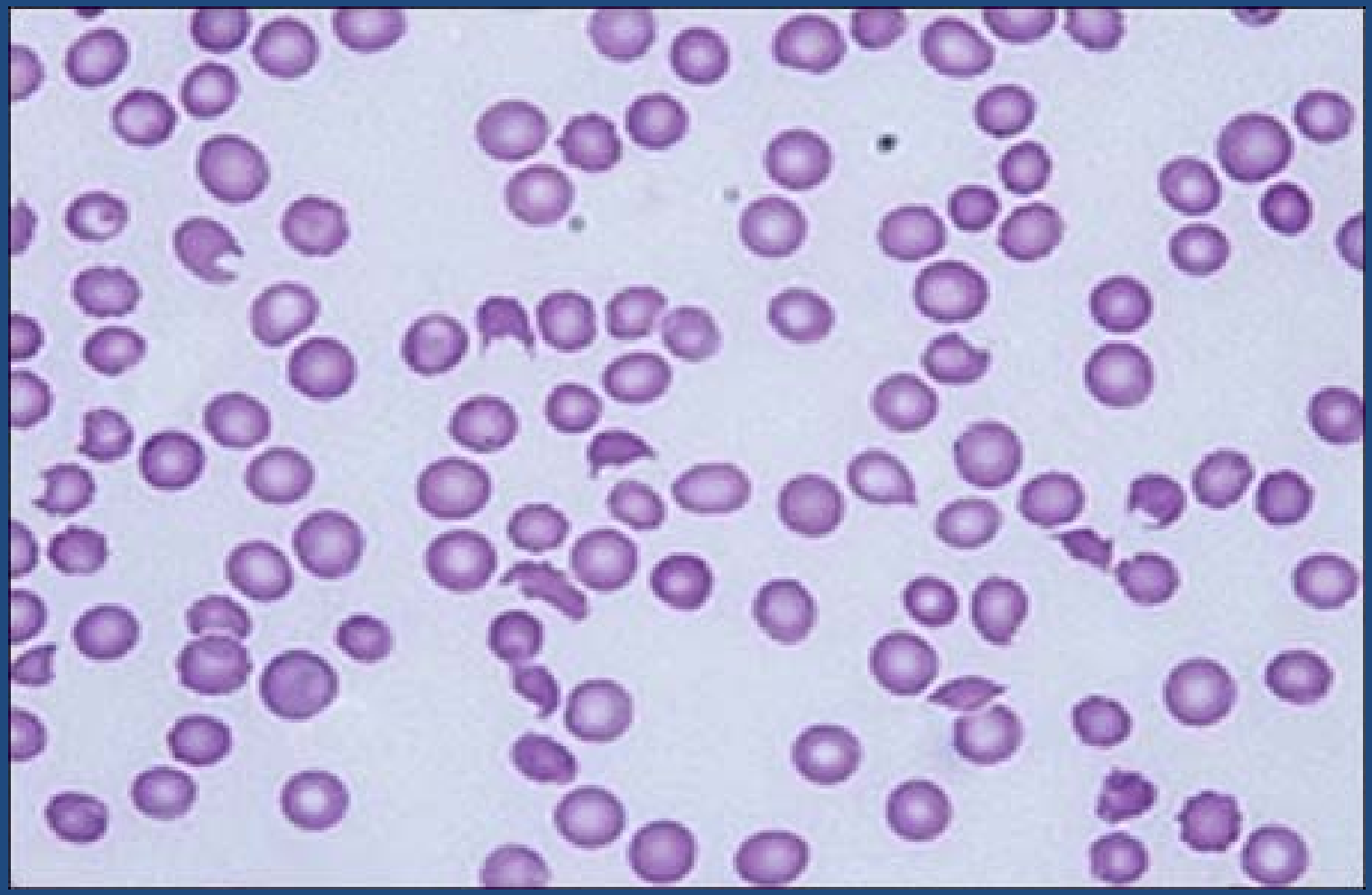
Question 12 (Figure 3)



Question 14 (Figure 4)



Question 17 (Figure 5)



Question 19 (Figure 6.