

Hematology AHD Test Review

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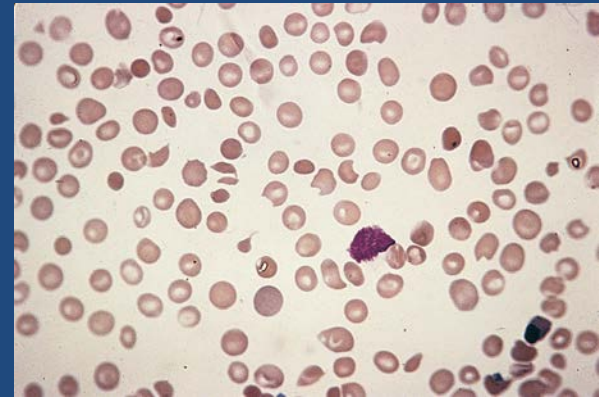
Question 1

- Which of the following is the most appropriate management of this patient's thrombocytopenia?
- A. Emergent delivery
- B. Intravenous immune globulin
- C. Plasma exchange
- D. Prednisone

Manage thrombocytopenia in pregnancy.

Thrombotic Microangiopathy of Pregnancy (spectrum)

1. Pre eclampsia
 - Hypertension
 - Proteinuria
 - Edema
2. Acute Fatty Liver of Pregnancy
3. HELLP
 - Hemolysis
 - Elevated Liver enzymes
 - Low Platelets
4. TTP – consider if low platelets and hemolytic anemia worsen post delivery



Gestational Thrombocytopenia cause of low platelets in 75% of pts.

Platelets >50,000 No schistocytes

Immune Thrombocytopenic Purpura (ITP)

- Normal coagulation studies & no schistocytes
- can treat with IgG during pregnancy
- Want Platelets >50,000 3rd trimester

Question 2

Which of the following is the most appropriate anticoagulation option for this patient?

- A: Apixaban
- B: Dabigatran
- C: Fondaparinux
- D: Rivaroxaban
- E: Warfarin

Point of Question: Treat a patient with VTE who wishes to breastfeed

Helpful Facts:

Pregnancy : **five-fold** increased risk for VTE

- highest risk first 6 weeks postpartum
- **D dimer** always positive in pregnancy so **not predictive**
- Weight based LMW Heparin treatment of choice
- Anticoagulation should be continued for at least **6 weeks postpartum**, for a therapy duration of at least 3 months
- **LMWH and warfarin** are acceptable to take while **breastfeeding** but fondaparinux and the new oral anticoagulants are not

Question 3

Which of the following is the most appropriate management of this patient's anemia?

- A: Bone marrow aspiration
- B: Erythropoiesis-stimulating agent therapy
- C: Oral iron supplementation
- D: Continue current management

Manage inflammatory anemia

Laboratory findings in iron deficiency anemia, thalassemia, and anemia of chronic disease/inflammation

Test	Iron deficiency anemia	Alpha or beta thalassemia	Anemia of chronic disease/inflammation
Complete blood count			
Hemoglobin	Decreased	Decreased	Decreased
Mean corpuscular volume (MCV)	Decreased	Decreased	Normal to decreased
Red cell distribution width (RDW)	Increased	Increased or normal	Normal to increased
Red blood cell count	Decreased	Increased or normal	Decreased
Iron studies			
Serum iron	Decreased	Normal or increased	Decreased
Total iron-binding capacity (TIBC); transferrin	Increased	Normal	Decreased
Transferrin saturation	Decreased	Normal	Decreased
Serum ferritin	Decreased	Normal	Increased
Erythrocyte protoporphyrin*	Increased	Normal or increased	Increased
Soluble transferrin receptor*	Increased	Increased	Normal
Reticulocyte hemoglobin equivalent (Ret-he or CHR)	Decreased	Decreased	Normal
C-reactive protein	Normal	Normal	Increased

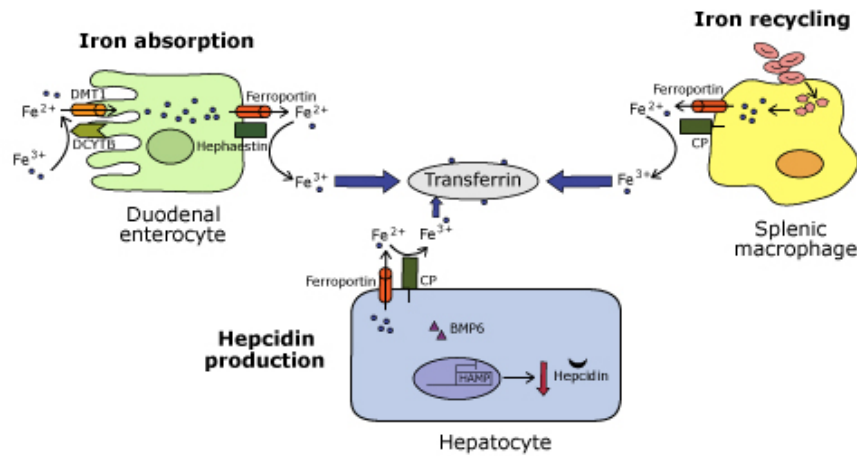
Refer to UpToDate topics on anemia for further details of the evaluation and interpretation. Refer to UpToDate topic on iron deficiency anemia for early changes associated with iron deficiency (before anemia develops).

* Not used in the routine evaluation of anemia.

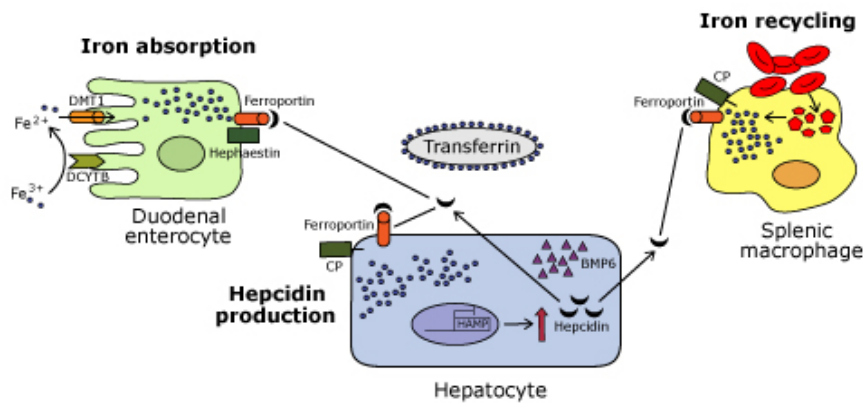
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Key – MCV normal; Serum Iron low; Ferritin >35; TIBC Decreased
 Once Diagnose Inflammatory Anemia – focus on treatment of underlying condition – there is no specific treatment for Inflammatory Anemia

A Iron deficiency



B Iron overload



↑ Inflammation leads to inflammatory cytokines: tumor necrosis factor- α , interleukin (IL)-6, IL-1, and interferon, leads to altered erythropoietin responsiveness
IL-6 causes hepatic synthesis of the small peptide **Hepcidin**, which regulates iron absorption.

Hepcidin

- decreases iron absorption and
- decreases iron release by macrophages

No laboratory test is commercially available for measuring hepcidin levels
Should be low in Iron deficiency and high in Inflammatory anemia

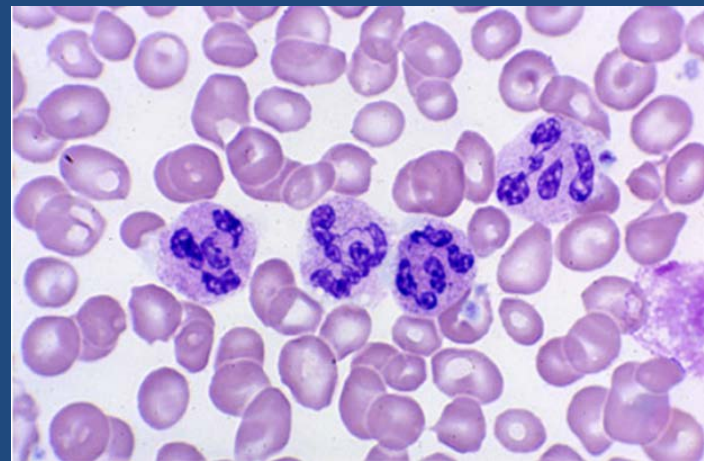
Question 4

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

- A. Bone marrow biopsy
- B. Folate level measurement
- C. Homocysteine level measurement
- 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 methylmalonic acid and Homocysteine level
- 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 \uparrow = B12 def so if suspect Vit B12 check MMA**
 - **Homocysteine only \uparrow = folate def**



Diagnose Cobalamin Deficiency

- Find REASON for B12 deficiency:

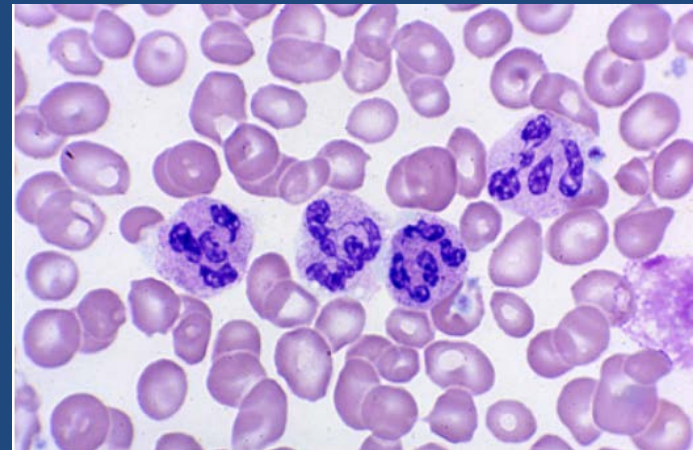
- 3 partner dance:
- Protein + B12 enters stomach → acid
- R Factor + B12 enters duodenum → pancreatic proteases
- Intrinsic factor (IF) + B12 → ileum absorption

- 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 5

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

A: MRI of the cervical, thoracic, and lumbar spine

B: Serum β 2-microglobulin measurement

C: Serum free light chain testing

D: Serum lactate dehydrogenase measurement

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:

Free light chains helpful for prognosis

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

Diagnostic Criteria for Smoldering (Asymptomatic) Myeloma:

(Both must be met)

1. Serum monoclonal protein \geq 3 gm/dL and/or \geq 10% and <60% bone marrow clonal plasma cells
2. NO end organ damage

MGUS

Common

- 3.2% age >50
- 5.3% age >70

Risk factors

1. Non-IgG M protein
2. M protein at least 1.5 g/dl
3. Abnormal Free Light Chain ratio

Risk of Progression to MM over next 20 years is based on number of risk factors

0 = 5%

1 = 21%

2 = 37%

3 = 58%

Question 6

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

A. 1,25-Dihydroxyvitamin D (calcitriol) measurement

B. Intact parathyroid hormone measurement

C. Parathyroid hormone–related protein measurement

D. Serum protein electrophoresis and free light chain test

Diagnose Multiple Myeloma Requiring Therapy

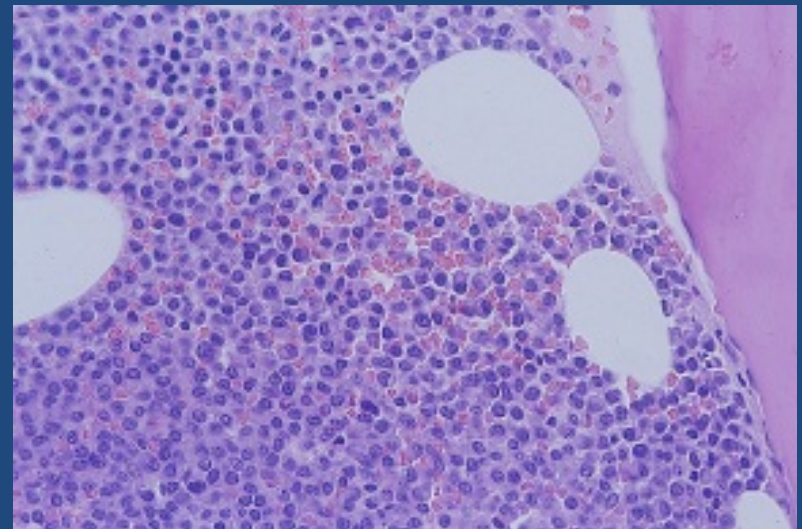
Diagnostic Criteria for Multiple Myeloma

(All 3 must be met):

1. Presence of a serum or urine monoclonal protein
2. Presence of $\geq 10\%$ 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

require therapy: CRAB

- HyperCalcemia
- Renal failure
- Anemia
- Lytic Bone lesions



Question 7

Which of the following is the most appropriate management?

A. Transfuse ABO-matched platelets

B. Transfuse HLA-matched platelets

C. Transfuse washed platelets

D. Observation

Treat platelet transfusion refractoriness

Definition: increase platelet count $<10,000/\mu\text{L}$ after 10- 60mins post transfusion x2

Non-immune causes (this patient doesn't have)


- Sepsis/fever
- DIC
- Splenomegaly
- Meds

Allo-immunization from previous pregnancies

Treat with HLA-matched platelets (ABO matched wont' help, Washed reserved for severe allergic rxn. Goal to get above 10,000)

Question 8

Which of the following is the most appropriate management of this patient's anemia?

- A. Erythrocyte transfusion
 - B. Erythropoiesis-stimulating agent
 - C. Intravenous iron
 - D. Continue current management
- 

Manage anemia in a critically ill hospitalized patient

Thresholds for red blood cell transfusion in adults

Condition	Hgb threshold for transfusion
Symptomatic patient (eg, myocardial ischemia, tachycardia)	10 g/dL ^{*[1,2]}
Hospitalized patient	
Preexisting coronary artery disease	8 g/dL ^{*[2]}
Acute coronary syndromes	8 to 10 g/dL ^{‡[2,3]}
Heart failure	7 to 8 g/dL [‡]
Intensive care unit (hemodynamically stable)	7 g/dL ^{*[4,5]}
Gastrointestinal bleeding (hemodynamically stable)	7 g/dL ^{*[6]}
Non-cardiac surgery	8 g/dL ^{*[1]}
Cardiac surgery	7 to 8 g/dL ^{*[7]}
Ambulatory outpatient	
Oncology patient in treatment	7 to 8 g/dL [‡]
Palliative care setting	As needed for symptoms; hospice benefits may vary

These thresholds are not a substitute for direct assessment of the patient and clinical judgment. Refer to UpToDate topics on red blood cell transfusion and specific clinical settings for further details.

Hgb: hemoglobin.

* Based on results from clinical trial(s).

‡ There are no large clinical trials yet performed in this setting. These recommendations are based on the authors' opinions.

References:

1. Carson JL, Terrin ML, Noveck H, et al. Liberal or restrictive transfusion in high-risk patients after hip surgery. *N Engl J Med* 2011; 365:2453.
2. Carson JL, Brooks MM, Abbott JD, et al. Liberal versus restrictive transfusion thresholds for patients with symptomatic coronary artery disease. *Am Heart J* 2013; 165:964.
3. Cooper HA, Rao SV, Greenberg MD, et al. Conservative versus liberal red cell transfusion in acute myocardial infarction (the CRIT Randomized Pilot Study). *Am J Cardiol* 2011; 108:1108.
4. Hebert PC, Wells G, Blajchman MA, et al. A multicenter, randomized, controlled clinical trial of transfusion requirements in critical care. *Transfusion Requirements in Critical Care Investigators, Canadian Critical Care Trials Group [see comments]. N Engl J Med* 1999; 340:409.

Question 9

Which of the following dietary constituents should this patient be advised to avoid?

A. Calcium supplements

B. Raw or undercooked seafood

C. Red meat

D. Vitamin C-containing fruits and vegetables

Diagnose infectious complications of iron overload syndromes

Organisms with Increased virulence in patients with iron overload: *Vibrio* species (*vulnificus*, *cholerae*)

V. Vulnificus – raw seafood i.e. Oysters

Other organisms with increased virulence:

Escherichia coli

Yersinia enterocolitica

Listeria monocytogenes

Cytomegalovirus

Hepatitis B and C viruses

HIV

Fungi *Aspergillus fumigatus* and *mucor*.

Question 10

Which of the following is the most appropriate treatment?

A. Ascorbic acid

B. Iron chelation therapy

C. Monthly phlebotomy

D. No treatment indicated

Treat a patient with secondary iron overload from β -thalassemia major

After 15 – 20 units of pRBC at risk for iron overload

check Ferritin levels – consider treatment if > 1000 ng/ml & elevated transferrin saturation

Treatment is with Iron chelation therapy –
Deferosirox (oral)

Ascorbic Acid – potential chelator but rapidly mobilizes iron in plasma so can cause iron toxicity – not first line

Question 11

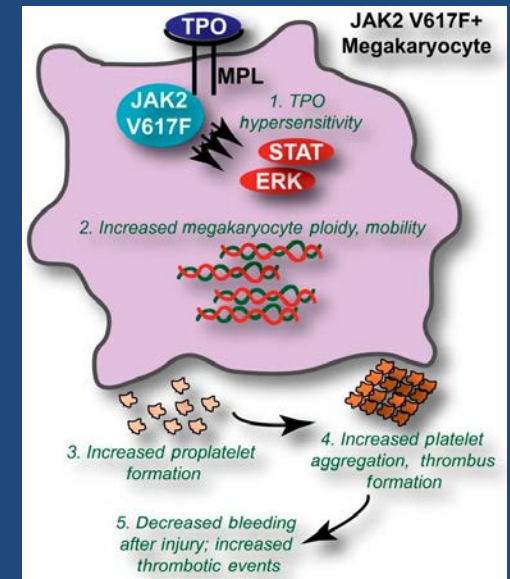
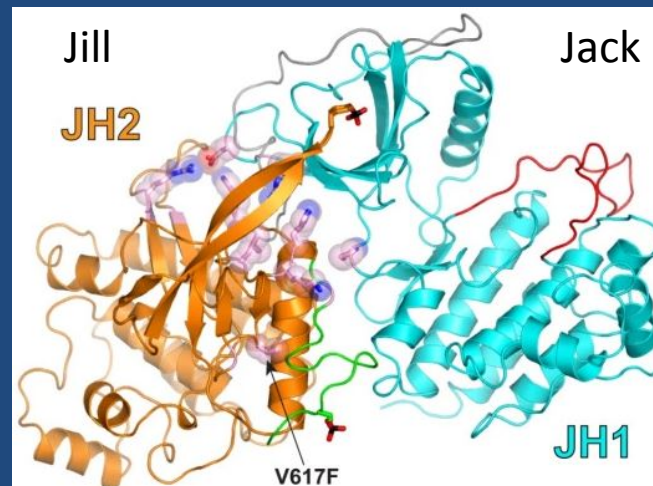
Which of the following diagnostic tests is most likely to explain the cause of this patient's condition?

- A. Antiphospholipid antibody
- B. Factor V Leiden
- C. JAK2 V617F activating mutation
- D. Prothrombin gene mutation (G20210A)

Objective: Diagnose Budd-Chiari syndrome associated with *JAK2 V617F* activating mutation

Why was this the right answer?

- An activating mutation of JAK2 (JAK2 V617F) is present in 97% and 50% of patients diagnosed with PV and ET, respectively
- Also present in 50% of patients with idiopathic portal vein thrombus, especially in women taking oral contraceptive pills
- What is JAK2 and why does V617F mutation promote thrombosis?
...Just Another Kinase?



Were the other answers wrong?

No, but they were less right... “which of the following... is *most likely*...?”

- Antiphospholipid Abs not specific (must be positive on 2 tests 3 months apart) and more commonly associated with DVT/PE, arterial thrombosis, and placental thrombosis
- Factor V Leiden most commonly associated with DVT/PE, rarely cerebral thrombosis and even less frequently associated with portal vein thrombosis
- Prothrombin gene mutation (G20210A) also associated with increased risk for DVT >> splanchnic vein thrombosis

Question 12

Which of the following is the most appropriate treatment?

- A. Anagrelide plus low-dose aspirin
- B. Hydroxyurea plus low-dose aspirin**
- C. Ruxolitinib
- D. Warfarin
- E. Observation

Objective: Treat essential thrombocythemia based on risk stratification

What do you need to know to answer this question?

1. Indications for treatment of Essential Thrombocythemia (based on International Prognostic Score):
 - Age \geq 60 years
 - leukocyte count $> 11,000$
 - No history of thrombosis
2. Type of treatment:
 - Platelet lowering therapy (hydroxyurea superior to anagrelide in RCT)
 - Plateletpheresis is indicated if patient has platelet count $>1,000,000$ and patients are symptomatic (digital ischemia, erythromelalgia, TIA, visual disturbances, bleeding/VTE)
3. Why were other choices incorrect:
 - warfarin has not been studied in primary prophylaxis of ET
 - Ruxolitinib (JAK2 V617F inhibitor) only approved for primary myelofibrosis and only 50% of patients with ET have this mutation

Question 13

Which of the following is the most appropriate next step in the evaluation?

- A. Bone marrow biopsy
- B. Escherichia coli O157:H7 titer measurement
- C. MRI of the brain
- D. Peripheral blood smear

Objective: Evaluate a patient with suspected thrombotic thrombocytopenic purpura

What do you need to know to answer this question?

1. Suspect TTP based on the pentad: thrombocytopenia, microangiopathic hemolytic anemia, neurologic deficits, kidney impairment, and fever
2. Criteria for diagnosis:
 - microangiopathic hemolytic anemia (schistocytes on peripheral blood smear) and increased serum LDH levels
 - thrombocytopenia
 - **ADAMTS13 activity/inhibitor not helpful for initiating therapy**

TEST TIP: If Hematology question gives the option to do a “peripheral blood smear”, better have a very good reason that is NOT the answer

3. Why were the other answers not correct?
 - MRI of the brain could show stroke and E Coli O157:H7 stool study would support, but neither are dx of TTP-HUS
 - Bone marrow bx if pancytopenia or abnormal leukocytes on smear

TEST TIP: If question has you managing an urgent issue, correct response is NOT selecting an exam with long turnaround time

Question 14

Which of the following is the most appropriate next step in management?

- A. Await platelet factor 4 immunoassay before initiating anticoagulation
- B. Await serotonin release assay before initiating anticoagulation
- C. Initiate argatroban**
- D. Initiate heparin
- E. Initiate warfarin

Objective: Manage Heparin-induced Thrombocytopenia

What do you need to know to answer this question?

1. Heparin is used during CABG (tricky MKSAP)!
2. How do you determine pretest probability of HIT? ... 4T score
 - Degree of Thrombocytopenia? (30-50%=1pt, >50%=2 pts)
 - Timing of thrombocytopenia (5-10 days or ≤ 1 day if prior heparin exposure ≤ 30 days)
 - Thromboses
 - Not Thinking other etiology?

MD calc: [4T score](#)

3. If high pretest probability of HIT, treat immediately!

TEST TIP: If question has you managing an urgent issue, correct response is probably not to “await ...dx test”

4. Appropriate tx of HIT: stop heparin, tx with nonheparin AC... but not warfarin due to delayed AC onset and risk of warfarin skin necrosis

EXTRA TIP: If pt does not have clot, AC until platelets $\geq 150,000$

Question 15

Which of the following is the most appropriate management??

- A. Continue anticoagulation indefinitely
- B. Discontinue warfarin in another 3 months
- C. Discontinue warfarin now
- D. Discontinue warfarin and perform thrombophilia testing

Objective: Determine duration of anticoagulation in a patient with venous thromboembolism.

Why was this the correct answer and for which patients would the other answers be correct?

1. Patients who should receive indefinite anticoagulation:
 - unprovoked proximal DVT
 - recurrent DVT
 - provoked with persistent, irreversible, or multiple risk factors
 - ... and low bleeding risk
2. When should patients be treated with only 3 months of AC (C)?
 - provoked DVT with major transient risk factor (e.g., trauma, surgery, or recent immobilization)
3. Which patients should receive 6-12 months of AC (B)
 - persistent risk factor or unresolved provoking event (e.g., immobilized patient undergoing physical therapy)
 - Cancer is a special case: AC until cancer is cured
4. Which patients should be tested for thrombophilia (D)? ...Grade 2C
 - Patients with minor risk factors for provoked DVT (e.g., travel)
 - Patient with provoked DVT and family history of DVT <45 y/o

Question 16

In addition to withholding warfarin, which of the following is the most appropriate management of this patient's anticoagulation?

- A. 4-Factor prothrombin complex concentrate
- B. Fresh frozen plasma
- C. Oral vitamin K
- D. No additional therapy

Objective: Manage a supratherapeutic INR in a patient receiving vitamin K antagonist therapy

Recommended management of a suprathreshold INR

INR	Bleeding present	Recommended action*
>Ther to 5.0	No	Lower warfarin dose, or
		Omit a dose and resume warfarin at a lower dose when INR is in therapeutic range, or
		No dose reduction needed if INR is minimally suprathreshold
>5.0 to 9.0	No	Omit the next one to two doses of warfarin, monitor INR more frequently, and resume treatment at a lower dose when INR is in therapeutic range, or
		Omit a dose and administer 1 to 2.5 mg oral vitamin K*
>9.0	No	Hold warfarin and administer 2.5 to 5 mg oral vitamin K1. Monitor INR more frequently and administer more vitamin K1 as needed. Resume warfarin at a lower dose when INR is in therapeutic range.
Any	Serious or life-threatening	Hold warfarin and administer 10 mg vitamin K by slow IV infusion; supplement with four-factor prothrombin complex concentrate (4-factor PCC) or fresh frozen plasma, depending on clinical urgency. Monitor and repeat as needed.

*Consider in patients at increased risk for bleeding (eg, history of bleeding, stroke, renal insufficiency, anemia, hypertension)

Retrospective study found the following predicted suprathreshold INR two days after stopping warfarin:

- Older age (odds ratio [OR] 1.2 per decade of life)
- Higher index INR (OR 1.25 per unit of elevation)
- Lower warfarin maintenance dose (OR 0.87 per 10 mg increase in total weekly dose)
- Decompensated heart failure (OR 2.79; 95% CI 1.30-5.98)
- Active cancer (OR 2.48; 95% CI 1.11-5.57)

Question 17

Which of the following is the most likely cause of the patient's coagulation abnormality?

- A. Disseminated intravascular coagulation
- B. Liver failure**
- C. Vitamin K deficiency
- D. Warfarin overdose

Objective: Diagnose coagulopathy of liver disease

What do you need to know to answer this question?

1. This patient is presenting with sepsis likely 2/2 PNA and (suspicious) self-medication with tylenol q2-3 h X 7 days (?!!)

2. How do you distinguish between **DIC** and **liver disease**?

Factor VIII ...Why?

- Consumed in DIC (like other coagulation factors)
- Produced by endothelial cells (not hepatocytes)
- Cleared by the liver
- So overall, high in liver disease and low in DIC

Not helpful: **fibrinogen** (consumed in DIC, underproduced in liver disease) and **D-dimer** (elevated in DIC, not cleared in liver disease)

3. What about vitamin K deficiency and warfarin toxicity?

Factor V would **NOT** be **low** in either context

Question 18

Which of the following is the most likely diagnosis?

- A. Acquired hemophilia
- B. Factor XI deficiency
- C. Lupus inhibitor
- D. Occult liver disease

Objective: diagnose acquired hemophilia

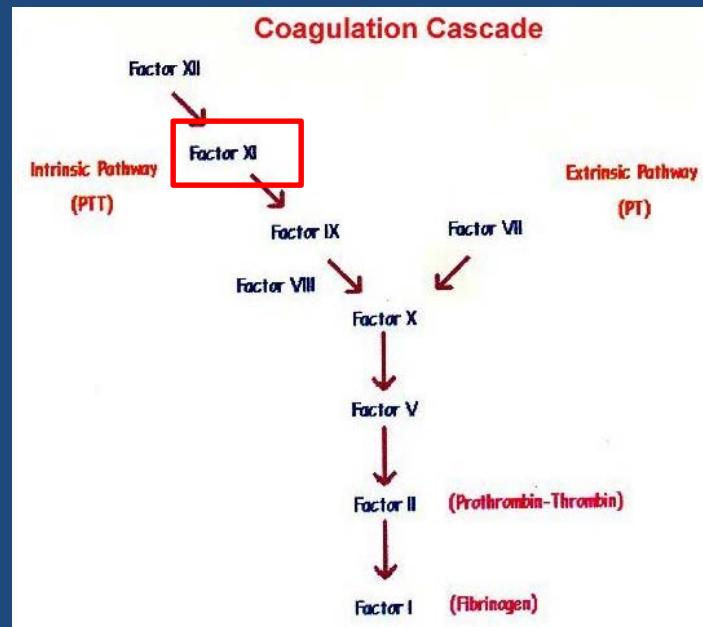
How to approach? Eliminate one by one...

1. The clinical presentation is consistent with a bleeding disorder (hematuria, bruising, nosebleed)
Eliminate: Lupus inhibitor (C) associated with increased V/ATE
2. PT is not prolonged (hematology not my strength, but I trained at BUMCP)
Eliminate: Liver disease (D)
3. You're left with 2 choices: acquired hemophilia and Factor XI deficiency...

How to approach? Eliminate one by one (continued)

4. Factor XI is a **red herring**:

- Occurs in patients of Ashkenazi Jewish descent
- Heterogenous bleeding manifestations (might manifest early to late life)
- aPTT would be prolonged but corrects with mixing



5. Didn't this study correct with mixing?

No, normal aPTT is 25-35 s (tricky MKSAP)correct answer is acquired thrombophilia (typically FVIII inhibitor in the elderly)

Question 19

Which of the following is the most likely diagnosis?

- A. Diffuse large B-cell lymphoma
- B. Follicular lymphoma
- C. Hodgkin lymphoma
- D. Mantle cell lymphoma

Objective: Diagnose mantle cell lymphoma

What do you need to know to answer this question?

1. MCL is comprised of small monoclonal lymphoid cells that are CD20+ (B-cell marker)... can **eliminate (A)**
2. MCL is associated with the chromosomal translocation [t(11:14)], which results in overexpression of cyclin D1

Why?

- Ig heavy chain expression
- Increased

↑ cyclin D1

→ S)

with LAD, B symptoms and (in blood stream)

3. 85% of cases sites of diffuse



Question 20

Which of the following is the most appropriate management?

- A. Cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP)
- B. Psoralen plus ultraviolet A (PUVA) therapy
- C. Topical glucocorticoids
- D. Rituximab

Objective: Treat a patient with stage I mycosis fungoides

What do you need to know to answer this question?

1. What you don't need to know:



This is mycosis fungoides,
i.e., mushroom rash

2. Staging:

- Early disease (stage I and II): skin +/- LN involvement (no significant involvement of blood, no organ involvement)
- Advanced disease: significant blood involvement and organ involvement

3. Treatment based on staging:

- Early disease (stage I and II): topical glucocorticoids → add retinoids and PUVA
- Advanced disease: external beam radiation, CHOP, alemtuzumab (CD52 Ab)

Why not rituximab?