

UC San Diego

Independent Study Projects

Title

Enhancement of Team-Based Learning (TBL) Modules for the Hematology Curriculum

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PROJECT SUMMARY

Independent Study Project
University of California, San Diego
School of Medicine

Title

Enhancement of Team-Based Learning (TBL) Modules for the Hematology Curriculum

Category

Medical Education

Rationale

Hematology is a broad topic that is only visited near the end of the first year of medical school at the University of California San Diego (UCSD). Students are scheduled to learn about numerous topics: hematopoiesis, the role of the different blood cell lineages, the physiology of blood, the coagulation cascade and thrombosis, and the importance and interpretation of lab tests. In the same course, students are also responsible for learning about the pathophysiology, treatment, and management of various genetic and acquired anemias, bleeding and clotting disorders, leukemias and lymphomas, and adverse reactions to blood transfusions.

The Hematology course is also the first largely clinically-based curriculum, with most of the knowledge achieved through small group case discussions and team-based learning (TBL) sessions. Team-based learning encourages participation in small groups, which better simulates a clinical encounter and allows the students to implement their critical reasoning skills and make decisions as a team on how to work up and manage the patient presented in the case.

In addition, Pediatrics is a core clinical rotation that is not explored in the first two years of the medical school curriculum. However, when students begin their third year rotation, they are expected to manage pediatric patients with hematologic problems, but the clinical course of certain hematologic conditions in children is not the same as in adults. There are clinical pearls in pediatric hematology that can provide some exposure to management and help prepare students prior to starting their pediatric rotation. For this reason, it is also relevant to learn about pediatric management of common hematologic problems.

Due to the short duration of this course, it is crucial that the information is presented in a high-yield format. This project enhances the team-based learning modules through the emphasis of profession-specific skills by allowing medical students to exercise their clinical reasoning to establish a differential diagnosis and treatment plan, and pharmacy students to contribute their knowledge about therapeutics to solve the cases. Alternate forms of multimedia will be introduced to maximize the learning offered in this course. Finally, the project also allows for the creation of pediatric cases to demonstrate differences in identification and treatment of hematologic diseases.

Project Objectives

Objectives of this project include:

- Analyze current TBL cases and identify concepts that would benefit from alternative summarization techniques
- Optimize team collaboration for learning by adding profession-specific questions throughout the cases
- Add cases relevant to the current modules to include pediatric management of hematologic disease.
- Incorporate alternate forms of multimedia to help emphasize important concepts and increase the quality of the TBLs.

Methods

The student:

1. Reviewed the current TBLs and identified topics and concepts that would benefit from additional summarization techniques.
2. Met with the course director to discuss the desired changes to be implemented.
3. Identified common hematologic pathologies highlighted in the course and structured cases to illustrate differences between pediatric and adult diagnosis and management of disease.
4. Wrote specific questions to utilize the profession-specific skills of medical and pharmacy students and engage collaboration between the team members.
5. Incorporated new forms of multimedia, including videos and the presentation software Prezi to provide alternative ways of mastering the material.
6. Obtained feedback from the ISP chair and committee members on the current and proposed cases for accuracy and presentation and incorporated their suggestions to optimize the learning from the TBL experiences.
7. Reviewed each module created for accuracy and interpretation.

Achievements

The student identified case topics that benefited from the profession-specific contribution and crafted questions to encourage pre-clinical students to share their expertise on skills they are honing throughout their training. The student created new cases to demonstrate the difference in treating children. The student also acknowledged difficult concepts presented throughout the course and designed summary presentations and visual complements on Prezi to help the students understand the subject matter.

PEDIATRIC HEMATOLOGY

****LEARNING OBJECTIVES****

By the end of this case, students should be able to:

- Identify risk factors for thrombosis
- Know classes and target sites of anticoagulation medications
- Be aware of medication interactions and effect on anticoagulation
- List anticoagulation monitoring methods

CASE 1 – AN INCIDENTAL FINDING

20 yo F with uncontrolled Type 1 Diabetes admitted to Pediatric ICU for severe diabetic ketoacidosis (DKA) secondary to pancreatitis

- Abdominal pain
- Prior hx of pancreatitis so CT abdomen/pelvis ordered to assess severity of illness, but revealed a **right lower lobe pulmonary embolus**
- ROS: Denies shortness of breath, chest pain, dyspnea on exertion, upper/lower extremity pain or swelling.
 - With her IVDU, she states her veins would "blow up" with thickened blood of coffee ground consistency
- Medications:
 - Insulin
 - Combined Oral Contraceptive (OCP)
 - 7-day course of Metronidazole for bacterial vaginosis

CASE 1 HISTORY (CONT.)

■ Past Medical Hx:

- DM1
- 1 miscarriage at age 18

■ SocHx:

- Current smoker 1ppd for past 3 yrs
- Meth IV drug use past 1.5 yrs

■ FamHx:

- (+) for miscarriage in maternal aunt and possibly in mother
- HTN in multiple family members on maternal and paternal sides
- Unaware of DVT/PE, early MI/stroke, breast ca

WHICH OF THE FOLLOWING THROMBOEMBOLIC RISK FACTORS ARE PRESENT IN THIS PATIENT?

■ Thromboembolic risk factors

- Prior history of VTE
- Family history of blood clots
- Hx of miscarriages
- Smoking
- Atrial fibrillation
- Liver disease
- Use of combined oral contraceptives
- IV drug use
- HTN
- Breast cancer and other malignancies

WHICH OF THE FOLLOWING THROMBOEMBOLIC RISK FACTORS ARE PRESENT IN THIS PATIENT?

■ Thromboembolic risk factors

- Prior history of VTE
- Family history of blood clots
- **Hx of miscarriages**
- **Smoking**
- Atrial fibrillation
- Liver disease (depends on extent of liver damage)
 - This can be a clotting risk (if Protein C and S aren't being made) or bleeding risk (if clotting factors are not being produced)
- **Use of combined oral contraceptives**
- **IV drug use**
- HTN
- Breast cancer and other malignancies

PHYSICAL EXAM

- **Vitals:** T 37.1, HR 88, BP 122/82, RR 20, SpO2 100%
- **General:** Awake, alert, no acute distress.
- **Respiratory:** Clear to auscultation, good air exchange, no wheezes, rales, or rhonchi.
- **Cardiovascular:** Regular rate and rhythm, no murmurs, gallops, or rubs, 2+ pulses bilateral upper and lower extremities, No clubbing, cyanosis, or edema.
- **Gastrointestinal:** Soft, non-tender, non-distended, normoactive bowel sounds, no hepatosplenomegaly or mass, 2cm subcutaneous nodule at RLQ insulin injection site. Bruising on LLQ insulin injection site.
- **Skin:** Warm, Dry, Pink, Numerous healing scars from drug injection sites on bilateral forearms, Mobile subcutaneous nodules on right dorsal and lateral forearm, Tattoos on left arm and across upper chest at collarbone, No bruising on upper and lower extremities, No petechiae.

LABS & IMAGING

- CBC: WBC 5.5, Hgb 10.5 (MCV 78 fL), Plt 273
 - Iron Panel: Fe Level 35 mCg/dL(Low), Fe Sat 9%(Low), TIBC 399 mCg/dL Ferritin 14.7 ng.mL
- Basic Metabolic Panel: Na 135, K 4.2, Cl 100, CO2 27, BUN 17, Cr 0.4, Gluc 234
- Amylase 207 (High), Lipase 5,289 (High)
- Urinalysis: Gluc 500, Ketones 5, Protein/LeukEsterase/Nitrites Neg

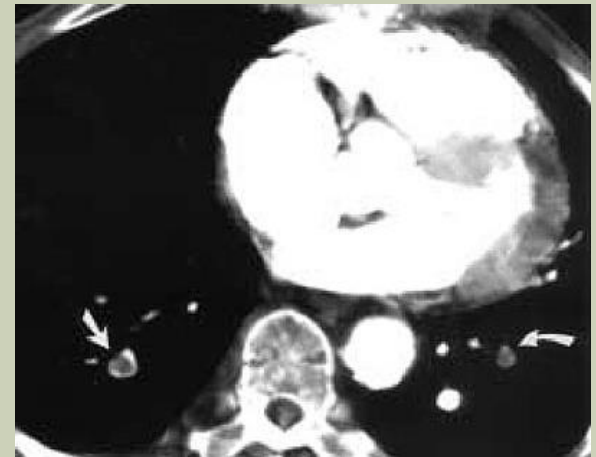
LABS & IMAGING (CONT.)

IMAGING

- Bilat Lower Extremity U/S: No evidence of lower extremity DVT
- CT Angiogram: Small embolus on posterior basal segment of right lower lobe, confirming finding from CT

THROMBOSIS WORKUP LABS

- Homocysteine 5.5 $\mu\text{Mol/L}$ (normal)
 - Fibrinogen 372 mg/dL (normal)
 - D-dimer 0.71 mcG/mL (High)
 - Antithrombin III (AT3) 139% (High)
-
- Baseline PT/INR 11.4 sec/0.85, PTT 24.3 sec



BACK TO OUR PATIENT... SHOULD WE ANTICOAGULATE?

- Thrombus was incidentally found on abdominal CT which was ordered for pancreatitis; what should we do with the information?
 1. What information from the hx is helpful to make your decision?
 2. What options are available for anticoagulation?

ANSWERS

1. Risk factors: current smoker, previous miscarriage, thickened blood with coffee-ground consistency
 2. Warfarin (Coumadin), Enoxaparin (Lovenox), Direct thrombin inhibitor (Dabigatran, Lepirudin)
- Based on results of the CT chest and information from the hx (risk factors) listed above, patient should be started on anticoagulation
 - Patient was given the option between warfarin and Lovenox (since she is a Type I diabetic and already knows how to inject subcutaneous insulin). Patient prefers oral medication so she was started on warfarin w/ Lovenox bridging while awaiting therapeutic levels of warfarin (goal INR 2-3)

BUT WAIT...

- Pharmacist on inpatient service reviewed patient's medication list, which includes the following:
 - Insulin
 - OCP
 - Metronidazole for bacterial vaginosis

- 3. Which medications, if any, will affect anticoagulation?
 - **Please consult your pharmacist to discuss possible interactions and necessary modifications to plan**

MEDICATION INTERACTIONS DILEMMA

3. Which medications, if any, will affect anticoagulation?
 - Oral contraceptives
 - Metronidazole

MEDICATION DOSING DILEMMA

4. Will the patient's Warfarin dose have to be:

- a) Increased
- b) Decreased
- c) Remain the same

■ Pharmacy students: Please consult your references to determine proper dosage

MEDICATION DOSING ANSWER

4. Will the patient's Warfarin dose have to be:

■ **(b) Decreased temporarily**

- Pt is taking metronidazole which raises INR and increases bleeding risk

■ **(a) Increased**

- Pt is on birth control, which makes Warfarin less effective and can increase clotting risk, however, now that pt has been diagnosed w/PE (an absolute contraindication to combined OCPs), it is **highly recommended** to switch birth control method

WARFARIN DRUG-DRUG INTERACTIONS

■ Raise INR (bleeding risk):

- Fluconazole ("-azole" antifungals)
- Trimethoprim-Sulfamethoxazole (antibiotic)
- Metronidazole (antibiotic/antiprotozoal)
- Amiodarone (anti-arrhythmic)

■ Lower INR (clotting risk):

- Combined OCPs
- Antibiotics (Rifampin, Dicloxacillin)
- Antiepileptics (Phenobarbital, Carbamazepine)
- Bosentan (endothelin R antag for pulm HTN)

MEDICATION MONITORING

5. Consider different monitoring techniques or dosing regimen.
 - How should pt be monitored?

MEDICATION MONITORING ANSWER

5. Monitoring Techniques:

- **Anti-Xa levels** until patient is in therapeutic range (0.5-1.0), especially if wants to continue on Lovenox
 - Must be drawn 4 hours after dose (not sooner!)
- **Baseline INR** drawn when patient starts warfarin to aid in titrating the medication
- **Coumadin Clinic: INR checks**
 - First outpatient check after 3 doses of medication
 - Usually medication is prescribed for dinnertime so when patient goes to Coumadin clinic the next morning and gets INR level, medication can be adjusted before next dose later that evening
 - Once patient is in therapeutic range for INR (usually 2-3), Lovenox can be discontinued after 7-10 days

MEDICATION MONITORING (CONT.)

- Patient would also need to follow up in outpatient Hematology clinic to obtain results of pending thrombotic workup labs:
 - Protein C and S activity levels and antigens
 - Factor VIII activity
 - Antiphospholipid Ab, Anticardiolipin Ab
 - Lupus anticoagulant
 - Factor V Leiden
 - Prothrombin mutation

****LEARNING OBJECTIVES****

By the end of this case, students should be able to:

- Know signs and symptoms of iron deficiency anemia
- Be able to correlate blood smear findings with type of anemia
- Be able to identify whether need for transfusion is present

CASE 2 – WELL CHILD CHECK

18mo previously healthy full-term girl who was at PCP for well-child visit.

- Mom noted she has been picking at strings and fibers off of fabrics and loose strands of hair for the past 2 months and threads and hair have been found in the stool
- ROS: dry cough still present from viral illness 2 weeks ago. Parents deny any fevers, hematemesis, melena, hematochezia, SOB. Activity level unchanged.

HISTORY (CONT.)

- Diet: cow's milk 9oz 4-5x/day, 1 cup juice, variety of fruits, some veggies, oatmeal, dry cereal, bread/pasta, yogurt, occasional chicken/turkey/ham
 - NOTE: Normal milk intake for toddler ~16oz/day
- FamHx:
 - Iron deficiency anemia in maternal grandmother and older sister as toddler.
 - No hx of thalassemia or sickle cell anemia. Both parents from Mexico.
- Spot Hgb at PCP: 6.6, but at visit 6 months prior was 11.6

PHYSICAL EXAM

- **Vitals:** T 36.9, HR 145 (*high even for toddler*), BP 121/70, RR 22, SpO2 100%
- **General:** Awake, alert, interactive, no acute distress, Slightly pale. Well nourished.
- **HEENT:** Mild conjunctival pallor. Moist mucous membranes, no erythema, no exudate.
- **Neck:** Supple, no lymphadenopathy.
- **Respiratory:** Clear to auscultation, good air exchange, no wheezes, rales, or rhonchi.
- **Cardiovascular:** RRR, no murmur appreciated, Cap refill = 2 sec.
- **Gastrointestinal:** Soft, non-tender, non-distended, normoactive bowel sounds, no hepatosplenomegaly or mass.
- **Integumentary:** Warm, Dry, Pale.

QUESTIONS

1. What parts of the history and physical exam stand out?

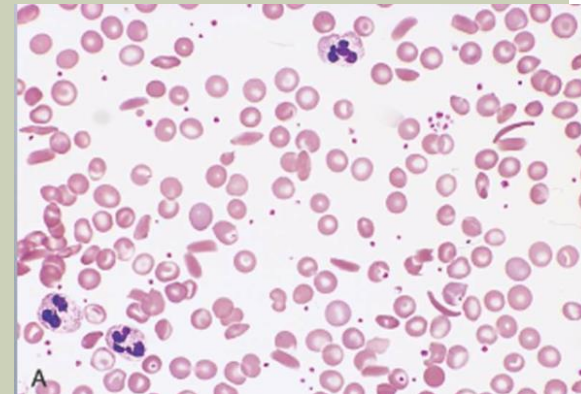
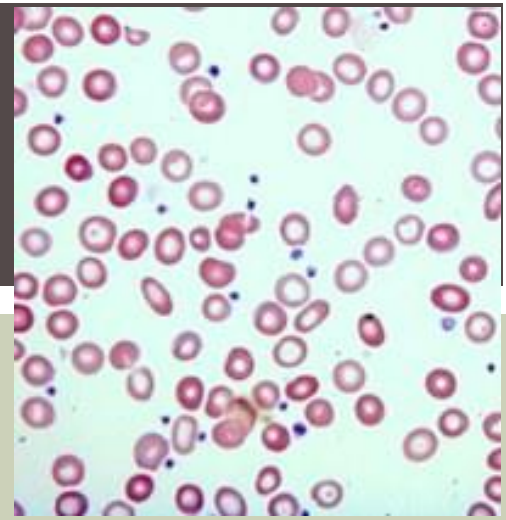
ANSWERS

1. Findings on history:

- Pica (appetite for non-nutritive substances, i.e. ice, dirt, clay, fibers, paint)
- High milk intake, little iron in diet
- Pallorous on exam (skin, conjunctiva)
- Family hx of anemia

LABS

- WBC 22.8, Hgb 6.7, Plt 292
 - MCV 46 (ref 80-95), MCHC 24.1, RDW 21.2%
 - LDH 641 (ref 160-370 U/L)
 - PT 14.4, PTT 27.4
2. What abnormal features can you identify on the following smear(s)?
 3. What other labs would you order to classify this anemia?
 4. How can you explain the elevated WBCs?



ANSWERS

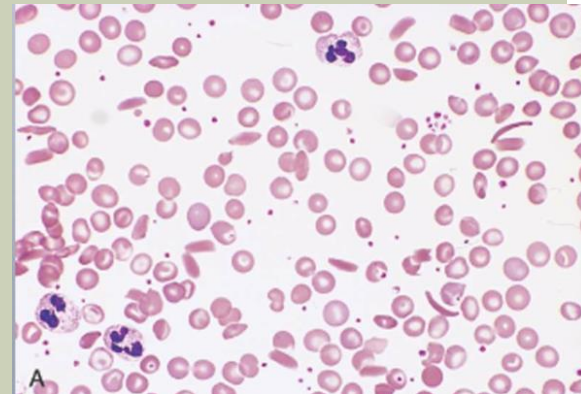
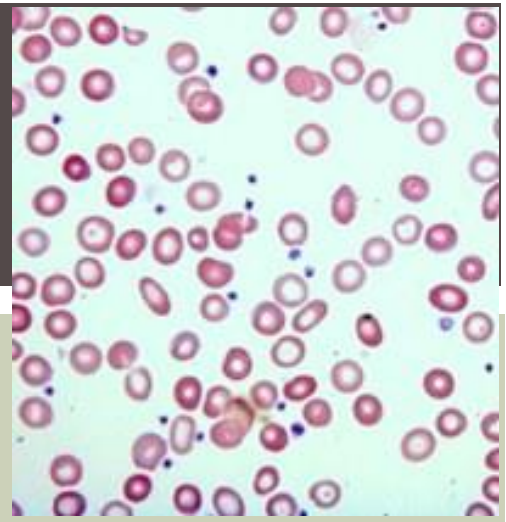
2. Anisocytosis, hypochromasia (central pallor), microcytosis (MCV 46)
3. Retic count 2.6% (HI)
Iron panel: Iron level <10 mcG/dL (Low), TIBC 526 (HI), Iron Sat <2% (Low), Ferritin 2.4 ng/mL (Low)
Total bilirubin 0.5, Direct bilirubin 0 (if indirect is high, can be due to hemolytic anemia)
Blood Type and Screen (in case there's the need for transfusion): O positive, negative Ab screen
4. Leukocytosis could be due to recent infection or hyperactive bone marrow due to lack of adequate erythropoiesis. Not concerning due to normal morphology on smear and has no signs of infection (fever, congestion, lymphadenopathy)

TRANSFUSE?

5. Should we transfuse?

a) Yes

b) No



ANSWERS

5. Should we transfuse?

a) Yes

b) No, pt is asymptomatic

- She continues to be an active toddler.
- She has severe iron deficiency anemia (based on results from iron panel – low iron stores, low Fe saturation, low ferritin, high TIBC, RDW >20%) so we will start iron supplementation (6mg/kg/day) to take with orange juice
- Encourage diet modification (decreasing milk intake to <16oz/day, adding high-iron foods)

****LEARNING OBJECTIVES****

By the end of this case, students should be able to:

- Identify risk factors for thrombosis
- Be able to suggest inpatient and outpatient management options of deep venous thrombosis (DVT)/venous thromboembolism (VTE)
- Be able to determine duration of anticoagulation therapy
- Become aware of lab tests ordered for thrombophilia and how an acute thrombus or anticoagulation therapy can effect the lab results

CASE 3 – CALF PAIN AND SWELLING

16 yo M with ADHD presented with 3 days of L popliteal/upper calf pain and swelling

- Denies recent trauma, although recalls an ankle sprain while skateboarding 1 month ago. No chest pain or SOB. No recent airplane travel or long road trips
- Past Medical Hx: ADHD
- FamHx: Pt is adopted; no contact with biological family to obtain bleeding/clotting history

PHYSICAL EXAM

- **Vitals:** T 36.9 deg C, HR 79, RR 19, BP 110/63, SpO2 97%
- **General:** Awake, alert, no acute distress.
- **Respiratory:** Clear to auscultation, good air exchange, no wheezes, rales, or rhonchi.
- **Cardiovascular:** Regular rate and rhythm, no murmurs, gallops, or rubs, 2+ pulses bilateral upper and lower extremities, Capillary refill < 2 seconds.
- **Musculoskeletal:** Normal range of motion, Normal strength, Increased swelling and TTP of left popliteal region and calf.
- **Integumentary:** Warm, Dry, Pink, No rash, No petechiae, No bruising.

QUESTIONS

1. What predisposing factors does this patient have to developing a blood clot?
2. What imaging/tests would you like to order?

ANSWERS

1. Predisposing factors:

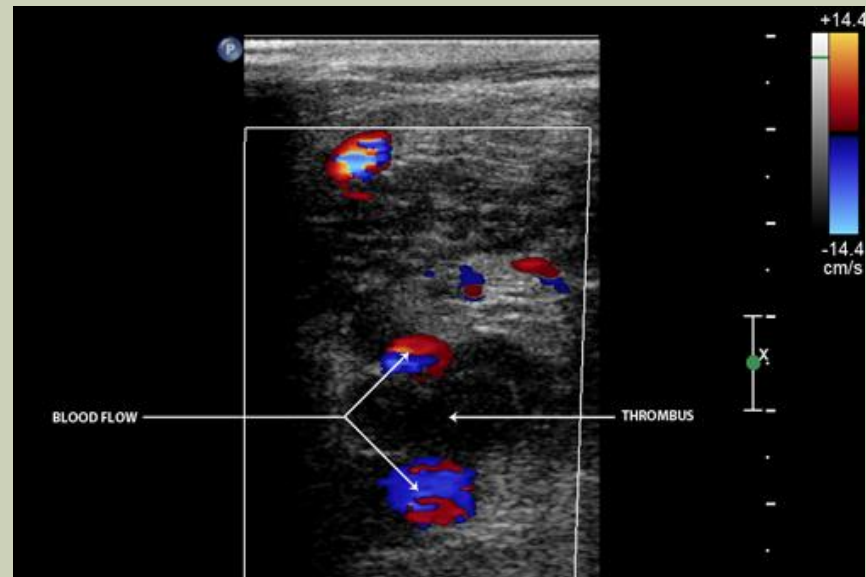
- Recent ankle sprain (but it was about 1 month ago, so very unlikely to have contributed to his current complaint)
- Unknown if there's a family hx of blood clots

2. Labs/Imaging to Order:

- *Baseline coagulation panel (PT/INR, PTT)
- *Imaging: LLE Venous Doppler U/S
- *D-dimer (but this will likely be elevated due to the acute thrombus and will not be clinically useful for management)
- *Thrombotic workup labs to follow-up
- If clinical suspicion for DVT is low and D-dimer is low, no Bilat LE U/S needed because DVT not suspected.
- If D-dimer is positive but there is a suspicion for thrombus, it is insignificant to rule out thrombus

LABS/IMAGING

- Baseline coags – normal PT/INR, PTT
- D-dimer: 3.85 mcG/mL (elevated due to acute thrombus)
- LLE Venous Doppler U/S: noncompressible occlusive thrombus of distal superficial femoral and popliteal veins



MANAGEMENT OPTIONS

■ Inpatient Management Options:

- Thrombectomy (IR procedure, depends if staff available to perform and site of thrombus)
- Thrombolysis via tPA drip (tissue plasminogen activator)
 - Local infusion to thrombus site, rapid breakdown of acute clot; follow with anticoagulation for duration of therapy of 3-6 months
- Anticoagulation w/Heparin drip (goal PTT 60-85 sec)

■ Outpatient Management Options:

- Warfarin w/Lovenox bridging -> therapeutic goal INR 2-3
- Lovenox -> monitor via Anti-Xa level (goal 0.5-1.0), but once therapeutic, usually monitoring not as frequent as warfarin

HOSPITAL COURSE

- Catheter and sheath in place for TPA infusion followed by IR thrombectomy
 - Heparin drip (15units/kg/hr) and TPA drip (0.5mg/kg/hr) resumed post-procedure
 - Heparin titrated for goal PTT 60-85sec
- Heparin discontinued -> Transitioned to Warfarin with Lovenox bridging until therapeutic (INR 2-3)
- Patient discharged with follow-up in Coumadin Clinic

TREATMENT DURATION

3. How long would you recommend treatment for?

- a) 3 months
- b) 6 months
- c) Indefinitely

TREATMENT DURATION ANSWER

3. How long would you recommend treatment for?

- a) 3 months**
- b) 6 months
- c) Indefinitely

This first episode appears to be an unprovoked thrombus, therefore at least 3 months of anticoagulation

PROVOKED VS UNPROVOKED DVTS

- Provoked = risk factor (either inherited or acquired) that leads to DVT
 - Tx: usu at least 6mo of anticoagulation
- Unprovoked = no risk factor identified as cause for DVT
 - Tx: usu at least 3mo of anticoagulation
- Indefinite anticoagulation if high risk of recurrent VTEs
 - Active malignancy
 - Antiphospholipid syndrome
 - High-risk thrombophilia (congenital ATIII deficiency)

Risk factors for developing DVTS

Inherited thrombophilia

Factor V Leiden mutation
Prothrombin gene mutation
Protein S deficiency
Protein C deficiency
Antithrombin (AT) deficiency
Rare disorders
Dysfibrinogenemia

Acquired disorders

Malignancy
Presence of a central venous catheter
Surgery, especially orthopedic
Trauma
Pregnancy
Oral contraceptives
Hormone replacement therapy
Tamoxifen, Thalidomide, Lenalidomide
Immobilization
Congestive failure
Antiphospholipid antibody syndrome
Myeloproliferative disorders
Polycythemia vera
Essential thrombocythemia
Paroxysmal nocturnal hemoglobinuria
Inflammatory bowel disease
Nephrotic syndrome

Rate of venous thromboembolism (VTE) recurrence

VTE type	First year	Annual rate after first year
First episode of unprovoked VTE	10 percent	5 percent
Second episode of unprovoked VTE	15 percent	7.5 percent
First VTE provoked by surgery	1 percent	0.5 percent
First VTE provoked by non-surgical factor	5 percent	2.5 percent

Data from: Kearon C, Akl EA, Comerota AJ, et al. Antithrombotic therapy for VTE disease: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest 2012; 141:e419S.

THROMBOTIC WORKUP LABS

- Protein C and S activity levels and antigens
- Factor VIII activity
- Antiphospholipid Ab, Anticardiolipin Ab
- Lupus anticoagulant
- Factor V Leiden
- Prothrombin mutation

4. This patient's Protein C and S activity levels were low; does this mean the patient has an inherited thrombophilia?

- a) Yes
- b) No

ANSWERS

4. This patient's Protein C and S activity levels were low; does this mean the patient has an inherited thrombophilia?
- a) Yes
 - b) No
- No, these proteins can be lowered in acute thrombosis due to rapid consumption to breakdown the clot, so these labs should be repeated after anticoagulation treatment has completed (in 3-6 mo)

Clinical settings that 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 ^Δ
Protein S (deficiency)	Can be lowered*	NC	Cannot measure ^Δ
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			

Thrombotic Workup Labs

Lab values in thrombophilia workup that can be affected by acute thrombus or anticoag therapy → values might not be reflective of true thrombophilia and would need to be reordered after treatment is completed

*Results can be affected by acute thrombosis; most cost-effective to avoid testing during initial presentation

^ΔIt is important to measure for these deficiencies while the pt is still anticoagulated with LMWH and not on warfarin for at least 2 weeks