Mechanisms of Human Disease
Small Group Sessions

The Thrombotic Patient

Demonstrations:
1. Proper Blood Draw
2. Whole Blood, Plasma, Serum
3. Appropriate Blood Collection Tubes
4. Whole Blood Clot
5. Lysis of Clot with Urokinase

Case Studies:
1. 45 yo female with shortness of breath
2. 72 yo male with acute bilateral leg pain
3. 19 yo male with a laceration

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EDUCATIONAL OBJECTIVES
THROMBOSIS PATIENT CASE STUDIES

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1. Identify the important technical aspects of a proper blood draw and specimen handling to allow for accurate lab measurements.
2. Define the components of whole blood, serum and plasma.
3. Describe proper blood collection tubes for coagulation blood samples.
4. Briefly describe how blood clots (in vivo vs. in vitro) and how clots are lysed.
5. Know that current laboratory screening assays detect a hypocoagulable state not a hypercoagulable state.
6. Recognize that there are specific assays for protein C, AT, APC resistance/FV Leiden, and fibrinolytic parameters, and that immunologic and functional assays provide different information.
7. Identify the pathophysiologic risk factors for venous thrombosis.
8. Recognize the “double hit” theory and the risk factors that precipitate a thrombotic event.
10. Describe the mechanisms which cause thrombosis in these pathologic disorders:
    - Antithrombin deficiency
    - Protein C deficiency
    - Activated Protein C Resistance/FV Leiden
    - Antiphospholipid antibody/Lupus anticoagulant
    - Heparin-induced thrombocytopenia
    - Prothrombin G20210A
11. Illustrate how defects in the coagulation cascade lead to thrombin generation producing a hypercoagulable state.
12. Illustrate the mechanisms by which heparin and vitamin K antagonists (oral anticoagulants) effect the PT and APTT assays and how these tests are used to monitor anticoagulant therapy.
14. Discuss treatment regimens for patients with heparin-induced thrombocytopenia.
15. Discuss the laboratory diagnosis of the antiphospholipid syndrome: lupus anticoagulant vs. other antiphospholipid antibodies such as anticardiolipin antibody.
16. Discuss how increased platelet activation can lead to a hypercoagulable state.
17. Discuss how decreased fibrinolytic activity can lead to a hypercoagulable state.
18. Discuss how Thrombin Time test/fibrinogen levels can be used to monitor thrombolytic therapy.
19. Describe the antithrombotic drugs used to treat an established thrombus or used for prophylaxis against venous/arterial thrombosis.
History and Physical:

**Patient:** 45 year-old woman.

**Chief Complaint:** This patient was admitted because of shortness of breath and pain upon breathing.

**Medical History:** The first episode of thrombosis occurred after the birth of the patient’s second daughter. Ten days after delivery she was placed on oral anticoagulants for superficial venous thrombosis. However, a few days later a diagnosis of left femoral vein thrombosis was established on the basis of a venogram and she was placed on subcutaneous low molecular weight heparin, followed by an oral anticoagulant.

Uneventful pregnancies followed two and four years later, then a spontaneous abortion in the fifth year at which time she was placed on oral contraceptives. Over the next several years she twice experienced bilateral superficial thrombosis, and the oral contraceptive was discontinued. After elective tubal ligation at the age of 40, a venous thrombosis developed in her left calf. Over the next two years she experienced several bouts of superficial thrombosis occurring either spontaneously or associated with minor trauma.

**Family History:** Patient’s paternal grandfather died at 32 years of age of “swollen legs,” and her father had a pulmonary embolism at 27 years of age, a history of thrombophlebitis, and he died suddenly at 42 years.

**Drug History:** At the time of the evaluation the patient was taking Coumadin.

**Physical Examination:** Superficial varices were noted over her legs.

QUESTIONS

1. What are the first steps taken to diagnose this patient?
2. What hereditary and acquired clinical disorders can account for the occurring symptoms of this patient?
3. Discuss “precipitating events” that initiate blood clotting in at-risk patients.
4. What laboratory tests can aid in the differential diagnosis of this patient?
5. Of what value are PT/APTT/platelet count as screening tests in this patient?
6. Describe the disorder in this patient and any relation to a precipitating event (lab test results will be provided).
7. Did the patient’s shortness of breath develop from a local problem?
8. What drugs can be used to treat this patient as she presents today and how is this treatment regimen managed?
9. How would this patient’s thrombosis have been treated if she were pregnant?
MECHANISMS OF HUMAN DISEASE
SMALL GROUP SESSIONS

The Thrombotic Patient
Case Study 2

October 1, 2018

History and Physical:

**Patient:** 72 year-old male was treated in the hospital for an acute coronary syndrome. Upon admission the patient was immediately started on intravenous heparin.

**Chief Complaint:** On the fifth hospital day, this patient presented with acute pain in both legs. Acute bilateral lower extremity arterial ischemia secondary to diffuse arterial thrombosis was found. Peripheral angiography showed total thrombotic occlusion of the proximal right common femoral artery with no distal blood flow and partial thrombotic occlusion of the left common femoral artery with sluggish distal flow.

**Medical History:** Upon admission and continually throughout the hospital stay, the patient had been treated with intravenous heparin for an acute myocardial infarction. The patient had previously received heparin 3 months earlier during an interventional cardiology procedure to implant a stent in his left anterior descending artery.

QUESTIONS

1. What is important in the patient’s medical history that leads to what suspicion for the cause of his thrombosis?
2. What screening lab tests can be ordered? How often?
3. What specific laboratory tests would aid in the diagnosis?
4. What is the mechanism of this disorder?
5. What is the treatment for thrombosis in a patient with this disorder?
6. What determines when this patient is out of the acute phase of this disorder?
7. How should this patient be treated if he returns to the hospital in the future for treatment requiring anticoagulation?
Patient: 19 year-old male

Chief Complaint: Admitted to the Emergency Department (ED) of a local hospital with a severe laceration on the palm of the left hand. The patient was attending the Lollapalooza concert in downtown Chicago, cut his hand on the fence that he was climbing, and then fell in the mud that was present from the rain that had fallen a few hours earlier.

Medical History: A young, healthy male with no significant medical or surgical history upon admission to the ED. Family History is non-contributory.

Progress Notes: In the ED cultures of the wound were taken, and the patient’s hand was sutured. Patient was placed on amoxicillin, an oral antibiotic. One week later the patient returned to the ED with a 40°C fever associated with pain, redness and swelling around the sutured wound. Such a wound is considered contaminated; even appropriate and extensive surgical irrigation cannot make such a wound clean. A progressive skin and subcutaneous infection developed and has now become systemic. The wound cultures grew *Staphylococcus aureus* and multiple rare organisms. Systemic IV antibiotics were required, so a peripherally inserted central catheter (PICC) line was placed so the patient could receive IV therapy at home.

QUESTIONS

1. A few days later at home the patient experienced an acute onset of respiratory distress (shortness of breath, tachypnea, and chest wall pain) immediately following injection of the antibiotic through the PICC line. What could have happened?

2. What laboratory tests could help with the diagnosis?

3. Assuming all first line lab tests are normal on this patient, what mechanism could have been at play?

4. How would the patient be treated now?

5. Discuss whether a similar type of health risk would exist in a young, healthy individual with an Achilles’ tendon rupture who was placed in an ambulatory plaster cast for 6 weeks.