**Lecture 8 Outline**

**Hemostatic Disorders of Thrombosis**

1. Introduction
   1. General Information
      1. If when you are clotting, there are irregularities that can develop.
      2. Thrombosis/cardiovascular disease: major cause of death in USA.
      3. General info: 780,000 died from cardiac disease; of all deaths, 32% were due to major cardio vascular disease.
      4. Disorders: acquired or inherited
      5. Risk factors include:
         1. Smoking
         2. ↑ cholesterol
         3. ↑ BP
         4. Obesity
         5. Diabetes
         6. Lack of exercise (can make b🡪e better)
         7. Stress
         8. Alchohol
      6. Other triggers:
         1. Surgery
         2. Major trauma
         3. Malignancy
         4. Inflammatory diseases
         5. Pregnancy
         6. Oral contraceptives: increase of clotting factors
         7. Venous situations
            1. Venous stasis in extremities
            2. Venous obstruction
            3. Increased blood viscosity (thicker)
   2. Definition of Terms
      1. Thrombosis: inappropriate formation of platelet or fibrin clots which block blood vessels
      2. Thrombophilia: predisposition to thrombosis secondary to an inherited or acquired disorder
      3. Hypercoagulability: alteration of blood coagulation mechanism that predisposes a person to thrombosis
      4. Thromboembolus: blood clot which has become detached from its site of formation, travels, and blocks a vessel
      5. DVT: deep vein thrombosis—blood clot in one of the veins usually of the leg or pelvis; may be asymptomatic; problem occurs when breaks off and travels elsewhere
      6. PE—pulmonary embolus—clot which has formed elsewhere and travels to the lungs; when obstruct blood flow to lungs, puts strain on heart 🡨 problems
      7. When clot blocks arterial blood flow supplying heart, brain, or other organs, have ischemia [=local and temporary deficiency of blood supply to the tissues]
      8. May have infarction [=reduction in blood flow to a cell or organ; more of a complete cutoff of blood supply than, e.g. ischemia]
      9. Infarction may lead to necrosis [=pathologic death of one or more cells of a portion of tissue or organ]
2. Inherited Disorders
   1. General
      1. If a person has reoccurring thrombosis and they are under 40, there may have inherited disorder.
      2. Usually a deficiency in one of the naturally occurring regulators.
      3. Homozygous deficiency: going to have problems
      4. Heterozygous deficiency: going to have problems if not working properly.
   2. AT III
   3. Heparin Cofactor II
   4. Protein C
   5. Protein S
   6. Factor V Leiden
   7. Prothrombin Gene Mutation G20210A
   8. Homocysteine
   9. Other
      1. Factor XII deficiency: XII activates breakdown of plasminogen. If you don’t have XII, you won’t break down clot, may thrombose.
      2. Dysfibrinogenemia: make an abnormal molecule, may have thrombosis.
      3. Elevated factor VIII: high factor VIII, but no inflammation, predisposition to thrombosis
3. Acquired Thrombotic Disorders – more common than inherited
   1. Situations
      1. Pregnancy
      2. Medications
         1. Oral contraceptives
         2. I-aspariginase: inhibits protein synthesis in leukemic cells, but also inhibits production of liver proteins
      3. Certain cancers
      4. Major trauma
      5. Increased levels of various clotting factors (VIII, fibrinogen)
   2. APA Syndrome
   3. HIT [Heparin-Induced Thrombocytopenia]
      1. Definition:
         1. Two types:
            1. Type 1: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_
            2. Type 2: \_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_
      2. Mechanism
         1. Platelets contain PF4 in alpha granules (PF4 = heparin neutralizing factor)
         2. If/when heparin somehow activates platelets, there is a release of PF4 from the alpha granules into the circulation. Heparin then binds