Essential Learning
Hemophilia

- **Important components of history taking in patients with hemophilia**
  - What type of hemophilia and what is the severity?
  - Who is the patient's hematologist?
  - Is the patient on prophylaxis? (dosing and route, last dose, port in place?)
  - Has the patient had a history of a severe bleed?
  - Does the patient have inhibitors?
  - Does the patient have an emergency plan or factor replacement on them?

- **What coagulation tests measure factor activity?**
  - PT/INR- tests extrinsic and common pathways, including factors V, VII, X (5, 7, 10), prothrombin, and fibrinogen
    - assess for inherited or acquired factor deficiencies
    - more sensitive than the aPTT for deficient levels of some factors
  - aPTT- tests intrinsic pathway including factors V, VIII, IX, XI, XII (5, 8, 9, 11, 12), prothrombin, and fibrinogen
    - assess for inherited or acquired factor deficiencies

- **Types of hemophilia**
  - All are disorders of the intrinsic coagulation pathway
  - Hemophilia A
    - Deficiency or inactivation of Factor VIII (also called antihemophilic globulin)
    - Most common X-linked recessive genetic disease
    - 2nd most common factor disorder after vWD
    - ~1/3 of cases involve new mutations
    - ~70% have severe disease
  - Hemophilia B
    - Deficiency or inactivation of Factor IX
    - Also called Christmas disease
  - Hemophilia C
    - Deficiency or inactivation of Factor XI
    - Very rare autosomal recessive disorder
    - Affects males and females equally
  - Acquired hemophilia
    - Autoimmune disorder predominantly seen in the elderly (> 60-years-old)
    - Most commonly affects Factor VIII
    - 50% will have concurrent autoimmune disorder (i.e., lupus, RA, Sjogren, etc.)
    - Joint bleeding is infrequent

- **Expected lab abnormalities seen with hemophilia**
    - Prolonged PTT (2-3x normal in severe disease) and typically a normal PT/INR (consistent with disruption of intrinsic pathway)
        - PT and PTT will be normal if factor activity ≥ 30%
    - Factor VIII assay levels determine severity of disease and expected symptoms:
        - Factor level 5-30% (mild)- bleeding with major trauma or surgery
        - Factor level 1-5% (moderate)- occasional spontaneous bleeding or bleeding into joints/muscles after minor trauma
        - Factor level < 1% (severe)- frequent spontaneous hemorrhage, internal bleeding after trauma/surgery

- **Indications for sending a Factor Inhibitor assay**
    - Bleeding is not controlled after infusion of adequate amounts of factor concentrate
    - When PTT fails to normalize with mixing study

- **Treatment guidelines for factor replacement**
    - Always consult Hematology
    - For patients with life-threatening bleeding, begin immediate therapy with appropriate factor replacement.
    - For treatment of acute bleeds, target levels by hemorrhage severity are as follows:
        - Skin lacerations: usually don't require factor, treat with pressure and topical thrombin
        - Mild (early hemarthrosis, gingival bleeding): 20-40%
        - Moderate (hemarthrosis, moderate muscle or oral bleeding): 30-60%
        - Major (retropharyngeal, GI, intra-abdominal): 60-100%
        - Life-Threatening Hemorrhages (CNS, major trauma or surgery, advanced or recurrent hemarthrosis): maintain an FVIII level of 100%

- **How much factor should be given?**
    - Formula for dosing Factor VIII (hemophilia A):
        - Units of Factor VIII = [Desired factor level] x Wt (kg) x 0.5
        - 1 IU factor VIII/kg increased activity by 2%
        - General guideline for initial replacement in severe disease:
            - Mild = 15 U/kg
            - Major = 25 U/kg
            - Life-Threatening = 50 U/kg
        - For reference, Factor VIII costs about $1/unit
    - Formula for dosing Factor IX (hemophilia B)
        - Units of Factor IX = [Desired factor level] x Wt (kg)
        - 1 IU factor IX/kg raises activity by 1%
        - General guideline for initial replacement in severe disease:
            - Mild = 30 U/kg

- Major = 50 U/kg
- Life-Threatening = 100 U/kg

- **Patients with factor inhibitors**
  - If a patient has known inhibitors to Factor VIII, additional treatment considerations include:
    - High doses of FVIII for low-titer inhibitors
    - Activated recombinant FVII (rFVIIa) at 90 µg/kg
    - Activated prothrombin complex concentrate (e.g., FEIBA- factor eight inhibitor bypassing activity)
    - Porcine FVIII

- **What should be given if factor is unavailable?**
  - For Hemophilia A (F8 def): give Cryoprecipitate 10 bags (1 bag = 80 U FVIII)
  - For Hemophilia A or B (F9 def): give FFP 15 mL/kg (1U FVIII per 1 mL FFP)
  - Volume overload often limits transfusion amounts necessary for hemostasis

- **What can be used to treat mild bleeding in patients with mild hemophilia?**
  - Desmopressin (DDAVP)
    - Stimulates release of vWF which promotes Increase in FVIII levels
    - IV dose is 0.3 mcg/kg
    - Intranasal dose is 150 mcg (single spray) for children (< 50 kg) and 300 mcg (2 sprays) for adults

- **Compartment syndrome and how it presents**
  - Tissue pressure > venous pressure **>** impaired blood flow **>** ischemia
  - Acute compartment syndrome is most commonly associated with traumatic injuries
  - Subacute or chronic “exertional” compartment syndrome is associated with repetitive microtrauma
  - “Classic” presentation includes the 5 P’s (pain, paresthesia, pallor, pulselessness, poikilothermia)
    - Not clinically reliable
    - Often only found with late stage disease
  - Patients often experience severe pain (“pain out of proportion”) described as deep, aching, or burning
  - Earliest exam findings include pain with passive stretch, a firm “wooden” muscle compartment on deep palpation, and decreased 2-point discrimination
  - Crucial to perform serial exams on patients at risk for development of compartment syndrome to notice changes early on

- **Management of compartment syndrome in patients with hemophilia?**
  - Normalize clotting derangements with factor replacement

- If compartment symptoms persist despite maximal factor replacement, measure compartment pressures and consider fasciotomy in consultation with a hematologist
- Exhaustion of non-surgical management is critical due to the significant functional surgical morbidity associated with a fasciotomy in a hemophilia patient

- **Diagnosis and treatment of compartment syndrome**
  - Diagnosis is made by measuring intra-compartmental pressure (often with Stryker pressure tonometer)
    - Use sterile technique
    - The compartment to be measured should be at the same level as the heart
    - Position so that the needle can be introduced perpendicularly to the muscular compartment
    - If there is a fracture, measure as close to fracture site as possible
  - No consensus regarding a specific compartment pressure threshold that should prompt a fasciotomy
    - General guidelines include compartment pressure > 30 (> 15-20 in hand) or compartment pressure > diastolic BP-30

- **The 4 compartments of the lower leg**
  - Compartments of the lower leg include:
    - Anterior (foot dorsiflexion, toe extension)
    - Lateral (ankle eversion, deep and superficial peroneal nerve- generally anterior lower leg and foot innervation)
    - Superficial posterior (foot plantar flexion)
    - Deep posterior (toe flexion, posterior tibial artery and vein, tibial nerve- generally posterior lower leg and foot innervation)

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