Cases

- 13 yr old male presents to the ER with chest pain, and shortness of breath. He had been at football practice when the symptoms began 3 days prior to admission. Symptoms have worsened over the past 2 to 3 days. Pain is worse with inspiration. He denies fever or cough.
- 17 yr old female referred for increased calf swelling and tenderness. She had started BCP one month prior to symptoms. She was hospitalized and treated for DVT. One day before discharge she developed chest pain. At her first follow-up visit, she still complained on right chest pain, pleuritic in nature.

Incidence of DVT in pediatrics

- Idiopathic thrombosis is rare in pediatrics
- 95% of VT is associated with underlying serious conditions
- Highest risk in infants< 1 yr and teenagers
- Central venous catheters are the most important predisposing factor
- 2/3 of children with VT have 2 or more risk factors
- Mortality is 2.2%-all patients who died had a CVC related upper extremity thrombosis (Canadian Thrombophilia registry)
Risk Factors
- Neonates—imbalance of maturation rates of coagulation proteins, maternal hormones
- Central venous catheters
- Nephrotic syndrome—loss of proteins in the urine esp antithrombin III
- Oral contraceptives
- Dehydration
- Cancer
- Congenital heart disease
- Systemic lupus erythematos
- Trauma
- Surgery
- Infection
- Obesity
- Previous thrombosis
- Pregnancy
- Smoking

Presentation of DVT
- Extremities present with swelling, pain, color changes and/or prominent surface vessels
- Superior vena cava thrombosis presents as upper extremity swelling, pain, superficial vein dilation. May also have facial swelling with altered level of consciousness. Usually associated with central venous catheters.
- Renal vein thrombosis occurs in newborns, present with hematuria, oligouria, and palpably enlarged kidneys
- Cerebral vein/venous sinus thrombosis present with headache, seizures, hemiparesis, coma, increased intracranial pressure.
- Hepatic vein thrombosis is rare but presents with ascites, abdominal pain, vomiting, hepatomegaly, abn LFT. Has a high mortality.
CVC and Thrombosis

- 1/3 of children with cancer and a CVC will develop catheter-related thrombosis
- Children at increased risk
  - Relative size of catheter compared to the vessel
  - Down regulation of the fibrinolytic system in children
- 3 types of thrombosis
  - Clots at the tip
  - Fibrin sheath
  - Proximal vein thrombosis
- Patients with clots may be at increased risk for infection
- Treatment-as with other DVT
- Prevention-catheters are flushed daily to 2 times daily with heparin. Studies using warfarin to prevent catheter-related thrombosis showed no efficacy

Diagnosis of DVT in Children

- Labs- CBC, PT/PTT, fibrinogen
- D-dimer-while used in adults as an indication of thrombosis, data in children is scarce. In ill children, will be of no value. May be useful in new onset upper or lower extremity DVT in otherwise healthy child
- Doppler ultrasound for upper or lower extremities
- US with doppler for renal or portal thrombosis
- MRI or MRV- for cerebral or thoracic thrombosis
- Angiogram is gold standard but is invasive and expensive.
The Congenital Prothrombotic States

Evaluation for Hypercoagulable State
- Laboratory studies: Draw before starting anticoagulation
  - Baseline PT/PTT, fibrinogen
  - Protein C Ag and function
  - Protein S Ag and function
  - Antithrombin III
  - Anticardiolipin antibodies
  - Lupus anticoagulant screen
  - May be drawn at a later date
  - Factor V Leiden (APC resistance)
  - Prothrombin gene mutation 20200
  - Homocysteine
  - MTHFR mutation ?
  - Factor VIII level
  - Lipoprotein a
  - Lipid profile

Pulmonary Emboli
- Rare in pediatrics
- Incidence on autopsy is 0.73 to 4.2%
- Highest rates in infants age 1-23 months, with second peak in adolescence age 15 to 17.
- 2.38 higher incidence in black children
Risk Factors for Pulmonary Emboli
- Burns
- Central venous catheters
- Deep vein thrombosis
- Dehydration
- Heart Disease
- Hematologic diseases
- Immobility
- Neoplasm
- Obesity
- Renal disease-nephrotic syndrome
- Septic
- Shock
- Stem cell/bone marrow transplant
- Surgery
- Preexisting thrombophilic conditions
- Trauma
- Vascular malformation

Symptoms of Pulmonary Emboli
- 90% present with dyspnea and tachypnea
- 50% are apprehensive
- Pain-usually sudden onset and pleuritic
- Unexplained hypoxia
- 50% cough
- Hemoptysis
- Syncope
- May be asymptomatic
- May have fever

Differential Diagnosis of PE
- Pneumothorax
- Fractured rib
- Lobar pneumonia
- Pericarditis
- Congestive heart failure
- Rarely in children, mitral stenosis or myocardial infarction

Diagnosis of PE in Children
- CXR often normal but pulmonary infiltrate with elevated hemidiaphragm is suggestive of pulmonary infarct
- EKG may show acute cor pulmonale (S1-Q3-T3) pattern
- Spiral CT is most commonly used today
  - Advantages: High sensitivity and specificity, identifies other diagnoses, visualizes non obstructive emboli
  - Disadvantages: Radiation exposure, use of contrast
- Pulmonary angiography remains the gold standard but is expensive and invasive.
- Ventilation-perfusion scans can be used but V/Q mismatch can also be seen with asthma, pneumonia, pulmonary artery stenosis, cardiac diseases
- MRA (magnetic resonance imaging) is non invasive, high sensitivity and specificity.
Treatment of DVT and Pulmonary Emboli in Children

- Use of low molecular weight heparin is preferred because of less potential for hemorrhage and less invasive laboratory monitoring.
- Coumadin is started 1 to 3 days after heparin.
- Use of thrombolytics (Tissue plasminogen activator) is less well studied in children but should be considered for life threatening thrombosis.
- Duration of therapy depends on predisposing risk factors and continued presence of risk factors.
- IVC filters can be used in patients who are at high risk for PE or cannot take anticoagulants.
- Surgical intervention can be considered for life threatening pulmonary emboli.

Low Molecular Weight Heparin

- Binds to Antithrombin and has specific activity against FXa
- Advantages over unfractionated heparin
  - Reproducible pharmacokinetics
  - Subcutaneous administration
  - Minimal monitoring
  - Decreased risk of heparin induced thrombocytopenia
  - Possible decreased risk of osteoporosis
- Dosing
  - 1 mg/kg/dose q 12 hrs subcutaneously
  - Infants require higher doses 1.2 mg/kg/dose q 12 hrs
  - Preterm infants may require even higher doses
  - Monitor with Factor Xa levels 4 hrs after the dose
- Monitoring in children is more frequent than in adults due to growth and weight changes in children

Prevention of Thrombosis

- Avoid dehydration-caffeine
  - No oral contraception, estrogen patches
  - Pts using OCP had a 5 fold increase in thrombosis
  - Increased risk with higher doses of estrogen
  - Risk highest in first 3 months of use, risk decreases with time on OCP
- Move when on long car rides or plane rides
- Support stockings 20-30 mm pressure
- Prophylaxis for surgery or prolonged immobilization
  - Low molecular weight heparin
  - Pneumatic boots
- Avoid smoking and alcohol
- WEIGHT CONTROL
Long Term Complications of DVT and Pulmonary Emboli in Children

- Recurrent thrombosis
  - Continued presence of risk factors
  - Congenital thrombophilic states esp. prothrombin mutation and factor V leiden
  - Antiphospholipid syndrome
  - Residual obstruction present
  - Post thrombotic syndrome
  - Pulmonary hypertension
  - Little information on long term effects of small pulmonary emboli
  - Large emboli result in acute cor pulmonale and/or death

Postthrombotic Syndrome

- Clinical condition of limb pain along with physical findings that range from swelling to stasis ulcers following one or more episodes of deep vein thrombosis.
- Diagnosed 6 months or more from time of DVT.
- Prevalence in children is 9.5 to 70%. Rate increases with time.
- Caused by obstructed and refluxed blood flow
- Risk factors: elevated factor VIII and D-dimer, clot persistence, number of venous segments involved, duration of observation after DVT.
- Treatment: elevation, compression, moderate exercise, and maintaining ideal body weight

Development of PTS

- Normal Venous Function: Valve prevents backwards blood flow
- Venous Insufficiency: Faulty valve allows backwards blood flow
Cases

15 yr old male presents to the ER with chest pain, and shortness of breath. He had been at football practice when the symptoms began a days prior to admission. Symptoms have worsened over the past 2 to 3 days. Pain is worse with inspiration. He denies fever or cough.

- Risk factors-obesity (weight > 350 lbs, dehydration)
- No DVT found. Multiple Pts found by spinline CT.
- Found to have Antiphospholipid antibody syndrome and remains on anticoagulation.
- 17 yr old female referred for increased calf swelling and tenderness. She had started BCP one month prior to symptoms. She was hospitalised and treated for extensive bilateral femoral-femoral DVT. One day before discharge she developed chest pain. At her first follow-up visit, she still complained of right chest pain, pleuritic in nature.
- Risk factors-obese, BCP, multiple family members with clot.
- Spinal CT as outpatient confirmed pulmonary emboli.
- Remains on Coumadin.
- No other risk factors found.
- Developed post thrombotic syndrome.

Summary

- Most children with venous thrombosis have a serious underlying condition.
- CVC are a major cause of thrombosis.
- Pulmonary emboli are rare but potentially fatal in children.
- Symptoms of PE range from asymptomatic to acute cardio-respiratory failure.
- Aggressive treatment of peripheral DVT is necessary to prevent progression of the clot, pulmonary emboli and postthrombotic syndrome.
- The use of thrombolytic agents remains limited and experimental in children but should be considered if life or limb is threatened.

References