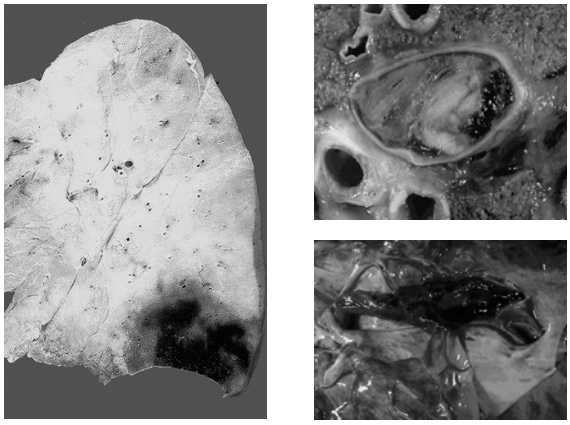
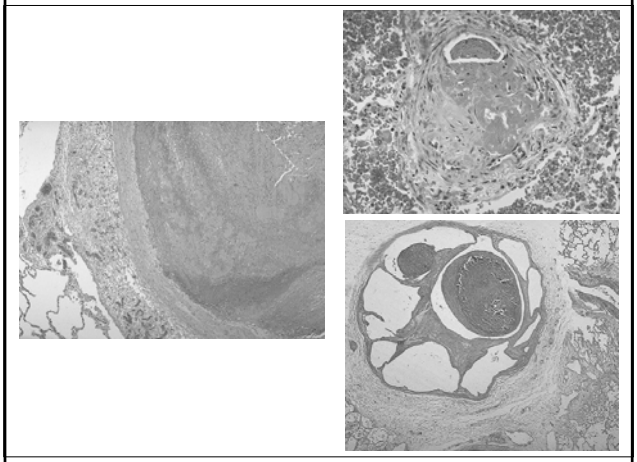
# Pulmonary Thromboembolism

James Allen, MD



# Epidemiology of Pulmonary Embolism

- 1,500,000 new cases per year in the United States
- Often asymptomatic
- 300,000 deaths per year
- DVT or PE present in 10% of ICU patients
- Untreated mortality is 25%

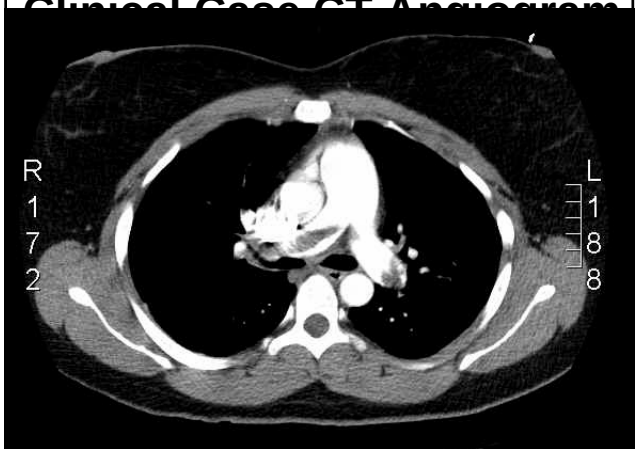


# Clinical Case

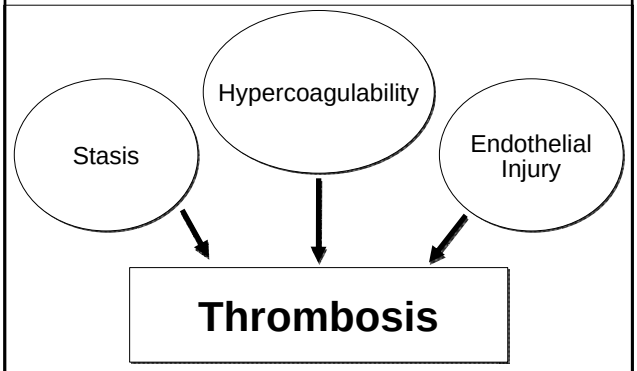
- 18 year old woman
- Recently started oral contraceptives
- Syncope, dyspnea, & chest pain
- In ED:
  - ✓BP = 96/50; HR = 120
  - ✓pO2 = 62 on room air
  - ✓CXR = normal

# Why Did She Clot?

## Clinical Case: CT Angiogram




## Virchow's Triad



## Venous Stasis

- Immobility
- Bed rest
- Surgery
- Pregnancy
- Cor pulmonale

## Heritable Hypercoaguability

- Factor V Leiden mutation
- Prothrombin G-A20210 mutation
- Hyperhomocysteinemia
- Protein C deficiency
- Protein S deficiency
- Anti-thrombin III deficiency
- Elevated factors VIII, IX, & XI

## Endothelial Injury

- Previous DVT
- Trauma
- Surgery
- Femoral venous catheters

## Factor V Leiden

- Causes resistance to activated protein C
- 4% of Americans are heterozygotes
- Contributes to about 20% of DVT/PE
- Heterozygotes = 5-10 fold increased risk
  - ✓plus OCPs = 35 fold increased risk
- Homozygotes = 80 fold increased risk

## The Genetic Epicenter of Factor V Leiden

## Prothrombin G-A20210 Mutation

- Causes increased prothrombin levels
- Contributes to about 14% of all DVT/PE
- Heterozygotes = 3 fold increased risk
  - ✓heterozygote + factor V Leiden = very high risk
- Homozygotes = very high risk

## United States Racial Distribution of Factor V Leiden

- 5.3% Caucasian Americans
- 2.2% Hispanic Americans
- 1.2% African Americans
- 1.2% Native Americans
- 0.4% Asian Americans

## Hyperhomocysteinemia

**Causes**

- Genetic
- Poor nutrition
- Renal insufficiency
- Malignancy
- Hypothyroidism
- High animal fat diet

**Drug causes**

- Methotrexate
- Phenytoin
- Carbamazepine
- Theophylline

# Acquired Hypercoaguability

- Hyperhomocysteinemia
- Anti-phospholipid antibody
- Malignancies
- Estrogens
- Heparin-induced thrombocytopenia

# Thrombocytopenia and Heparin

**Non-Immune**

- Platelets > 100,000
- Days 1-5 of heparin
- Not thrombogenic

**Immune**

- Platelets fall by > 50% (usually < 100,000)
- Between day 5-14 of heparin
- Highly thrombogenic

# Anti-Phospholipid Antibodies

**Associated Conditions**

- SLE
- Sjogren's
- Rheumatoid arthritis
- Systemic sclerosis
- HIV
- Syphilis

**Associated Drugs**

- Phenytoin
- Oral contraceptives
- Phenothiazines
- Hydralazine
- Procainamide

# Heparin-induced Thrombocytopenia

- When suspected, discontinue all heparin pending HIT study
- Initial treatment = argatroban or lepirudin
- Long-term (3-6 month) coumadin

# Deep Venous Thrombosis Diagnosis

- **Duplex ultrasound**
  - ✓**Sensitivity & specificity = 99%**
  - ✓**Accuracy best for femoral DVT**
- **Impedance plethysmography**
- **Venography**
- **CT scanning**
- **MRI**

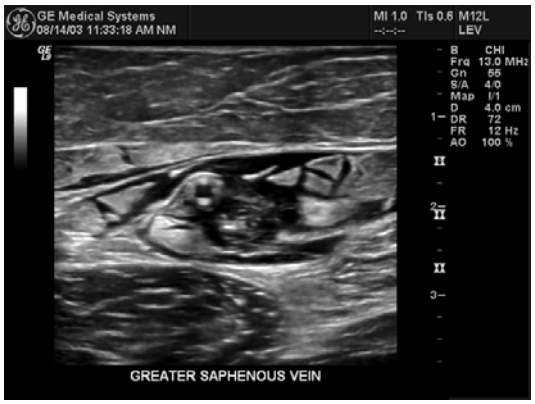


Image courtesy of GE Healthcare; used with permission

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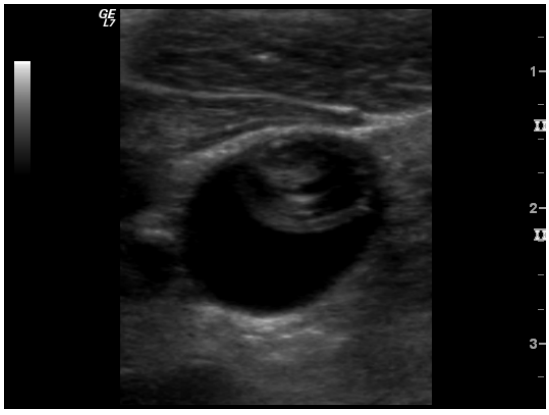
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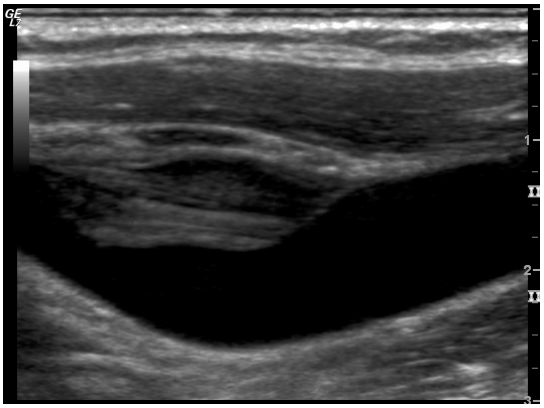


Image courtesy of GE Healthcare; used with permission

# Pulmonary Embolism

**Symptoms**

- Dyspnea 80%
- Pleurisy 70%
- Cough 50%
- Hemoptysis 30%

**Signs**

- Increased A-a gradient 95%
- Tachypnea 92%
- Tachycardia 44%
- Fever 43%

# Calf Vein Thrombosis

- 20% propagate into popliteal vein
- Anticoagulation necessary if propagate
- Safest approach is to treat all cases
- Serial duplex ultrasounds if anticoagulation is risky

# Well's Criteria for PE

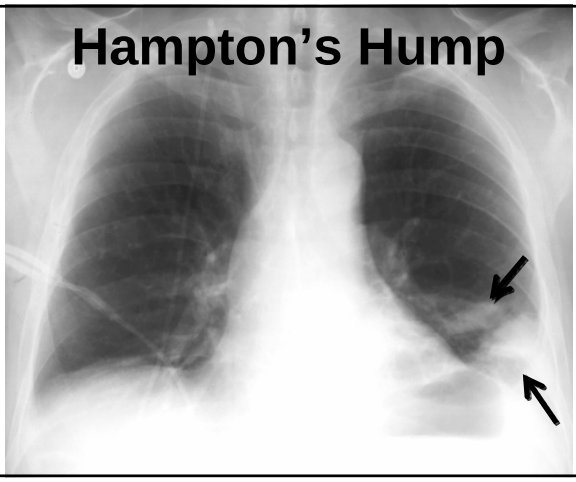
| | |
|---|---|
| 3.0 Signs of DVT | |
| 1.5 HR > 100 | |
| 1.5 Immobilization for > 3 days or surgery in past 4 months | |
| 1.5 Previous PE | |
| 1.0 Hemoptysis | |
| 1.0 Malignancy | |
| 3.0 PE as or more likely than other diagnoses | |

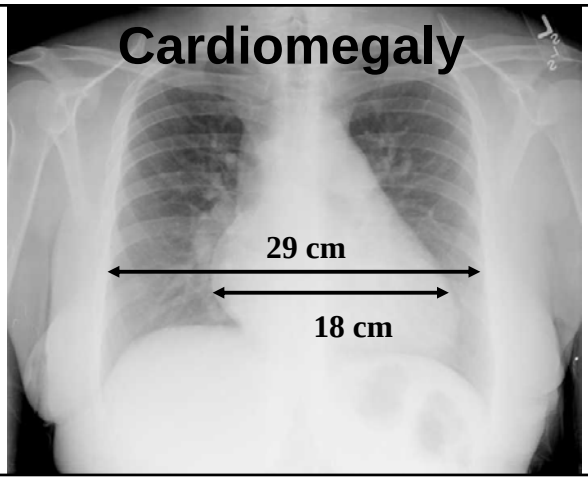
| Probability | |
|---|---|
| <2 | Low |
| 2-6 | Intermediate |
| >6 | High |

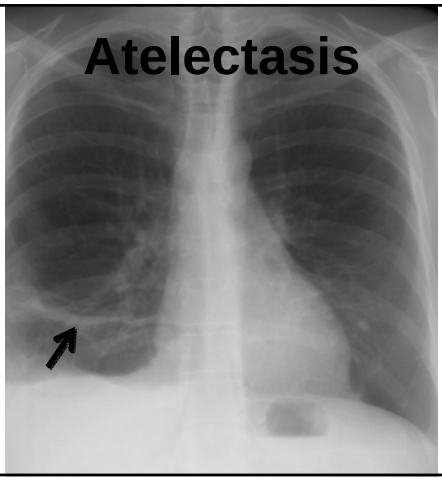
Thromb Haemost. 2000;83:416-20

# Chest X-Ray Findings

- Cardiomegaly
- Enlarged pulmonary artery
- Atelectasis
- Elevated hemidiaphragm
- Regional oligemia
- Pleural effusion
- Hampton's hump



# D-Dimer In Pulmonary Embolism

- **Negative test is strong evidence against DVT/PE in patients with low clinical suspicion**
- **False negatives can occur (especially in cancer)**
- **False positives are frequent**
- **Only validated for outpatients**

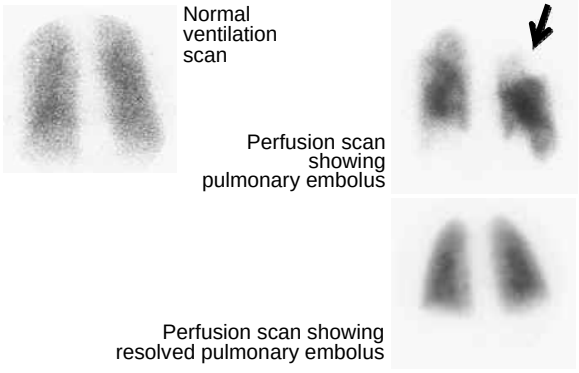
# Ventilation Perfusion Scan

- **Still the best initial test for some patients**
- **Most valuable if normal**
- **Clinical decision making requires:**
  - ✓**V/Q scan probability**
  - ✓**Clinical probability**

# Troponin I

- **Elevated in 30-50% of moderate to large PE**
- **Correlates with embolism size and worse outcome**

# Ventilation/Perfusion Scan



# Probability of Pulmonary Embolus

| V/Q Probability | Clinical Suspicion: High | Intermediate | Low |
|---|---|---|---|
| High | 96% | 88% | 56% |
| Intermediate | 66% | 28% | 16% |
| Low | 40% | 16% | 4% |

JAMA 1990; 263:2753-9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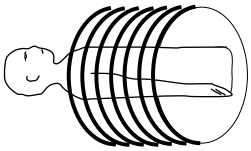
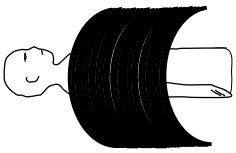
## Pulmonary Angiogram

- "Gold standard"
- Usually performed following V/Q scan
- Relatively low complication rate
- False positives rare



**One channel CT:**
**Fewer image slices per scan**
**Less sensitive for PE**



**Quad channel CT:**
**More image slices per scan**
**More sensitive for PE**

## CT Pulmonary Angiogram

- Specificity about 90%
- Sensitivity about 80%
- Optimal study requires:
  - ✓Recent generation CT scanner
  - ✓Technician experience
  - ✓Radiologist experience

## CT Pulmonary Angiogram

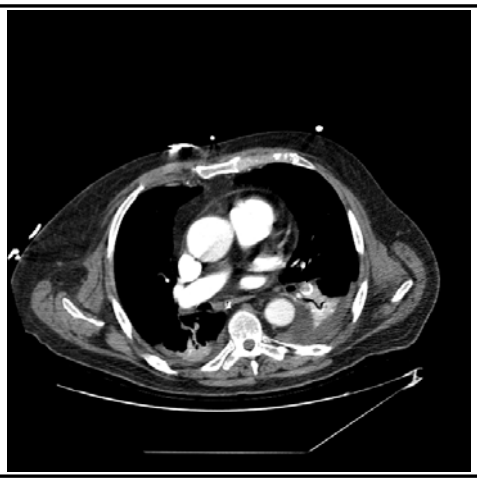
Normal

Pulmonary emboli

Inadequate technique

## Reconstructed high speed multi-channel CT angiogram

Image courtesy of GE Healthcare; used with permission

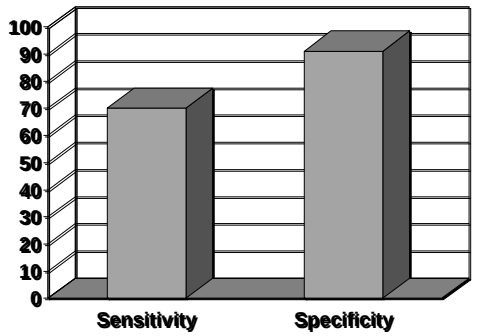


# Probability Of True PE

| | High Clinical Suspicion | Medium Clinical Suspicion | Low Clinical Suspicion |
|---|---|---|---|
| CTPA/CTV Positive | 96% | 90% | 57% |
| CTPA/CTV Negative | 18% | 8% | 3% |

N Engl J Med 2006; 354:2317-27

# CT Angio in the ED




Perrier, et. Al. Intensive Care Med 2001; 27:1481-6

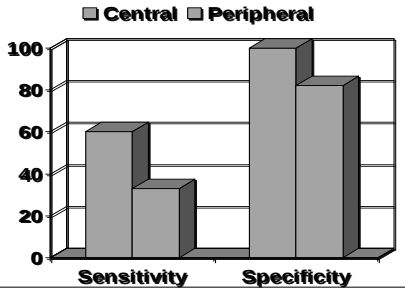
# PIOPED II Conclusions

- **CTPA should not be used alone**
- **CT venogram may be useful with CTPA except in:**
  - ✓**Pregnant women**
  - ✓**Patients under 40**
- **CTPA positive in main or lobar arteries more accurate than CTPA positive in segmental arteries**

# CT Angio in the ICU

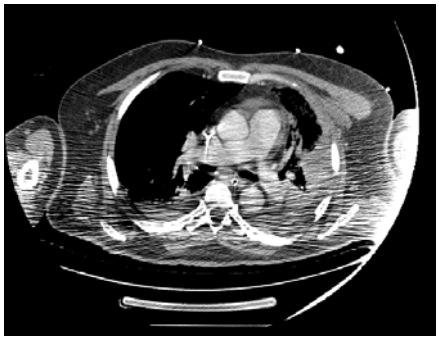
Surgical ICU

22 patients undergoing both CT & traditional angiogram




Arch Surg 2001; 136:505-11

## Typical CT-PA in the ICU



## Practical Use Of CT-PA

- If clearly positive = PE present
- If negative:
  - ✓Low clinical suspicion = no PE
  - ✓Intermediate or high clinical suspicion = additional testing

## CT Angio Conclusions

- Specificity is good
- CT misses 20-30% of pulmonary emboli in outpatients
- CT misses up to 50% of PE in ICU patients

## What Rules Out PE?

- Normal V/Q scan
- Low clinical suspicion and D-dimer less than 500 ng/ml
- Low probability V/Q and D-dimer less than 500 ng/ml
- Negative CT-PA plus negative LE duplex
- Low/intermediate probability V/Q and low/moderate clinical probability and either D-dimer < 500 ng/ml or serial duplex ultrasounds
- Normal angiogram

## What does NOT rule out PE? If the clinical suspicion is high:

- Low probability V/Q scan alone
- Negative CT-PA alone
- Normal D-dimer test
- Negative MRI

## Sometimes the best test is the one that you can do

## So, what is the best initial test?

- CT scan:
  - ✓Previous PE
  - ✓Significant underlying lung disease
- V/Q scan:
  - ✓Dye allergy
  - ✓Renal insufficiency
  - ✓?Patients with normal CXR
- Duplex ultrasound:
  - ✓Pregnancy
  - ✓Patients with transportation risks
- D-dimer
  - ✓Low risk outpatients

## Predictors of worse outcome

- Shock
- Severe hypoxemia
- Elevated troponin I
- BNP > 90
- RV dysfunction by echo

# Pulmonary Embolism Treatment

- Heparin
- Low molecular weight heparin
- Fondaparinux
- Coumadin
- Thrombolytics
- IVC filters
- Catheter extracation/fragmentation
- Surgical embolectomy

# Heparins

- DVT:
  - ✓ Low molecular weight heparin or unfractionated heparin
  - ✓ Outpatients or inpatients
- PE
  - ✓ Low molecular weight heparin
  - ✓ Unfractionated heparin in:
    - Renal failure (creatinine clearance less than 25 ml/min)
    - Morbid obesity (greater than 150 kg)
    - Most ICU patients
  - ✓ Inpatients only

# "Shoot first, ask questions later"

# Heparin Dosing

- Bolus with 80 u/kg
- IV infusion of 16-18 u/kg
- Check PTT Q6 hrs until stable, then QD
- Keep PTT 60-105 seconds*
- Check platelets every other day
- Minimum 5 day infusion

* Appropriate therapeutic range may vary by hospital lab

## Low Molecular Weight Heparins

- Equally or more effective than heparin
- Equal or less bleeding than heparin
- Lower incidence of thrombocytopenia
- Longer half life
- Monitoring PTT unnecessary
- Problems: renal insufficiency & obesity

## Duration of treatment

- Reversible factor: 3 months
- First idiopathic: minimum of 3 months and consider indefinite therapy
- Second DVT/PE: indefinite anticoagulation

## Coumadin

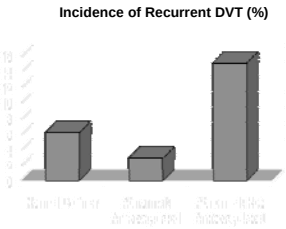
- Start on day #1 of heparin
- Initial dose = 10 mg
- Keep INR 2.0 - 3.0
- Genetic testing may help guide dosing in the future

## Thromboembolism in cancer

- Patients can clot through coumadin
- Use minimum of 6 months heparin or low molecular weight heparin

# D-dimer predicts recurrence

- 608 patients with venous thromboembolism treated > 3 months
- 233 had elevated D-dimer after treatment
- Patients randomly assigned to anti-coagulation or no treatment




N Engl J Med 2006; 355:1780

# Inferior Vena Cava Filters

- Indications:
  - ✓Contraindication to anticoagulation
  - ✓Failure of anticoagulation
  - ✓Complications of anticoagulation
- Complications:
  - ✓Recurrent PE = 2.4%
  - ✓Occlusion = 3.4%
  - ✓Doubled risk of recurrent DVT

# Anticoagulants on the horizon:

- Idraparinux – once weekly subcutaneous anticoagulant not requiring INR monitoring and recently found to be as effective as coumadin
- Rivaroxaban – oral anticoagulant not requiring INR monitoring and recently found to be superior to low molecular weight heparin for short term DVT prophylaxis

*Neither are currently approved by the FDA

# Upper extremity DVT

- Initial therapy: heparin (low molecular weight or unfractionated)
- Long term treatment with coumadin as per DVT

# Mortality of Pulmonary Embolus

- **Untreated: 25%**
- **Heparin Treated: 2%**

# Heparin vs. Thrombolytics In Pulmonary Embolism

| | Heparin Alone | Thrombolytics |
|---|---|---|
| Uncomplicated | X | |
| Shock | | X |
| Resp. Failure | | X |
| RV Dysfunction | ? | ? |
| High Troponin | ? | ? |

# Complications of Thrombolytics in Pulmonary Embolus

- **Cerebral hemorrhage 1.2%**
- **Major bleeding 6.3%**

Arcasoy SM. *Chest* 1999; 115:1695-1707

# Other Treatments

**Surgical embolectomy**

- **Mainly if thrombolysis is contraindicated**
- **20-30% operative mortality**

**Catheter techniques**

- **Clot removal**
- **Clot fragmentation**
- **28% mortality**

**Bottom Line: Pulmonary embolism is a medical disease in most patients**

## The Key to Improving Mortality from PE is to Prevent PE

## The new world of pay for performance

1. Your prophylaxis record will be publicly reported
2. Failure to prevent = failure to get paid

## DVT/PE Prevention Strategies

- SQ heparin
- Low molecular weight heparin
- Adjusted dose coumadin
- Pneumatic compression stockings
- Fondaparinux

## So, what can we do in our practices?

- Prophylaxis, prophylaxis, prophylaxis
- High degree of suspicion
- Remember: the CT-PA is NOT a perfect test
- Avoid femoral venous catheters
- Don't miss HIT

# Clinical Case Outcome

- **Cardiac echo = no RV dysfunction**
- **Prothrombin gene mutation (heterozygous)**
- **Treatment**
  - ✓**Heparin x 5 days**
  - ✓**Coumadin for 6 months**
  - ✓**No future oral contraceptives**