DVT/PE

Opposing Factors

- 75% of patients who present with suspected DVT/PE DO NOT have these conditions
- Untreated (UNDIAGNOSED) DVT/PE can have a FATAL OUTCOME
Diagnosis of DVT

- History and physical examination are often NOT suggestive of DVT.
- Phlebitis was present in only 32% of 327 patients with documented PE in the UPET phase I and II trials.
- Homan's sign is neither sensitive nor specific for the diagnosis of DVT.
Venous Thromboembolic Disease

CAVEAT

- ALWAYS CONSIDER THE DIAGNOSIS!
- High index of suspicion
- Low threshold for diagnostic evaluation
Risk Factors for Venous Thromboembolism

ACQUIRED

- Virchow's Triad
  (stasis, venous injury, hypercoagulable)
- Prior history of thromboembolic disease
- Prior surgical history or trauma
- Immobilization/paralysis
- Cancer
- Estrogen Therapy
- Pregnancy/Postpartum
- Antiphospholipid antibody syndrome
Venous Thromboembolism

- **Interesting Factoids on Cancer and VTE**
  - Occult cancer in 0.5 - 5% of VTE pts
  - 3x more likely to get cancer in next 3 yrs if idiopathic VTE
  - 19% of cancer pts have a VTE
  - Chemo increases risk of VTE because it increases tissue factor and expression of E-selectin, thereby increasing thrombus potential
Hypercoagulable states associated with BOTH Arterial and Venous Thrombosis

- Cancer
- Myeloproliferative syndromes
- Antiphospholipid antibodies (APA)
- Hyperhomocysteinemia
- Heparin-induced thrombocytopenia.
<table>
<thead>
<tr>
<th>Established or Potential Hypercoagulable States</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Activated protein C resistance</td>
</tr>
<tr>
<td>• Alpha-macroglobulin deficiency</td>
</tr>
<tr>
<td>• Anticardiolipin antibodies</td>
</tr>
<tr>
<td>• Antithrombin deficiency</td>
</tr>
<tr>
<td>• Dysfibrinogenemia</td>
</tr>
<tr>
<td>• Factor V Leiden</td>
</tr>
<tr>
<td>• Factor V deficiency/excess</td>
</tr>
<tr>
<td>• Factor VII excess</td>
</tr>
<tr>
<td>• Factor VIII excess</td>
</tr>
<tr>
<td>• Factor XI excess</td>
</tr>
<tr>
<td>• Heparin cofactor II deficiency</td>
</tr>
<tr>
<td>• Hyperhomocysteinemia</td>
</tr>
<tr>
<td>• Hyperfibrinogenemia</td>
</tr>
<tr>
<td>• Lupus anticoagulants</td>
</tr>
<tr>
<td>• PAI-1 excess</td>
</tr>
<tr>
<td>• Plasminogen deficiency</td>
</tr>
<tr>
<td>• Protein C deficiency</td>
</tr>
<tr>
<td>• Protein S deficiency</td>
</tr>
<tr>
<td>• Prothrombin G20210A</td>
</tr>
<tr>
<td>• tPA deficiency</td>
</tr>
<tr>
<td>• TFPI deficiency</td>
</tr>
<tr>
<td>• Thrombomodulin deficiency</td>
</tr>
</tbody>
</table>

PAI-1=plasminogen activator inhibitor-1; TFPI=tissue factor pathway inhibitor; tPA=tissue plasminogen activator
Table 1:

<table>
<thead>
<tr>
<th>Hypercoagulable State</th>
<th>General Population (%)</th>
<th>Patients with Single VTE (%)</th>
<th>Thrombophilic Families (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Factor V Leiden</td>
<td>3-7</td>
<td>20</td>
<td>50</td>
</tr>
<tr>
<td>Prothrombin G20210A</td>
<td>1-3</td>
<td>6</td>
<td>18</td>
</tr>
<tr>
<td>Antithrombin deficiency</td>
<td>0.02</td>
<td>1</td>
<td>4-8</td>
</tr>
<tr>
<td>Protein C deficiency</td>
<td>0.2-0.4</td>
<td>3</td>
<td>6-8</td>
</tr>
<tr>
<td>Protein S deficiency</td>
<td>N/A</td>
<td>1-2</td>
<td>3-13</td>
</tr>
<tr>
<td>Hyperhomocysteinemia</td>
<td>5-10</td>
<td>10-25</td>
<td>N/A</td>
</tr>
<tr>
<td>Antiphospholipid antibodies</td>
<td>0-7</td>
<td>5-15</td>
<td>N/A</td>
</tr>
</tbody>
</table>

N/A=not readily available or unknown.
**Heparin-Induced Thrombocytopenia & Thrombosis Syndrome (up to 30%)**

<table>
<thead>
<tr>
<th>Site</th>
<th>Venous, occasional arterial</th>
</tr>
</thead>
</table>
| **Mech**      | Heparin-dependent IgG has and Fc receptor that causes platelets to aggregate together  
                 -starts 3-14 days after initiation of heparin |
| **Dx**        | -suspect if plts ↓ by 50% or if Plts<100K  
                 -suspect if thrombosis in unusual area  
                 -ELISA usually used, but SRA more accurate |
| **Tx**        | -stop all heparin, including flushes  
                 -coumadin only if initially used w/ other anticoagulant due to initial prothrombotic state  
                 -cannot use LMW heparin (92% cross-reactivity)  
                 -Hirudin or argatroban or abciximab |
Diagnostic studies for DVT

1. Impedance plethysmography (IPG)
2. Doppler Ultrasound (DUS)
3. Contrast venography
4. I-125 Fibrinogen scan
D-Dimer for diagnosis of DVT/PE

- D-dimer is generated from degradation of circulating, crosslinked fibrin

- The test is elevated in patients with acute venous thrombosis
D-Dimer for diagnosis of DVT/PE

- Several assays are available to determine D-dimer levels
- Most common assays are ELISA and Latex Agglutination
<table>
<thead>
<tr>
<th>ELISA</th>
<th>LATEX</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quantitative</td>
<td>Semi Quant</td>
</tr>
<tr>
<td>Slow (hours)</td>
<td>Rapid (minutes)</td>
</tr>
<tr>
<td>Detects low levels</td>
<td>Needs higher levels</td>
</tr>
</tbody>
</table>

### D-Dimer Assay Characteristics

- **ELISA**
  - Qualitative
  - Slow (hours)
  - Detects low levels

- **LATEX**
  - Semi Quantitative
  - Rapid (minutes)
  - Needs higher levels
## D-Dimer Assay Characteristics

<table>
<thead>
<tr>
<th></th>
<th>ELISA</th>
<th>LATEX</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>97%</td>
<td>79%</td>
</tr>
<tr>
<td>Specificity</td>
<td>38% (high FP)</td>
<td>71%</td>
</tr>
</tbody>
</table>
**D-Dimers**

**Valuable screening test**

- High sensitivity; low specificity
  - Helpful only if *Negative*
  - *Strong Negative Predictive Value*—*Rules out PE when low probability*

- Safe, noninvasive
- Rapid, inexpensive
Treatment of DVT

- Intravenous Heparin
- SQ Low-molecular-weight heparin
- ? Thrombolytic Therapy
  Prevent post-phlebitic syndrome
  Perhaps for proximal obstructive DVT
- Oral Coumadin
Comparison of Fractionated and LMW Heparin

**Unfractionated**
- heterogeneous mixture of polysaccharide chains
- 3,000 to 30,000 MW

**LMW Heparin**
- Fragments of unfractionated heparin
- chemical or enzymatic degradation
- Multiple fragments
- (5,000 MW)
## Commercially Available LMWH

<table>
<thead>
<tr>
<th>Generic</th>
<th>Trade</th>
<th>MW</th>
<th>anti Xa/IIa</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dalteparin</td>
<td>Fragmin</td>
<td>5000</td>
<td>4</td>
</tr>
<tr>
<td>Exoxaparin</td>
<td>Lovenox</td>
<td>3800</td>
<td>3</td>
</tr>
<tr>
<td>Nadroparin</td>
<td>Fraxiparin</td>
<td>4500</td>
<td>2</td>
</tr>
<tr>
<td>Reviparin</td>
<td>Clivarin</td>
<td>4000</td>
<td>4</td>
</tr>
<tr>
<td>Tinzaparin</td>
<td>Innohep</td>
<td>4900</td>
<td>2</td>
</tr>
<tr>
<td>Certoparin</td>
<td>Sandoparin</td>
<td>7600</td>
<td>2</td>
</tr>
<tr>
<td>Parvoparin</td>
<td>Fluxum</td>
<td>5000</td>
<td>3</td>
</tr>
</tbody>
</table>
Low Molecular Weight Heparin

ADVANTAGES

- Longer half life
- Predictable dose response
- No lab monitoring
- Fixed dosing
- Less thrombocytopenia
# Monitoring Requirements of Anticoagulants

<table>
<thead>
<tr>
<th>Indication</th>
<th>Monitoring Requirement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prophylaxis</td>
<td>None</td>
</tr>
<tr>
<td>Treatment</td>
<td>APTT</td>
</tr>
<tr>
<td></td>
<td>None</td>
</tr>
</tbody>
</table>

*Check antiXa level in renal insufficiency, wt < 50 or > 80 kg*
Low M. Wt. Heparin for out patient TX of DVT

Two large randomized trials of selected patients with proximal DVT

Levine NEJM 1996; 334:677-81
Koopman NEJM 1996; 334:682-7

Showed that outpatient treatment with LMWH was as safe and effective as inpatient UH IV
## Results of a Randomized Trial Comparing Outpatient LMWH to Inpatient UH for DVT (LEVINE et al)

<table>
<thead>
<tr>
<th>EVENT</th>
<th>LMWH (N=247)</th>
<th>UH (N=253)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recurrent Thromboembolism</td>
<td>5.3 %</td>
<td>6.7 %</td>
</tr>
<tr>
<td>Major Bleeding</td>
<td>0.5 %</td>
<td>2.0 %</td>
</tr>
<tr>
<td>Death</td>
<td>6.9 %</td>
<td>8.0 %</td>
</tr>
</tbody>
</table>
### Results of a Randomized Trial Comparing Outpatient LMWH to Inpatient UH for DVT (KOOPMAN et al)

<table>
<thead>
<tr>
<th>EVENT</th>
<th>LMWH (N=202)</th>
<th>UH (N=198)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recurrent Thromboembolism</td>
<td>6.9 %</td>
<td>8.5 %</td>
</tr>
<tr>
<td>Major Bleeding</td>
<td>2.0 %</td>
<td>1.2 %</td>
</tr>
<tr>
<td>Death</td>
<td>4.0 %</td>
<td>6.3 %</td>
</tr>
</tbody>
</table>
COUMADIN
Clinical Points (1)

- Use INR (2.0 to 3.0)
- When starting coumadin, you must continue heparin for at least **FOUR DAYS**.
- Reason: Coumadin reduces protein c and Factor VII levels more quickly than the other Vit K factors - hypercoagulable
<table>
<thead>
<tr>
<th>Condition</th>
<th>Duration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calf Vein</td>
<td>3 to 6 months</td>
</tr>
<tr>
<td>DVT with transient risk</td>
<td>4 to 6 weeks or until risk resolves</td>
</tr>
<tr>
<td>DVT with cancer</td>
<td>3 to 6 months plus</td>
</tr>
<tr>
<td>Recurrent DVT</td>
<td>Indefinite (life)</td>
</tr>
</tbody>
</table>
Prothrombin Time and the INR (International Normalized Ratio)

- Thromboplastins from different animals or manufactures have significant effects on the PT obtained in different laboratories.

- The INR has been adopted as a method for standardizing the PT results from different laboratories.
INR = \left( \frac{PT \text{ (patient)}}{PT \text{ (group normals)}} \right)^{ISI}

ISI = International Sensitivity Index
Adjustment for the sensitivity of each type of thromboplatin
# Recommendations for Use of INR

<table>
<thead>
<tr>
<th>Clinical State</th>
<th>Recommended INR</th>
</tr>
</thead>
<tbody>
<tr>
<td>DVT/PE</td>
<td>2.0 to 3.0</td>
</tr>
<tr>
<td>Prosthetic Valve</td>
<td>2.5 to 3.5</td>
</tr>
</tbody>
</table>
Studies suggest that nearly every patient with thrombus in the upper leg or thigh will have a PE if a sensitive enough test is done to look for it.

Current techniques allow us to demonstrate PE in 60-80% of these patients, even though about half have no clinical symptoms to suggest PE.
Sources of Pulmonary Emboli

DVT

Propagation from calf vein thrombi

Pelvic vein thrombi

Caval Thrombi

Renal vein thrombi

Right heart thrombi

Upper extremity thrombi
Autopsy Specimens of Venous Thrombi

"Hmmm... Sounds grave, very grave. We'll know more after the autopsy!"
Clinical Syndromes

- Pts with **massive PE** present with systemic arterial hypotension and evidence of peripheral thrombosis
- Pts with **moderate PE** will have right ventricular hypokinesis on echocardiogram but normal systemic arterial pressure
- Pts with **small** to moderate PE have both normal right heart function and normal systemic arterial pressure
THE SPECTRUM OF PULMONARY EMBOLISM

- Stable hemodynamics
- RV dysfunction
- Hemo-dynamic instability
Clinical Signs and Symptoms of Pulmonary Embolism

Dyspnea
Hemoptysis
Chest pain
Tachypnea
Tachycardia
Syncope
Hypotension
# Wells’ Criteria for Assessment of Pretest Probability

The Wells Criteria for assessing pretest probability is important for diagnosing DVT and PE. Below describes the criteria and scoring system:

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Suspected DVT</td>
<td>3.0</td>
</tr>
<tr>
<td>An alternative diagnosis is less likely than PE</td>
<td>3.0</td>
</tr>
<tr>
<td>Heart rate &gt; 100 beats per minute</td>
<td>1.5</td>
</tr>
<tr>
<td>Immobilization or surgery in the previous four weeks</td>
<td>1.5</td>
</tr>
<tr>
<td>Previous DVT or PE</td>
<td>1.5</td>
</tr>
<tr>
<td>Hemoptysis</td>
<td>1.0</td>
</tr>
<tr>
<td>Malignancy (on treatment, treated in the past six months or palliative)</td>
<td>1.0</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Score range</th>
<th>Mean probability of PE</th>
<th>% with this score</th>
<th>Interpretation of risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;2 points</td>
<td>3.6%</td>
<td>40</td>
<td>Low</td>
</tr>
<tr>
<td>2 to 6 points</td>
<td>20.5%</td>
<td>53</td>
<td>Moderate</td>
</tr>
<tr>
<td>&gt;6 points</td>
<td>66.7%</td>
<td>7</td>
<td>High</td>
</tr>
</tbody>
</table>

### Table 1. Modified Wells Criteria for PE

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical signs of DVT</td>
<td>3.0</td>
</tr>
<tr>
<td>An alternate diagnosis is less likely than PE</td>
<td>3.0</td>
</tr>
<tr>
<td>Heart rate &gt;100 beats per minute</td>
<td>1.5</td>
</tr>
<tr>
<td>Immobilization or surgery in past 4 weeks</td>
<td>1.5</td>
</tr>
<tr>
<td>Previous DVT or PE</td>
<td>1.5</td>
</tr>
<tr>
<td>Hemoptysis</td>
<td>1.0</td>
</tr>
<tr>
<td>Malignancy (being treated, treated in past 6 months, or palliative)</td>
<td>1.0</td>
</tr>
</tbody>
</table>

### Traditional Clinical Probability Assessment

<table>
<thead>
<tr>
<th>Points</th>
<th>Probability of PE</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-1</td>
<td>Low probability</td>
</tr>
<tr>
<td>2-6</td>
<td>Moderate probability</td>
</tr>
<tr>
<td>&gt;6</td>
<td>High probability</td>
</tr>
</tbody>
</table>

### Simplified Clinical Probability

<table>
<thead>
<tr>
<th>Probability of PE</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>PE likely</td>
<td>&gt;4</td>
</tr>
<tr>
<td>PE unlikely</td>
<td>≤4</td>
</tr>
</tbody>
</table>
BioMarkers in Pulmonary Embolism

**BNP**

- Normal BNP: Benign Prognosis
- Elevated BNP associated with adverse outcome
- Other causes of elevated BNP in RV pressure overload:
  - Primary pulmonary hypertension
  - Chronic thromboembolic pulmonary hypertension
  - Chronic lung disease

*Circulation. 2003 Apr 1;107(12):1576-8*
BioMarkers in Pulmonary Embolism

Troponin

- In acute pulmonary embolism elevated troponin levels have been shown to predict an adverse outcome.

- Serum troponin levels should help stratify patients with submassive acute pulmonary embolism into a group in which aggressive medical or surgical intervention would be considered.

Techniques for diagnosis of PE

- EKG
- Chest Radiographs
- Echocardiogram
- V/Q Scans
- Helical CT
- MRI
EKG Findings of Pulmonary Embolism

- Tachycardia
- T-wave changes
- ST-segment changes
- Right axis deviation
- S1-Q3-T3
- RBBB
- p-pulmonale
Echocardiogram

- Useful for rapid triage of pts
- Assess right and left ventricular function
- Diagnostic of PE if hemodynamics by echo are consistent with clinical hx
Echocardiogram

- TEE more sensitive than TTE
- Demonstrate intracardiac clot or signs of right ventricular failure
- Emboli observed = 42-50% mortality rate
- Indirect evidence
  - right ventricular dilation
  - dilated pulmonary artery
  - abnl right ventricular wall motion
  - dilated vena cava
Right Ventricular Dysfunction

- Progressive right heart failure is the usual immediate cause of death from PE
- As pulmonary vascular resistance increases, right ventricular wall tension rises and perpetuates further right ventricle dilation and dysfunction
- Interventricular septum bulges into and compresses the normal left ventricle
Echocardiogram suggesting a PE. Diastole on the left, systole on the right.
MORTALITY with RV DYSFUNCTION

Chest X-Ray Findings of Pulmonary Embolism

NORMAL
Atelectasis
Pleural Effusion
Infiltrate
Elevated diaphragm
Hampton's hump
Westermark's sign
Westermark’s Sign
Hamptons
Hump
Pulmonary Infarction

Hampton’s Hump
V/Q Scan

Historically, the principal imaging test for the diagnosis of PE

- A perfusion defect indicates absent or decreased blood flow
- Ventilation scan obtained with radiolabeled gases
- A high probability scan is defined as two or more segmental perfusion defects in presence of normal ventilation scan
High Probability V/Q Scan

**Lung Perfusion**
- Rt Lat
- Anterior
- Lt Lat
- LPO
- Posterior
- RPO

**Lung Ventilation**
- Breath hold 15 sec
- Equilibrium
- LPO
- RPO
V/Q Scan

- Useful if the results are normal or near normal, or if there is a high probability for PE
  - As many as 40% of pts with high clinical suspicion for PE and low probability scans have a PE on angiogram
V/Q Lung Scan

- Normal V/Q Sensitivity 99%
  - Rules out PE
- High Prob V/Q Specificity 96%
  - Rules in PE
- But, >60% nondiagnostic
- Takes >2 hr to perform
- Not available at all times
Results from PIOPED V/Q (n=755)
255/755 (31%) had PE at Angiogram

<table>
<thead>
<tr>
<th>SCAN</th>
<th>INCIDENCE</th>
<th>+Predictive Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>HIGH</td>
<td>13 %</td>
<td>88 %</td>
</tr>
<tr>
<td>INTERMEDIATE</td>
<td>39 %</td>
<td>33 %</td>
</tr>
<tr>
<td>LOW</td>
<td>34 %</td>
<td>16 %</td>
</tr>
<tr>
<td>VERY LOW</td>
<td>14 %</td>
<td>9 %</td>
</tr>
</tbody>
</table>
**Treatment Algorithm**

*based on PIOPED Results*

**Normal Scan:**
No Treatment

V/Q Scan Findings

- **High**
  - Treat Heparin

- **Intermediate**
  - PAgarm

- **Low**
  - PAgarm
  - Low Low Clinical Suspicion
  - No Treat
CT Pulmonary Angiogram

- Identifies proximal PE (which are the ones usually hemodynamically important)
- Not as accurate with peripheral PE
# CT Angiogram

<table>
<thead>
<tr>
<th>TESTS</th>
<th>Accuracy</th>
<th>False Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Helical CT alone</td>
<td>70%</td>
<td>30%</td>
</tr>
<tr>
<td>CT plus Negative US</td>
<td>87%</td>
<td>21%</td>
</tr>
<tr>
<td>CT plus Neg US plus V/Q</td>
<td>94%</td>
<td>5%</td>
</tr>
</tbody>
</table>
CT Angiogram

- Prospective study of consecutive, nonselected patients in a Geneva ER included 299 with suspected PE
- 39% had confirmed PE
  - High prob V/Q, +US, or +Angio
- **CT Sensitivity 70%**
- **CT Specificity 91%**

Spiral CT for Dx PE
Spiral CT for Dx PE
# Spiral CT for PE

<table>
<thead>
<tr>
<th>Author</th>
<th>#pt / #PE</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Remy-Jardin</td>
<td>42 / 18</td>
<td>100</td>
<td>96</td>
</tr>
<tr>
<td>1992</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Remy-Jardin</td>
<td>72 / 39</td>
<td>91</td>
<td>78</td>
</tr>
<tr>
<td>1996</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Van Rossum</td>
<td>77 / 39</td>
<td>95</td>
<td>97</td>
</tr>
<tr>
<td>1996</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sostman 1996</td>
<td>28 / 21</td>
<td>73</td>
<td>97</td>
</tr>
<tr>
<td>Goodman 1996</td>
<td>20 / 11</td>
<td>86</td>
<td>92</td>
</tr>
<tr>
<td>Mayo 1995</td>
<td>139 / 46</td>
<td>87</td>
<td>95</td>
</tr>
<tr>
<td>Drucker 1998</td>
<td>47 / 15</td>
<td>60</td>
<td>81</td>
</tr>
</tbody>
</table>
Pulmonary Embolism by CT
MRI/MRA

- No radiation or contrast exposure
- Expensive
- Not uniformly available
- Limited data
- Role not established
Pulmonary Angiogram

- Most specific test available for diagnosis of PE
- Can detect emboli as small as 1-2 mm
- Most useful when the clinical likelihood of PE differs substantially from the lung scan or CTPA results
## Pulmonary Angiography

### Diagnostic Findings

<table>
<thead>
<tr>
<th>Diagnostic Findings</th>
<th>Intraluminal filling defects</th>
<th>Vascular Cutoffs</th>
</tr>
</thead>
</table>

In general, PIOPED has made PAgram MORE NECESSARY.
Pulmonary angiogram
Pulmonary angiogram
Treatment of Pulmonary Embolism

- Intravenous Heparin (most common treatment)
- SQ Low-molecular-weight heparin
- Thrombolytic Therapy (for massive PE with shock)
- Caval Interruption
## Low Molecular Weight Heparin Preparations

<table>
<thead>
<tr>
<th>PREPARATION</th>
<th>MW</th>
<th>AntiXa/IIa Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ardeparin (Normiflo)</td>
<td>6000</td>
<td>1.9</td>
</tr>
<tr>
<td>Dalteparin (Fragmin)</td>
<td>6000</td>
<td>2.7</td>
</tr>
<tr>
<td>Enoxaparin (Lovenox)</td>
<td>4200</td>
<td>3.8</td>
</tr>
<tr>
<td>Naroparin (Fraxiparin)</td>
<td>4500</td>
<td>3.6</td>
</tr>
<tr>
<td>Reviparin (Clivarine)</td>
<td>4000</td>
<td>3.5</td>
</tr>
<tr>
<td>Tinzaparin (Innohep)</td>
<td>4500</td>
<td>1.9</td>
</tr>
</tbody>
</table>
Plasma Half-life of LMW Heparin

- Plasma half-life of LMW heparin is 2 to 4 times that of unfractionated heparin
- **Intravenous** - 2 to 4 hours
- **Subcutaneous** - 3 to 6 hours
**LMWH in the Treatment of Venous Thromboembolism**

- The Columbus Investigators NEJM 1997; 337:657-62
- 1,021 patients randomly - about 1/3 had PE
- Fixed dose, LMWH (reviparin) or Adjusted dose, UH, IV
- Followed for 12 weeks
Results of a Randomized Trial Comparing LMWH to UH for DVT/PE
The Columbus Investigators

<table>
<thead>
<tr>
<th>EVENT</th>
<th>LMWH (N=510)</th>
<th>UH (N=511)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recurrent Thromboembolism</td>
<td>5.3 %</td>
<td>4.9 %</td>
</tr>
<tr>
<td>Major Bleeding</td>
<td>3.1 %</td>
<td>2.3 %</td>
</tr>
<tr>
<td>Death</td>
<td>7.1 %</td>
<td>7.6 %</td>
</tr>
</tbody>
</table>
**LMWH vs UH for Acute Pulmonary Embolism**

Simonneau et al. NEJM 1997; 337:663-9

612 pts with acute PE

- 304 pts SQ LMWH (tinzaparinin)
  175 U/kg/day - once
- 308 pts IV UH - adjusted
- coumadin - 3 month follow-up
LMWH vs UH for PE
(Simonneau et al)
Lytic Therapy for PE

When and Who

- Higher risk of bleed and higher cost than heparin

- When lytic Tx and heparin were compared, the mortality and degree of clot lysis were about the same by day 5.

- When rapid clot lysis is essential (i.e. hemodynamic instability) lytic therapy is warranted.
<table>
<thead>
<tr>
<th>AGENT</th>
<th>Dosage Regimen</th>
</tr>
</thead>
<tbody>
<tr>
<td>STREPTOKINASE</td>
<td>250,000 U IV loading dose over 30 min then 100,000 U/Hr for 24 hrs</td>
</tr>
<tr>
<td>UROKINASE</td>
<td>2,000 U/lb IV loading dose over 10 min then 2,000 U/lb/Hr for 12 to 24 Hr</td>
</tr>
<tr>
<td>TISSUE PLASMINOGEN</td>
<td>100 mg IV over 2 Hr</td>
</tr>
<tr>
<td>ACTIVATOR</td>
<td></td>
</tr>
</tbody>
</table>
Contraindications to Systemic Thrombolytic Therapy

**ABSOLUTE**

- Previous hemorrhagic CVA
- Intracranial Neoplasm
- Head Trauma or neurosurgery
- Active/recent internal bleeding

**RELATIVE**

- Bleeding diathesis
- Uncontrolled severe hypertension
- CPR
- Pregnancy
- Nonhemorrhagic CVA
Indications for Vena Caval Interruption

1. Contraindication to anticoagulation
2. Recurrent emboli on adequate Tx
3. Serious bleeding on anticoagulation
4. Massive pulmonary embolism
5. Psychosocial reasons
Embolectomy in Acute PE

METHODS

1. Surgical Embolectomy
   Requires Bypass
   High morbidity and mortality emergently?
   In-house
   Reserved for refractory patients

2. Catheter Embolectomy (fragmentation)
   No Bypass
   Can be done in-house
   Less technical expertise
Pulmonary embolism

Haemodynamically unstable

Thrombolysis contraindicated

No

Thrombolysis + ?
inferior vena cava filter

Consider: catheter embolectomy or surgical embolectomy

Yes

Haemodynamically stable

Anticoagulation contraindicated

No

Inferior vena cava filter

Yes

Anticoagulate: intravenous unfractionated heparin or subcutaneous low molecular weight heparin plus warfarin started day 1-3

Recurrent pulmonary embolism