PULMONARY EMBOLISM

PULMONARY EMBOLISM

INTRODUCTION

- 2/3 patients remained undiagnosed
- A mortality rate up to 30% if untreated due to recurrent embolization primarily and 2-8 % mortality if well treated
- Often occurring as a terminal event with comorbid disease

PULMONARY EMBOLISM

PATHOPHYSIOLOGY (1)

- Originate primarily from deep venous system of lower extremities
- Ilio-femoral thrombi and pelvic veins appear to be the most clinically recognized source
- Air, amniotic fluid and fat emboli are rarer causes

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PATHOPHYSIOLOGY (2)

The commonest scenario is a patient with a risk factor who becomes breathless suddenly, with a normal CxR and perhaps mild hypoxia, and no obvious cause

Most pulmonary thrombi are multiple, with the lower lobes being involved in the majority

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CLINICAL CHARACTERISTICS (1)

Risk factors for deep venous thromboembolism:

Triad of Virchow's

- **Endothelial injury**
- **Stasis**
- **Hypercoagulation status**

The last 2 components predominate in venous thrombosis

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CLINICAL CHARACTERISTICS (2)

- Most PE are small, and infarcts are usually associated with small PE
- Small embolism may produce dyspnea, pleuritic chest pain, and occasionally hemoptysis
- Small embolism will reach the periphery of the lung, sometimes producing wedge-shaped shadow on CxR, and may cause pulmonary infarction

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CLINICAL CHARACTERISTICS (3)

- A large embolism suddenly obstructing a major pulmonary vessel has marked effects on cardiac function, often associated with anterior chest pain and collapse
- Pulmonary infarct following a large embolism is less common
- A distinguish between small and large embolism is important

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CLINICAL CHARACTERISTICS (4)

Chronic recurrent pulmonary embolism may develop pulmonary hypertension and right ventricular failure

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CLINICAL CHARACTERISTICS (5)

The most common risk factors identified in the PIOPED study:

1. **Immobilization**
2. **Surgery or trauma within the last 3 months**
3. **Increasing age**
4. **Malignancy**

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CLINICAL CHARACTERISTICS (6)

Idiopathic or primary venous thromboembolism should be further evaluated for the underlying abnormalities

For example: pancreatic cancer

prostate cancer

late in the course of breast, lung, uterine, or brain malignancies

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CLINICAL CHARACTERISTICS (7)

- Heart failure and underlying cardiac disease usually are associated with infarct formation

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CLINICAL CHARACTERISTICS (8)

Coagulation Factors

Resistance to activated protein C is found in Caucasians and occurs in 21% of patients with venous thromboembolic events

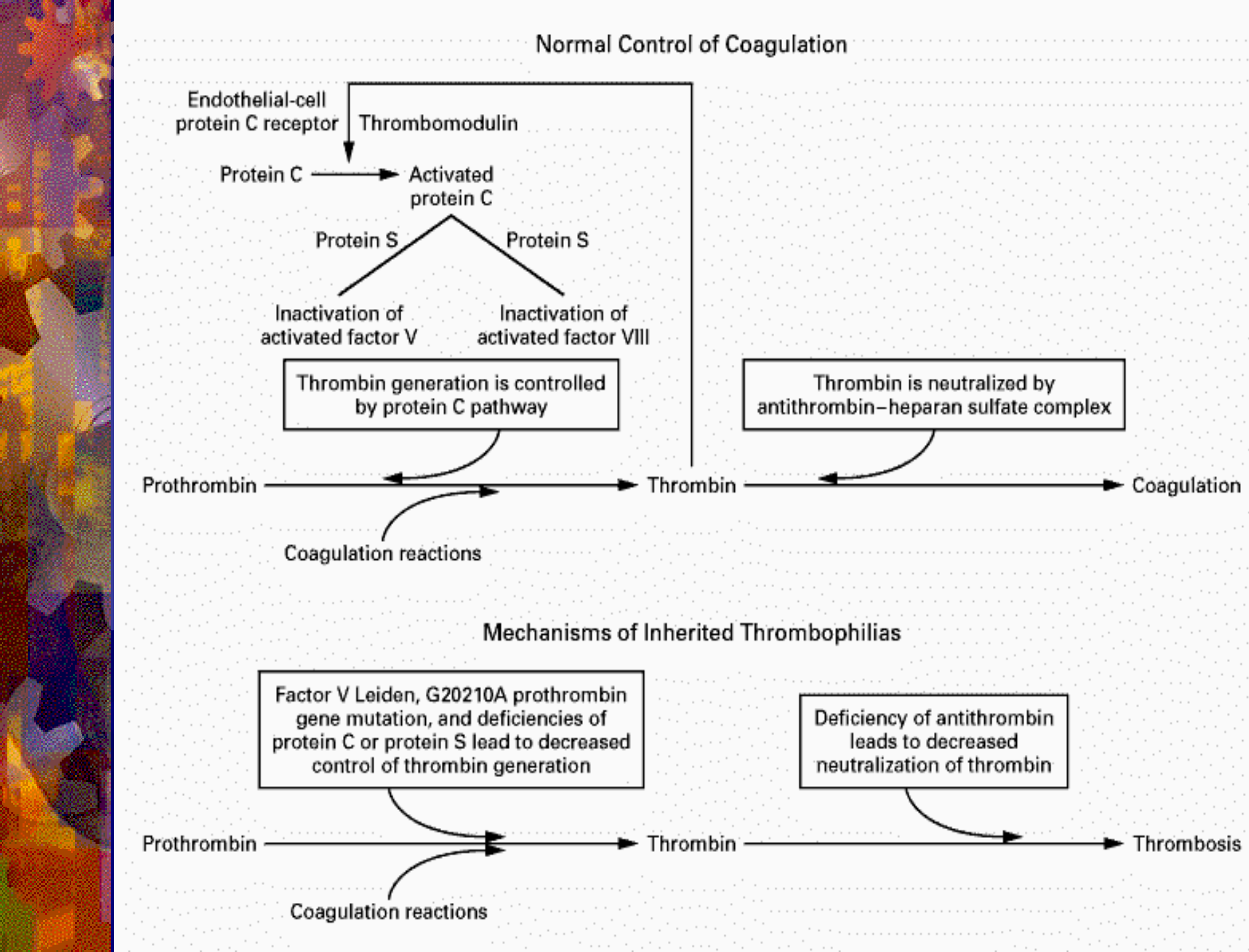
Normal Control of Coagulation
Endothelial-cell protein C receptor
Thrombomodulin
Protein C
Activated protein C
Protein S
Protein S
Inactivation of activated factor V
Inactivation of activated factor VIII
Thrombin generation is controlled by protein C pathway
Thrombin is neutralized by antithrombin–heparan sulfate complex
Prothrombin
Thrombin
Coagulation
Coagulation reactions
Mechanisms of Inherited Thrombophilias
Factor V Leiden, G20210A prothrombin gene mutation, and deficiencies of protein C or protein S lead to decreased control of thrombin generation
Deficiency of antithrombin leads to decreased neutralization of thrombin
Prothrombin
Thrombin
Thrombosis
Coagulation reactions

TABLE 1. INHERITED AND ACQUIRED CAUSES OF VENOUS THROMBOSIS.

Inherited
Common
G1691A mutation in the factor V gene (factor V Leiden)
G20210A mutation in the prothrombin (factor II) gene
Homozygous C677T mutation in the methylenetetrahydrofolate reductase gene
Rare
Antithrombin deficiency
Protein C deficiency
Protein S deficiency
Very rare
Dysfibrinogenemia
Homozygous homocystinuria
Probably inherited
Increased levels of factor VIII, factor IX, factor XI, or fibrinogen*
Acquired
Surgery and trauma
Prolonged immobilization
Older age
Cancer
Myeloproliferative disorders
Previous thrombosis
Pregnancy and the puerperium
Use of contraceptives or hormone-replacement therapy
Resistance to activated protein C that is not due to alterations in the factor V gene
Antiphospholipid antibodies
Mild-to-moderate hyperhomocysteinemia

*Levels of factor VIII and fibrinogen may also increase as part of the acute-phase response.

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SYMPTOMS AND SIGNS (1)

- Autopsy revealed that many pulmonary emboli are silent
- Less than 30% patients had S/S of lower extremity venous thrombosis

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SYMPTOMS AND SIGNS (2)

Without previous cardiopulmonary disease in PIOPED, the following frequency of S/S was noted:

SYMPTOMS	SIGNS
Dyspnea (84%)	Tachypnea (70%)
Pleuritic pain (74%)	Rales (51%)
Anterior chest pain (68%)	Tachycardia (30%)
Cough (53%)	S4 (24%)
Hemoptysis (30%)	Accentuated P2
Asymptomatic (10%)	

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SYMPTOMS AND SIGNS (3)

Symptoms of cardiac compromise are important and indicate a large PE, including collapse or dizziness on standing, severe dyspnea and severe anterior chest pain

Signs of right heart strain should prompt early, rapid action

DIFFERENTIAL DIAGNOSIS OF PULMONARY EMBOLISM

Differential diagnosis of any PE

- AMI
- Pneumonia
- Asthma
- Pneumothorax
- CHF and Acute Pulmonary Edema
- Tachyarrhythmia
- Pleurisy/Pericarditis
- Musculoskeletal/ rib fracture
- Lobar collapse, e.g. secondary to tumor

Differential diagnosis of large PE

- AMI
- Acute Pulmonary Edema
- Pericardial tamponade
- Hypovolemia
- Sepsis
- Aortic Dissection

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LAB ABNORMALITIES

- Nonspecific: leukocytosis, ESR elevation, LDH, SGOT elevation with normal bilirubin
- CK, CK-MB or Troponin-I should be checked to rule out AMI
- ABG usually revealed hypoxemia, hypocapnia, with respiratory alkalosis
- Respiratory collapse and hypotension due to massive pulmonary embolus may reveal combined respiratory and metabolic acidosis

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ECG CHANGES

ECG most commonly revealed nonspecific ST segment and T wave changes in submassive PE

More severe right ventricular dysfunction with obstruction of more than 50% of pulmonary vasculature in a previously healthy patient may reveal T wave inversion in the precordial leads V1-V3 or P pulmonale, RAD, RBBB

S1Q3T3 (seen in only 25% of large PE: Stein et al), or sinus tachycardia can also be found. On occasion, PE can precipitate atrial flutter or AF

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RADIOGRAPHY

- Atelectasis or a pulmonary parenchymal abnormality is the most frequent radiographic abnormalities
- Westermark's sign
- Hampton's hump

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CLINICAL PROBABILITY

High clinical probability (>80% chance)

- Presence of risk factors
- Radiological or ABG consistent finding, lack of evidence for another explanation

Intermediate clinical probability (20%-80% chance)

- Neither high nor low probability

Low clinical probability (<20% chance)

- No risk factors
- Clinical symptoms or signs explainable by other causes

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SPECIFIC DIAGNOSTIC STUDIES

Ventilation-Perfusion scans

It remains the first line investigation of possible PE. It should be performed in all clinically stable patients

A Ventilation-Perfusion scan is most useful when the result category is one of normal, low or high probability and is concordant with the pretest suspicion of physicians

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Likelihood of Pulmonary Embolism According to Scan Category and Clinical Probability in PIOPED Study†

Scan Category	Clinical probability of emboli		
	High	Intermediate	Low
High	95	86	56
Intermediate	66	28	15
Low	40	15	4
Near normal through normal	0	6	2

†Data from PIOPED Investigators, JAMA 1990; 263:2753.

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SPECIFIC DIAGNOSTIC STUDIES

Evaluation of DVT

It may support a diagnosis of thromboembolic disease in patients in whom a Ventilation-Perfusion scan is nondiagnosed

Noninvasive Techs in the thigh: IPG, compression ultrasonography, Venous duplex scanning (If this is positive with an intermediate probability lung scan, this is strong evidence of PE : >90% PE are secondary to DVT)

Invasive Techs: Venography (definitive diagnosis)

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SPECIFIC DIAGNOSTIC STUDIES

Pulmonary Angiography

- It should be performed whenever clinical data and noninvasive tests are equivocal or contradictory
- It is appropriate in patients with a high probability of PE by Ventilation-Perfusion scan, or if vena cava interruption or thrombolytic therapy is being considered
- It may be the appropriate initial diagnostic tests in patients with unstable hemodynamics
- It remains the gold standard investigation for PE but is invasive, time consuming, needs experienced radiologists

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SPECIFIC DIAGNOSTIC STUDIES

Pulmonary Angiography

TABLE 60-7 - INDICATIONS FOR PULMONARY ANGIOGRAPHY

When examination of clinical findings, V./Q. scan, and impedance plethysmography are inconclusive
When there are relative contraindications to anticoagulation
When thrombolytic therapy may be indicated
When inferior vena cava interruption or surgical therapy may be indicated
Recurrent pulmonary embolism, despite therapy
Young patient with uncertain predisposition to deep venous thrombosis

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SPECIFIC DIAGNOSTIC STUDIES

D-Dimer

<500 ng/ml is a powerful excluding tool for PE

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SPECIFIC DIAGNOSTIC STUDIES

SPIRAL COMPUTED TOMOGRAPHY

It may be used as a first-line investigation when V/Q Scan is delayed and when a large PE is suspected and early diagnosis is needed

It is most sensitive and specific for main, lobar and segmental vessels, but is less good at detecting peripheral emboli, which may account for up to 30% of PE

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SPECIFIC DIAGNOSTIC STUDIES

ECHOCARDIOGRAPHY

It may be helpful after a large PE in a compromised patient, as it can show right heart dilatation, occasionally thrombus and increased pulmonary arterial pressure readings if tricuspid regurgitation developed

Convenient and rapidly available

PULMONARY EMBOLISM

TREATMENT

Prevent death and morbidity acutely

Reduce the incidence of recurrence

PULMONARY EMBOLISM

TREATMENT

PREVENTION

See next Table

TABLE 60-3 - PROPHYLAXIS AGAINST DEEP VENOUS THROMBOSIS PULMONARY EMBOLISM FOR SPECIFIC PATIENT GROUPS

Patient Group	Prophylaxis
Medical or surgical patients under 40 years of age with no clinical risk factors	Early ambulation
Medical patients with one or more risk factors (Table 60-1) or surgical patients over 40 years of age undergoing major operations but with no additional risk factors	GCS; LDH every 8-12 h, fixed-dose LMWH, or IPC
Surgical patients over 40 years of age undergoing major operations and with additional risk factors	GCS; adjusted-dose subcutaneous unfractionated heparin or fixed-dose LMWH (IPC is an alternative in patients prone to hematomas or infection)
Very high risk general surgery patients with multiple risk factors	GCS; IPC and adjusted-dose subcutaneous unfractionated heparin or fixed-dose LMWH; in selected patients, perioperative warfarin (INR 2.0-3.0)
Total hip replacement	GCS; adjusted doses of warfarin (INR 2.0-3.0) or unfractionated heparin (APTT 1.5-2.5 times control 6 h after injection); when available, LMWH (without laboratory control)
Hip fractures	GCS; warfarin (INR 2.0-3.0) or LMWH
Knee surgery, neurosurgery	GCS; IPC; LMWH
Acute spinal cord injury with paralysis	GCS; adjusted-dose unfractionated heparin (APTT 31-36 s 6 h after injection); LMWH; low-dose warfarin (INR 2.0-3.0)
Multiple trauma	GCS; IPC; warfarin (INR 2.0-3.0); LMWH
Myocardial infarction	GCS; LDH (IVH if anterior infarct or increased risk factors); IPC if heparin is contraindicated
Ischemic stroke with lower extremity paralysis	GCS; LDH (alternative: LMWH, IPC, warfarin)
Long-term indwelling central vein catheter	GCS; warfarin, 1 mg/day
Hip or knee surgery in high-risk patients with history of serious, previous pulmonary embolism	GCS; warfarin; consider prophylactic inferior vena cava filter

Note: GCS, graded compression stockings; LDH, low-dose subcutaneous heparin; LMWH, low-molecular-weight heparin; IPC, intermittent pneumatic compression; INR, International Normalized Ratio; APTT, activated partial thromboplastin time; IVH, intravenous heparin.

Source: Modified from Dalen and Hirsh.27

PULMONARY EMBOLISM

TREATMENT

PRIMARY TREATMENT

- Supplemental oxygen for hypoxemia if the PE is small
- Specific treatment is with intravenous heparin infusion following an initial bolus dose of 5000 units
- aPTT should be monitored 4-6 hours after initiation, 6-10 hours after any dosage change, then daily with a target of 1.5-2.5 times normal
- Heparin does not reduce acute mortality but significantly reduces further events

PULMONARY EMBOLISM

TREATMENT

PRIMARY TREATMENT

- LMWH are now first line treatment for DVT and are as effective as Heparin IVD
- LMWH could be used as an alternative choice of Heparin IVD in PE as 30mg, sc, bid
- If the PE is large, supportive treatments for hypotention or reduced CO should be given IVF, Levophed, or Dopamine
- Spiral CT should be performed if the patient is once stable

PULMONARY EMBOLISM

TREATMENT

THROMBOLYTIC THERAPY

- Thrombolytic therapy is used when there is significant cardiac compromise, RV strain, or hemodynamic changes not responding to IVF and vasopressor resuscitation
- Thrombolytic therapy achieves faster resolution of the thrombus and more rapid recovery of normal vascular flow than simple anticoagulation

PULMONARY EMBOLISM

TREATMENT

THROMBOLYTIC THERAPY

Cerebral hemorrhage can occur in up to 1% of cases

It has been used successfully and safely in a pregnant woman and this is not a contraindication unless immediately postpartum

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Regimens for Thrombolysis in Pulmonary Embolus

DRUG	REGIMEN
Streptokinase	250 000 UNITS IN 20-3- MINUTES FOLLOWED BY 100 000 UNITS/HOUR UP TO 24 HOURS
t-PA	10 MG INTRAVENOUSLY OVER 1-2 MINUTES FOLLOWED BY AN INFUSION OF 90 MG OVER 2 HOURS

PULMONARY EMBOLISM

TREATMENT

PULMONAY EMBOLECTOMY

This is reserved for severe cardiac compromise where thrombolysis has either failed or is contraindicated

It requires an experienced team to be successful and, although used infrequently, small studies (Doerge et al, 1999) have shown favorable outcomes

PULMONARY EMBOLISM

TREATMENT

SECONDARY PREVENTION

Oral anticoagulants (and LMWH subcutaneously)

Vena cava filters

PULMONARY EMBOLISM

TREATMENT

ANTICOAGULATION

- LMWH keeps aPTT between 1.5-2 for 5-10 days when warfarin is contraindicated (e.g. pregnancy)
- Oral warfarin can be given with the initiation of Heparin keep INR between 2-3 with initial dose of 5mg/day for 2 days
- An overlap of 4-5 days with a therapeutic INR and aPTT is recommended
- Persistent oral warfarin should be prescribed for 3 months till the absence of risk factors

PULMONARY EMBOLISM

TREATMENT

ANTICOAGULATION

- After the first episode of PE, treatment is recommended for 3-6 months. Studies revealed that 3 months therapy is adequate (British Thoracic Society, 1992)
- Permanent anticoagulation is recommended with repeated PE unless there is an obvious reversible cause. Repeat Doppler ultrasound scans of the legs or repeat V/Q scans have been used to confirm complete resolution of thrombus before stopping anticoagulation

PULMONARY EMBOLISM

TREATMENT

ANTICOAGULATION

- Permanent anticoagulation is recommended with repeated PE unless there is an obvious reversible cause. Repeat Doppler ultrasound scans of the legs or repeat V/Q scans have been used to confirm complete resolution of thrombus before stopping anticoagulation

PULMONARY EMBOLISM

TREATMENT

INFERIOR VENA CAVA INTERRUPTION

- These have been used in patients with recurrent venous thromboembolic disease where anticoagulation is contraindicated or has been ineffective

PULMONARY EMBOLISM

TREATMENT

INFERIOR VENA CAVA INTERRUPTION

Potential Indications for Thrombolytic Therapy in Venous Thromboembolism

- Presence of hypotension related to PE†
- Presence of severe hypoxemia
- Substantial perfusion defect
- Right ventricular dysfunction associated with PE
- Extensive deep vein thrombosis

† This indication is widely accepted; the other potential indications require careful review of relative contraindications to thrombolytic therapy.