

A SURVEY OF PULMONARY THROMBOEMBOLIC DISEASE*

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Incidence

When bacterial pneumonia was conquered by antibiotic therapy, pulmonary embolism took its place as the most common serious lung disorder among Americans.

Pulmonary embolism causes 47,000 deaths per year in the U. S. The Peter Bent Brigham Hospital of Boston states it is the third most common cause of death according to their records. Embolism to the lungs is far more common; but also, on the average, rather less serious than was once thought. Recent post-mortem studies have elucidated evidence of emboli in as many as 50% of patients dying from all causes.

Smith et al studying patients at the Brigham Hospital with post mortem pulmonary arteriography found 4-5 times as many emboli than when usual gross methods were used. Emboli were invariably multiple and most frequent in the lower lobes.

50% of emboli are large enough to cause significant morbidity and mortality. 50% studied had no signs of embolism and had died from other non-related conditions.

Hampton et al investigated 370 cases of pulmonary embolism. 40% occurred post-operatively, 30% were on medical regimens for cardiac disease, 30% were non-cardiac medical patients in the same hospital.

Pulmonary emboli are closely related to the following conditions: congestive heart failure; acute myocardial infarction, especially right ventricular myocardial infarction; pelvic and prostatic surgery; women on oral contraceptives, according to Inman there is a nine-fold increase in the incidence of mortality from pulmonary emboli between pill users and non-users.

Pathophysiology and Clinical Manifestations

Pulmonary emboli may arise from thrombophlebitis or phlebothrombosis, in fact many investigators feel that the later "silent" condition actually gives rise to more. The site of the embolus is most commonly the lower extremities, but occasionally pelvic or prostatic venous channels may give rise to emboli. Less commonly the right atrium in CHF or atrial fibrillation, right ventricle in massive septal infarction, idiopathic cardiac hypertrophy, endocardial fibrosis, or fibro-elastosis. In a large retrospective study of patients dying from pulmonary embolism greater than 80% had thrombi in the veins of the lower extremity.

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Venous stasis, endothelial damage or physical and chemical properties of the blood which promote coagulation are considered to be the most important causative mechanisms. Fibrin is the major component of venous thrombi, while platelets are dominant in arterial thrombosis. This becomes an important distinction when consideration of therapy is discussed.

Evidence accumulated points to transient rises of venous pressure being implicated in the dynamics of dislodgement of thrombi giving subsequent use to pulmonary emboli. Experimental evidence has shown that most large emboli are fragmented in the right ventricle; it is for this reason that massive or saddle emboli, blocking the bifurcation of the pulmonary artery are uncommon. Most often emboli are multiple and block smaller subdivisions of the pulmonary vascular tree. Pulmonary infarction does not occur when the main pulmonary or its primary division or very small vessels are occluded. It is most likely to occur if a medium-sized pulmonary arterial branch is occluded, or if there is preexistent pulmonary stasis and the patient survives more than two days. In general, pulmonary infarction occurs in about 10% of patients with pulmonary embolism.

Experimental studies have shown that infarction is not dependent on mechanical blockage of an artery, but also depends on some undetermined factor in the embolus. Thus, emboli containing extracts from fatal human embolus caused typical pulmonary infarcts, whereas atelectasis but no infarction occurred in experimental emboli prepared from ordinary clots of human blood. Other studies have implicated antigen-antibody reactions in the evolution of infarcts.

Experimental evidence shows that serious circulatory disturbances in the lung occur only after 65% of the pulmonary circulatory cross-sectional area is cut-off and that death usually follows 85% obstruction. Factors which have been cited to explain death in patients with fatal embolization involving less than 85% are as follows: reflex pulmonary vasoconstriction mediated through neurohumeral mechanisms; myocardial ischaemia mediated by sudden fall in cardiac out-put or caused by the so-called pulmono-coronary reflex, by way of the vagus nerve; or impaired coronary drainage by way of thebesian vessel due to the rise in right ventricular and diastolic pressure. The weight of evidence, according to Freidberg, however, still favours extensive mechanical obstruction with increased resistance to flow and subsequent drop in right ventricular output.

Bronchospasm is frequently seen in pulmonary embolism. Indeed in few patients the admitting symptoms may only be that of asthmatic-like wheezes. Since the bronchospasm appears related to the site of occlusion it was originally thought to be due to a local neurogenic effect. Subsequent studies, however, suggest this effect is due to the release of serotonin from platelets. Indeed, the effectiveness of heparin in the therapy of pulmonary embolism rests not only on its anticoagulant properties but also on its direct effect on platelets preventing them from releasing serotonin.

Clinical Features

The clinical features of pulmonary embolism are so varied and are so non-specific that the diagnosis must be considered whenever a host of unexplained symptoms occur in a

patient in heart failure, in postoperative patients, and elderly individuals subjected to prolonged bedrest.

In general, three major syndromes may result.

- I. Massive pulmonary embolism due to occlusion of the main or two or more major pulmonary arteries. The clinical syndrome is dominated then by shock, pulmonary hypertension, tachycardia, tachypnea, and EKG signs of acute right ventricular strain.
- II. Pulmonary embolism of medium-sized pulmonary arteries causing clinical and radiographic signs of pulmonary infarction, but without significant pulmonary hypertension or right ventricular strain.
- III. Small pulmonary emboli with varied clinical manifestations such as unexplained fever, transient tachypnea, and tachycardia, hypotension, or the development of chronic exertional dyspnea, and fatigue with chronic cor pulmonale. Wheezes or an asthmatic-like picture in a previously anapathic patient may likewise be a clue.

In a large series of patients with pulmonary embolism, the following frequency of symptoms were found:

— Accentuated pulmonic second sound	—95%
— Tachypnea	—90%
— Tachycardia	—90%
— Fever	—80%
— Chest pain (pleuritic)	—75%
— Rales	—60%
— Dyspnea	—45%
— Hemoptysis	—30%
— Friction rub	—25%
— Hypotension	—25%
— A pulmonic systolic murmur heard best over the subscapular region of the chest may occasionally be heard. It is thought to be pathognomonic.	

Diagnosis

The diagnosis of pulmonary embolism rests largely on a battery tests which may elucidate the basic pathophysiology underlying the disease.

CBS—As first shows slight leukocytosis which becomes markedly increased if infarction occurs.

Sedimentation Rate— Is usually normal unless infarction evolves.

Chest X-ray— Initially it is negative except for increased hilar shadows and signs of pulmonary engorgement. If an infarct develops, 20% will show a positive x-ray. According to Wharton et al the earliest detectable changes are clouding at the

base of the lung fields observing the costophrenic sulcus on the affected side. The right lower lobe is most commonly affected. According to Hampton et al American Journal of Radiology—plate-like atelectasis with elevation of the diaphragm on the affected side is a reliable sign. According to Stein infarcts most often occur at the junction of two pleural surfaces and pleural effusion is a common radiographic finding. With recurrent emboli one finds radiologic signs of cor pulmonale.

Chemical Tests—The recently acclaimed classical triad of chemical tests has been questioned by Schnell et al at Edinburgh. However, most investigators still feel them to be useful when pulmonary infarction has occurred.

SGOT—is normal in the absence of severe right-sided failure with hepatic congestion. This helps to rule out acute myocardial infarction.

Bilirubin —is slightly increased.

LDH (lactic dehydrogenase)— rises to high values on the 4th–5th day.

Pulmonary function studies— reveal decreased maximal breathing capacity, decreased alveolar PCO_2 , and increased arterial PCO_2 with decreased O_2 saturation.

EKG— The pattern seen is that of systolic and diastolic overloading of the right ventricle as described by Cabrera et al.

These are the classical $S_1Q_3T_3$ pattern with ST-T changes

- 1) Right axis deviation
- 2) Incomplete to complete RBBB
- 3) Tall, slurred R waves; right precordium with inverted T-waves of the ischemic variety over the same area.
- 4) Tall, peaked P waves lead II
- 5) Tall, R waves AVR
- 6) Arrhythmias of which atrial fibrillation, and nodal tachycardia are most common.

Lung scan—Radioactively-tagged albumin aggregates are injected into the venous circulation and their perfusion of the pulmonary vascular bed is then revealed by the pattern elucidated by a scintillation counter which scans the lung fields measuring the relative radioactivity. Areas of no radiation, due to failure of the tagged albumin to reach that area because of occlusion, are presumptive evidence of embolism.

Pulmonary arteriography — The pulmonary vasculature is defined by using a benign contrast material injected into the outflow track of the right ventricle through a CVP catheter. Occlusions of vessels in the pulmonary vessels is thereby delineated.

Prophylaxis and Treatment

Prophylaxis is mainly directed at avoidance of venous thrombosis. This includes local measures such as avoidance of prolonged periods of bedrest, leg exercises, early ambulation, and in selected cases anticoagulation. Elastic stockings or bandages have been employed in

the prophylaxis of postoperative thromboembolism, but proper application and management of these is very important if they are to be efficacious. Immediate treatment of congestive heart failure when present is a very important consideration.

The routine used of anticoagulation has been recommended following operations, injuries or other conditions requiring complete bedrest. The value of anticoagulation is now well established in the therapy of acute MI and CHF. A recent study has proved its value in the prolonged treatment of elderly patients needing extended immobilization.

In high risk patients, daily examination of the lower extremities for incipient venous thrombosis is mandatory. Those patients that develop this condition should be considered for immediate treatment with anticoagulants and/or venous ligation with or without thrombectomy.

Anticoagulation—The value of coagulation is now widely accepted. Considerable evidence has accumulated that adequate anticoagulation with heparin results in decreased mortality in acute pulmonary embolism. Similar evidence of efficacy with coumadin, which is utilized when anticoagulation is to be prolonged is not quite as clear. There are many different regimens proposed for the administration of heparin but the Lee-White clotting time must be followed closely. The normal range is 7-14 minutes and the adequately anticoagulated individual will have a clotting time of 2-4 times as the control 4-6 hours after the previous dose. The addition of coumadin of course necessitates lab control of the prothombin time which is kept at 15-25% of normal.

Venous ligation—venous interruption may be the preferred method of prophylaxis and has been used under three major circumstances.

- A) Patients with contraindication to anticoagulation
- B) Anticoagulation failure
- C) Patients with recurrent thrombophlebitis, chronic predisposition to pulmonary embolism, or a survivor of a well-documented massive pulmonary embolus.

Venous interruption may be complete with ligation or partial using plication or teflon clips. Most commonly inferior vena caval ligation is employed, but in some cases ligation of the common femoral bilaterally is the procedure of choice.

Treatment of Acute Pulmonary Embolism

If recognised massive embolization can be treated and mortality can be reduced.

Hypotension—must be treated with vasopressors

Hypoxia—must be treated with O₂

Arrhythmias—must be treated with appropriate cardiac medications.

Pulmonary oedema—must be treated in the routine manner.

Heparin—should be given early by the intravenous route and may reverse some of the clinical signs, i.e., bronchospasm immediately.

In institutions where the procedure is feasible, embolectomy must be prepared for and accomplished immediately. The indications for such a procedure are now widely held to be quite limited. It has been found that only very severe, massive emboli should be removed surgically since even with large emboli and cor pulmonale patients placed on a proper conservative regimen will survive. Dahan et al in their monograph on pulmonary emboli suggest emergency embolectomy only if the following criteria are met:

- 1) Unequivocal demonstration of obstruction of more than 60% of the pulmonary vasculature by embolism that can be removed surgically.
This implies pulmonary angiography be done.
- 2) Hemodynamic evidence of acute cor pulmonale. The absence of cor pulmonale indicates that embolism has not caused significant vascular obstruction and the patient should survive with conservative regimens.
- 3) Shock that is unresponsive to vasopressors. If vasopressors are required to maintain adequate blood pressure after 30 minutes of treatment, the outlook is grave and embolectomy should be considered.

In the realm of research, thrombolytic therapy is being investigated. A large study with urokinase is now in progress. Early reports have shown good results with rapid lysis of emboli and return of cardio-circulatory dynamics to normal after short periods of therapy; however, further study is necessary to assess the efficacy of this therapeutic approach to the problem which appears to many hospitalized patients.

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