Current Practice

CLINICAL PROGRESS

Diagnosis of Pulmonary Embolism

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Pulmonary embolism follows detachment of thrombus from a peripheral vein or from a chamber on the right side of the heart. If the volume of material is great it causes circulatory obstruction. If the particles are small they reach the small pulmonary arteries, where they produce either no overt disturbance or pulmonary infarction. Rarely, if embolism is very frequent the obstruction may lead to chronic thromboembolic pulmonary hypertension.^{1 2}

Air, fat, tumour, or amniotic fluid can also reach the pulmonary arteries as emboli. Fat embolism after fractures is common but usually only an incidental finding in fatal accident cases. Right atrial myxoma may present with recurrent pulmonary emboli. Haematogenous spread of a sarcoma or renal carcinoma may fill the vena cavae and even extend into the right atrium mimicking constrictive pericarditis before blocking the pulmonary artery. Choriocarcinoma cells may gradually fill the small pulmonary arteries and cause severe pulmonary hypertension. Amniotic fluid embolism is a dramatic but rare complication of obstructed labour or of precipitate delivery in a multiparous woman.

Pulmonary thrombo-embolism is common. Often it is predictable and therefore largely preventable. It develops during venous stasis from inactivity in chronic medical illness, reduced cardiac output in heart disease, during anaesthesia, and post partum. Changes in the clotting propensities of the blood also contribute—as in the puerperal or postoperative state (particularly after splenectomy), in polycythaemia, and during the taking of oral contraceptives containing oestrogens. When pulmonary embolism occurs in a patient who is already in heart failure or seriously ill postoperatively the typical features may be obscured; the diagnosis then depends on recognition that sudden deterioration or fever or tachypnoea or tachycardia or drop in blood pressure may have resulted from this complication.

Pulmonary embolism is not confined to the old and the ill, nor even to takers of the "pill." It can occur unheralded in the young and apparently healthy.³ Though previously thought to be rare in the African and almost non-existent in children this is now known not to be true either.⁴ Nevertheless it needs to be sought both by the clinician and by the pathologist as it is easily missed. In children pulmonary embolism occurs in the nephrotic syndrome, in blood dyscrasias, and postoperatively—particularly when veins have been interfered with, as after open-heart surgery. Prolonged sitting, as during air flights in economy class seats, has been incriminated as a predisposing factor in some otherwise healthy people who have sustained pulmonary embolism after such journeys. The first step towards diagnosing pulmonary embolism is to keep the possibility in mind and to remember the mundane as well as the more dramatic ways in which it may present.

Peripheral Pulmonary Embolism

When pulmonary embolism causes segmental infarction there may be fever and tachypnoea, a pleural rub, pleuritic

pain, haemoptysis, pleural effusion, or an unexpected opacity on the chest radiograph. In a few it may be clinically silent until chronic thromboembolic pulmonary hypertension produces symptoms through impaired gas exchange, restricted left ventricular output, or right ventricular failure. Lung signs do not occur unless there is infarction, which is said to be more likely when there is pulmonary venous obstruction (as occurs in left ventricular failure or mitral stenosis), but this may also depend on whether the embolism totally occludes the pulmonary artery inflow to the segment. If obstruction is partial the lung probably survives, the blood flow brings lytic agents, and resolution is rapid. In such patients no permanent damage results even if embolism is recurrent.

Central Pulmonary Embolism

When a pulmonary embolus lodges in the bifurcation or in the main branches of the pulmonary artery the right ventricle becomes obstructed, cannot empty, or transport blood to the left ventricle, whose stroke volume also suddenly falls giving rise to hypotension, tachycardia, and syncope. The rise in pressure behind the obstructed dilating right ventricle gives rise to jugular venous distension, but this cardinal physical sign is often obscured by the patient's dyspnoea and prostration. The arterial blood pressure is often maintained despite curtailment of the cardiac output. The sympathetic outpouring responsible for the vasoconstriction which keeps the blood pressure up also increases the contractile force of the left ventricle. The left ventricle is starved of blood but ejects what it receives at augmented velocity into a constricted arterial tree. The character of these pulses may lead to serious underestimation of the gravity of the problem.

Signs of pulmonary hypertension are absent because the failing and previously unprepared right ventricle cannot generate a high pressure. The cutting off of blood flow to parts of the lung which remain ventilated leads to an abrupt rise in dead space. Because over-compensating hyperpnoea and tachypnoea the arterial PCO_2 becomes reduced. Moreover, invariably hypoxaemia occurs owing to venous admixture of blood from the underventilated areas adjacent to those deprived of blood flow. In a few patients right to left shunting across a patent foramen ovale may further augment hypoxaemia.^{5 6}

The features of the clinical emergency of pulmonary embolism—with sudden collapse, respiratory distress, tachycardia, hypotension, and gallop rhythm—are well known. The tachypnoea and respiratory distress far exceed that in other catastrophes and are the most helpful signs. Breath sounds are loud and clear; the pulse is rapid, regular, sharp, and small; a diffuse systolic lift at the left sternal edge is sometimes present and a gallop rhythm is invariably audible.¹ Evidence of leg vein thrombosis is often absent, may never show itself, or may emerge only several days later.⁶

Diagnosis

Electrocardiogram

The electrocardiogram (E.C.G.) is usually very helpful in excluding underlying cardiac disease as well as in the actual

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diagnosis of pulmonary embolism. Nevertheless, the changes are often transient, reflecting the usually rapid improvement in the circulatory state. A normal E.C.G. does *not* preclude the diagnosis of pulmonary embolism. T-wave inversion in right precordial leads is the most common change; though often it does not occur immediately, it may persist for many days in the more seriously ill patients (Figs. 1 and 2). A q wave and inverted T wave in lead III is often associated with a rise in the diaphragm, pleuritic pain, and basal lung collapse (Fig. 3). In the most severely ill patients the E.C.G. sometimes shows changes resembling those in inferior or posterior infarction (Fig. 4); these may reflect myocardial necrosis secondary either to inadequate coronary blood flow or to interruption of flow down the right coronary artery

which may be stretched and flattened around the dilated right ventricle.

Evidence of right atrial enlargement or the development of right bundle branch block are less common but very helpful especially if previous normal E.C.G.s are available for comparison (Fig. 5). These changes are summarized in Table I.

FIG. 4.—E.C.G. mimicking posterior and inferior infarction in a man of 28 with massive pulmonary embolism. These changes persisted.

FIG. 5.—Extensive T-wave inversion and partial right bundle branch block in massive pulmonary embolism.

TABLE I.—E.C.G. Changes in Acute Pulmonary Embolism

Change	Reason
Normal E.C.G.	Transience of serious circulatory derangement in many instances. Delayed development of abnormality in others.
Atrial fibrillation	Right atrial distension
QIII TIII	Raised diaphragms
Resembling inferior or posterior infarction	Coronary insufficiency
T-wave inversion in R precordial leads	Right ventricular dilation or hyperventilation
Right atrial preponderance or right bundle branch block	Right ventricular failure
Tachycardia and low voltage	Reduced stroke output

Plain Radiology

The chest radiograph may look nearly normal in a patient who is close to death from massive pulmonary embolism but, like the E.C.G., the x-ray film is useful for identifying pre-existing cardiac disease. The heart size does not change abruptly, though a prominent pulmonary conus may be visible (Fig. 6). The lungs occasionally show a paucity of vascular markings, but the most useful sign is a peripheral opacity from the herald infarct, which so often precedes the major catastrophe (Fig. 6 and 7). Basal collapse and infarction may develop some days after admission due perhaps to

FIG. 1.—E.C.G. 12 hours after massive pulmonary embolism. Although there is tachycardia, slight right axis deviation, a qR in V₁ and a delayed vector to the right visible as qR in VR such minor changes are readily overlooked.

FIG. 2.—Same patient next day. T-wave inversion in V₁ to V₃ has appeared.

FIG. 3.—E.C.G. from patient whose chest radiograph is shown in Fig. 9. The q and T-wave inversion in III and VF are related to elevation of the diaphragm. It is similar to that seen commonly in pregnancy.

re-embolization within the lungs because clinical improvement is not interrupted (Figs. 8 and 9).

Lung and Leg Scans

Scanning of the lungs with a scintillation scanner or gamma camera after intravenous injection of ^{131}I or technetium-labelled macro-aggregates of human serum albumin⁸ cannot be used in the diagnosis of the sudden emergency; the material takes half to one hour to prepare for injection and scanning requires some posturing and co-operation which may not be possible in a sick patient. Nevertheless, the technique is very useful in the recognition and follow-up of minor or recurrent embolism.

FIG. 6.—Prominent pulmonary conus and consolidation at right lung base in a patient with acute pulmonary embolism and probable previous peripheral infarct.

FIG. 7.—Small peripheral opacities in right and left lung fields in a patient who presented with major acute embolism.

The macro-aggregates are distributed in the small arteries according to the blood flow. Areas of ill-perfusion are recognized as holes where radioactivity is absent, but this technique does not distinguish pulmonary embolism from pneumonia, tumour, or bullae except when the findings are considered in the context of the clinical circumstances and the chest x-ray film. Serial scans do enable pulmonary embolism

to be distinguished from other causes of poor perfusion largely because the former causes only a transient disturbance.

Scanning of the legs after injection of ^{125}I -labelled fibrinogen is the most sensitive means of recognizing venous thrombosis.⁹ The labelled fibrinogen is incorporated in developing thrombus, when it can be located by an external counter. Serial studies may show the thrombus creeping up the legs if treatment is not instituted. This technique is very useful in detecting calf vein thrombosis, but less accurate in the thigh, where an ultrasound method is probably more useful.¹⁰

Even these sensitive tests may not necessarily disclose peripheral venous thrombosis in patients with acute or even with recurrent pulmonary embolism. Nevertheless, when the tests are positive they may allow prompt action in time to prevent subsequent embolism.

FIG. 8.—Near normal chest radiograph in a young man with acute pulmonary embolism.

FIG. 9.—Later film in same patient whose E.C.G. is shown in Fig. 3. There is bilateral basal lung deflation.

Pulmonary Angiography

In patients with suspected massive embolism, pulmonary angiography is the definitive test and should be carried out as an emergency to confirm the diagnosis, indicate the distribution and severity of obstruction, and plan appropriate ther-

apy.^{11 12} In patients with recurrent peripheral pulmonary embolism pulmonary angiograms are frequently normal, and serial lung scans are much more useful. In chronic pulmonary hypertension the pulmonary angiograms permit differentiation between thromboembolic obstruction and the small vessel obliteration which is associated with normal architecture of the visible vessels in idiopathic and postpartum cases.

In an emergency angiography is best carried out via an arm vein to avoid possible dislodgement of thrombus from

FIG. 10.—Chronic thromboembolic pulmonary hypertension for comparison with the previous film of acute pulmonary embolism. The right atrium is enlarged and the main pulmonary arteries are dilated and sharply outlined. The lung fields look rather patchily perfused and this fact was confirmed on angiography.

FIG. 11.—Postpartum pulmonary hypertension due to symmetrical small vessel disease. The right heart chambers and the main pulmonary artery are dilated. The lung fields appear uniformly oligemic.

iliac veins if the saphenous route is used. The catheter should be placed in the pulmonary artery so that opacification of right heart chambers does not obscure the lung fields and so that the volume of contrast injected can be kept to the minimum. To combat systemic vasodilatation caused by the contrast medium 0.4 mg. phenylephrine is given down the catheter immediately before the former is injected. A drop in blood pressure from this cause is the main danger in patients whose precarious survival is dependent on maintenance of maximal vasoconstriction. With this precaution haemodynamic study and angiocardiology is surprisingly well tolerated even in desperately sick patients.

In massive embolism pulmonary blood flow may appear to be almost totally obstructed in patients who are investigated within an hour of their collapse. Embolic material is seen straddling the bifurcation of the pulmonary trunk and only a few spidery peripheral vessels may receive contrast beyond the central obstruction. Such patients may well die unless embolectomy is carried out immediately after the diagnosis has been confirmed in this way. Patients who are investigated several hours after their collapse usually show less definite interruption of the circulation, with restoration of adequate flow through at least one lobar branch. If more time has elapsed the filling defects are usually more peripheral and sometimes are very hard to pick up at first glance, though the experienced eye quickly spots the rounded leading edges of filling defects at the origins of branches, with contrast flowing round them.

Total occlusion of a main or lobar pulmonary artery in the absence of a proximal thrombus, and with no "ghost" filling around the obstruction, usually means that the obstruction is permanent and often that the condition is already chronic. In such cases the episode may have been caused by a small recurrent embolus in a patient who was already suffering from chronic thromboembolic pulmonary hypertension. These patients also show much more dilatation of the main pulmonary arteries than do patients whose obstruction is only recent (Figs. 10 and 11).

Measurement of Arterial Blood Gases

An Astrup machine or equivalent is now available in almost every hospital and using it to test an arterial blood sample allows major pulmonary embolism to be diagnosed with considerable confidence. Almost no other condition gives rise to arterial hypoxaemia with hypocapnia. In addition, there is usually a severe metabolic acidosis with a rise in lactic acid and other products of anaerobic metabolism. Despite this, however, the pH may be kept close to normal by hyperventilation, and hence by itself the pH is a poor guide to the severity of the condition.

Variable hypoxaemia and invariable hypocapnia are seen also in chronic thromboembolic pulmonary hypertension so that blood-gas analysis cannot distinguish between acute and chronic or acute-on-chronic embolism.

In the differential diagnosis of acute massive pulmonary embolism (Table II) the E.C.G. and chest x-ray film usually bring to light pre-existing chronic cardiac or lung disease in patients too collapsed to provide either a history or the physical signs of their underlying condition. However, the near

TABLE II.—*Clinical Differential Diagnosis of Acute Massive Pulmonary Embolism*

Acute myocardial infarction
Acute-on-chronic pulmonary embolism
Pulmonary embolism in a patient with pre-existing pulmonary hypertension due to other causes
Pulmonary embolism complicating pre-existing heart failure
Acute right ventricular failure complicating pre-existing chronic left ventricular disease
Acute cardiac tamponade
Acute haemorrhage

normality of the results of these two tests in many patients with massive pulmonary embolism often puts the unwary physician off the diagnosis. Chronic mitral valve or ischaemic heart disease are unlikely to provide normal records in this situation, but the difficulty is often to decide whether concomitant pulmonary embolism is also present. Pulmonary angiography provides the answer.

Acute myocardial infarction in shock is quite the most common problem in differential diagnosis, and too many such patients have been rushed to the operating theatre for emergency pulmonary embolectomy. The E.C.G. may be of little help in an emergency (Fig. 4) and, again, pulmonary angiography is mandatory before heroic therapy is instituted. Measurement of the wedged pulmonary artery pressure is

useful if practicable because this is invariably raised in acute myocardial infarction but is normal in pulmonary embolism.

A "paradoxical" arterial pulse, which falls at the onset of inspiration and rises on expiration by more than 15 mm. Hg—so that the change is detectable by the finger palpating the femoral pulse—is almost invariably present in acute cardiac tamponade from pericardial effusion. Unfortunately, it is also present sometimes in acute cardiac dilatation from any cause and is not infrequent in acute pulmonary embolism. Electrical alternans on the E.C.G. is a frequent sign of cardiac tamponade and is virtually a diagnostic finding.

Sudden internal haemorrhage as from a ruptured ectopic

pregnancy may cause collapse with air hunger and restlessness, tachycardia, and gallop rhythm. The arterial blood gases are usually normal but there may be hypocapnia and the site of bleeding usually very rapidly becomes obvious.

To sum up, the mainstays of diagnosis of acute pulmonary embolism are alertness to the possibility, the observation of tachypnoea and hyperpnoea in an acutely ill patient, measurement of the arterial blood gases, and pulmonary angiography. The clinical findings, aided only by electrocardiography and chest radiography allow the diagnosis to be made with confidence in most patients, but angiography should still be carried out for confirmation and for establishment of severity.

Massive Pulmonary Embolism—Medical Management

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Acute pulmonary embolism may be minor or massive; the distinction is important not only in terms of the differing symptomatology but also because the prognosis and treatment of the two conditions are very different. *Minor* pulmonary embolism, presenting with the symptoms and signs of pulmonary infarction, carries a good prognosis. Treatment is primarily directed at the deep venous thrombosis with the aim of preventing either subsequent massive embolism or recurrent minor pulmonary embolism, which can lead to chronic thrombo-embolic pulmonary hypertension. No specific therapy is needed for the pulmonary infarct itself except in those rare cases which progress to cavitation.

Massive pulmonary embolism may be defined as embolism involving at least half of the major pulmonary arterial branches; the condition may be suspected clinically, but definition of severity requires special investigations (e.g., pulmonary arteriography). In general, such special investigations are probably rarely performed, and massive embolism tends to be diagnosed most often at necropsy. Thus we lack figures for both the incidence and the mortality of massive embolism against which treatment can be assessed and the stage is set for controversy. In many cases massive pulmonary embolism is rapidly fatal; of 100 patients dying from pulmonary embolism studied by Gorham¹³ 41 were dead within 10 minutes and 66 within 2 hours. While this high initial mortality may be reduced by resuscitative measures (external cardiac massage, vasopressor drugs, oxygen therapy, and, possibly, D/C countershock) it is unlikely that any specific medical treatment will be effective in this group, for whom emergency embolectomy by the Trendelenburg technique may still be the treatment of choice.¹⁴ There remain those patients who, having survived for 2 hours, will still die over the next few hours or days (29% in Gorham's series¹³) and in whom there is time for specific medical therapy.

Assessment of Treatment

Any series of patients seen 2 hours or more after proved massive pulmonary embolism will also include an unknown proportion who would survive *without* any specific treatment. Assessment of treatment in this group of patients thus requires either a method for assessing prognosis in any individual at the time of study, or admission of all such patients to a randomized trial of treatment. While attempts have been made to assess prognosis,^{15 16} these have not found wide accep-

tance, and probably a properly controlled trial will be required to show the advantages of any particular form of therapy. Such a controlled trial of heparin and a thrombolytic agent, urokinase, is in progress in the U.S.A.¹⁷ and a similar trial of heparin and another thrombolytic agent, streptokinase, is presently being planned in Britain. In neither trial is it regarded as ethical to include an untreated control group since D. W. Barritt and S. C. Jordan¹⁸ in a controlled trial, showed a significant reduction in the mortality from pulmonary embolism when anticoagulants (heparin and Nicoumalone) were given.

In this study 35 patients with a clinical diagnosis of pulmonary embolism and no contraindication to anticoagulant therapy were admitted to the trial. By random selection 19 patients were admitted to the control group, of whom 5 died and 5 others had non-fatal recurrences of embolism. In the treated group there was only one death, which was due, in part, to anticoagulant therapy. No further patients were admitted to the control group but 38 more patients were admitted to the treatment group, with one further death from anticoagulant therapy. Of the 5 deaths occurring in the control group one was due to recurrent embolism, one to cerebral infarction and two were from progressive necrosis of infarcted lung. Only one patient died from the uncomplicated effects of the initial massive embolism.

This trial thus highlights the effect of anticoagulants in reducing the risk of further embolism but leaves unclear the mechanism whereby anticoagulants prevented death from occurring as a result of the initial embolus. Nonetheless the absence of mortality from embolism per se in the treated group is in striking contrast to the 33% mortality for untreated pulmonary embolism reported by H. Zilliacus.¹⁹ The optimal dosage of heparin to be employed remains uncertain, while the minimum dose required to prevent clot formation or propagation appears to be that which doubles or trebles the clotting time,²⁰ the dose needed to achieve this effect may vary considerably and may be much higher in patients with thrombo-embolism. Recently C. Crane and his colleagues²¹ have advocated massive dosages of about 100,000 U.S.P. units/day given not only to achieve anticoagulation but also to abolish the bronchoconstriction which occurs in pulmonary embolism and is abolished by intravenous heparin²²—possibly by preventing serotonin release from platelets.²³ This action of heparin may explain the rapid clinical improvement observed by some authors after the first intravenous dose of heparin.^{21 24 25} At present it seems reasonable to give an initial intravenous dose of 10-15,000 units of heparin as part of the resuscitative measures for massive pulmonary embolism;²⁶ continued high-dose treatment must carry risks from bleeding which may be no less than those from thrombolytic therapy.

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