ANAESTHESIA AND PULMONARY EMBOLISM*

LEONARD C. JENKINS, B.A., M.D., C.M., F.R.C.P.(C.),†
and HORACE B. GRAVES, B.A., M.D., C.M.‡

THIS REPORT is a review of 105 autopsy-proven cases of postoperative pulmonary embolism, which occurred during the four-year period, July 1, 1955, to June 30, 1959, at the Vancouver General Hospital. Pulmonary embolism was the sole cause of death or a major contributing cause in each of the 105 cases.

RESULTS

Incidence of Death from Pulmonary Embolism in the Postoperative Patient

Proof of pulmonary embolism can be obtained only at autopsy. However, it is of interest that Israel and Goldstein,¹ in a review of hospital clinical diagnoses, found pulmonary embolism to be more frequent than either pneumonia or bronchogenic carcinoma. The frequency with which the disease is detected at autopsy depends upon the age of the patients examined.² Not only is this disease being more frequently detected, but also the incidence is increasing, owing both to a generally aging population and to the greater life expectancy of individuals with chronic illnesses which predispose to thromboembolic disease. The anaesthetist will be called upon to provide anaesthesia for these patients, involving various surgical procedures. The relatively high incidence of pulmonary embolism as a cause of death in the postoperative patient becomes apparent from an analysis of Table I.

TABLE I

RESULTS: INCIDENCE OF AUTOPSY-PROVEN DEATHS DUE TO
PULMONARY EMBOLISM (July 1, 1955-June 30, 1959)

Anaesthetics	90,710		
Deaths	105		
Mortality rate	1:864		
Age			
Years	1-29	30-59	60-89
Nos.	2	32	71

Pathogenesis and Pathology of Pulmonary Embolism

(a) *Embolic material.* Under certain circumstances foreign materials such as air, fat (3 patients), amniotic fluid, bone, neoplasm (1 patient), or extraneous

*Presented at the Second World Congress of Anaesthesiologists, Toronto, Canada, Sept. 4-10, 1960.

†Department of Anaesthesiology, Vancouver General Hospital, and University of British Columbia, Vancouver, B.C.

‡Director, Department of Anaesthesiology, Vancouver General Hospital, Clinical Associate Professor of Surgery, Medical Faculty, University of British Columbia.

objects (bullets) may embolize to the lungs. The most common and clinically the most important foreign material is an intravascular blood clot (101 patients).

(b) *Sites of venous thrombi.* The usual sites of venous thrombi which detach and embolize to the lung are the veins of the lower extremities (94 patients), the chambers of the right heart (4 patients), and the pelvic veins (7 patients). The majority of reports indicate that well over half of fatal pulmonary emboli originate in the leg veins.

(c) *Predisposing factors.* Thrombosis of veins is related to three basic predisposing factors: venous stasis, injury to blood vessel wall, and physicochemical alterations in the blood constituents.^{3,4,5}

Conditions which cause stasis of blood in veins predispose to the formation of thrombi. One of the most common conditions is cardiac decompensation due to heart disease of all types (20 patients). Thrombi occur in veins of the lower extremities during the course of many chronic illnesses, particularly those associated with debility and requiring prolonged bed rest (26 patients). Pulmonary embolism is seen in patients with pulmonary emphysema⁶ (8 patients). It occurs during pregnancy (1 patient). In this series it occurred most commonly following abdominal and pelvic operations (Table II [51 patients]). Twelve patients (11.4 per cent) had fractured femurs. Only three cardiovascular surgical procedures were involved. Does the anaesthetic state or technique contribute to stasis and thus predispose to pulmonary embolism? Sixty-seven per cent of the patients had general anaesthesia and 30.4 per cent had spinal anaesthesia. More will be said of this aspect in the discussion to follow.

TABLE II
RESULTS: PREDISPOSING (?) FACTORS IN
AUTOPSY-PROVEN PULMONARY EMBOLISM

<i>Operation</i>	
Abdominal	27
Pelvic	24
Fractured femur	12
C.V.S.	3
<i>Anaesthesia</i>	
General	71
Regional	34
Hypotensive episode	27
Special techniques	19

Injury to blood vessel walls in the lower extremities may be complicated by the development of thrombophlebitis or phlebothrombosis of leg veins. Intravenous administration of fluids into leg veins may predispose to phlebothrombosis and to subsequent pulmonary emboli (8 patients or 7.6 per cent of the fatal cases). Thrombi may form within the right atrium or atrial appendage in those diseases which result in enlargement of the right atrium or atrial appendage (2 patients) and in atrial fibrillation (11 patients). Previous subendocardial injury of the right ventricle, as occurs in myocardial infarction (13 patients), may lead to the formation of mural thrombi which may subsequently detach and embolize to the lungs. Thrombosis of the pelvic veins results most often from infections

or tumours of the bladder, prostate (20 patients), rectum, uterus, or fallopian tubes.

Physicochemical changes in the blood constituents predispose to venous thrombi (3 patients, one each with anaemia, thrombocytosis, and polycythemia rubra vera).

(d) *Sequelae.* Trauma to small vessels is followed within 15 to 30 seconds by a localized vasoconstriction.^{7,8} Next, an agglutination of platelets occurs. This agglutination and subsequent lysis of the platelets is followed by the liberation of serotonin (5-hydroxytryptamine). Serotonin is a powerful vasoconstrictor for vessels both intact and injured, local and distant. This vasoconstriction may occur for as long as 30 min. Following the vasoconstriction the fibrin clot is formed within a few minutes. Because injected serotonin produces a rise in venous, right atrial, and pulmonary artery pressure, with a fall in systemic blood pressure,⁹ probably by the mechanism of pulmonary vasoconstriction, Smith and Smith¹⁰ have implicated serotonin release from blood clot and infarcted lung as a factor in the production of the systemic effects of pulmonary embolism. Sequelae which result from a pulmonary embolus are often unpredictable, differ in separate individuals, and vary according to the size and location of the embolus, the pre-existing state of the pulmonary and cardiovascular systems, the influence of autonomic reflexes, as well as to other poorly understood factors.¹¹

Experimental evidence in dogs¹² indicates that an acute obstruction of approximately 70 per cent of the cross-sectional area of the pulmonary circulation is required to lower the pulmonary blood flow sufficiently to decrease systemic blood pressure or to induce right heart failure. Occlusion of more than 80 per cent of the pulmonary vascular bed is necessary to cause death.

(e) *Natural history.* The true necrotic infarct heals by fibrosis. Eventually, only a shrunken scar remains at the original site of infarction. Cavitation or sloughing rarely develop. Pulmonary abscess may rarely occur. Large clots, which occlude the pulmonary artery or both main branches, lead to rapid death. An embolus which occludes a major branch of the pulmonary artery or occasionally one which terminates in a lobar branch may prove fatal. Death in this instance is usually attributed to acute pulmonary hypertension resulting from reflex or possibly serotonin-induced pulmonary arterial vasoconstriction. According to Weidner¹³ the reflex effect is initiated only in vessels less than 25–100 μ in diameter and is mediated through the sympathetic nervous system.

The normal pulmonary arterial pressure of 16/7 to 30/15 mm. Hg is dependent upon a balance between (i) right ventricular output, (ii) resistance of the pulmonary vascular bed, and (iii) respiratory thoracic pump mechanisms and possibly alterations in resistance to air flow.¹⁴ It is evident that mechanical blockade alone, from massive pulmonary emboli, may alter one or all of these factors markedly, leading to gross alterations in pulmonary blood pressure.

Pathologic-Physiology and Clinical Manifestations

Pulmonary embolization in surgical patients appears more often as a single massive episode and less often with preliminary non-fatal episodes than in

medical patients. Evidence of thrombophlebitis directing attention to the need for treatment is also less frequent in surgical patients (Table III). Pulmonary embolism was unsuspected in 103 of the 105 patients who died following operation. Some of these patients had serious, uncontrolled disease, and continued on a downhill course following operation. The clinical manifestations, in many instances, were caused by the primary disease. There was no evidence of pulmonary embolism until the terminal episode, except for 7 of the 105 patients studied. Apart from emboli of cardiac origin dislodged at operation, thromboembolic phenomena were rare in the first three days in most series studied.⁶ In our study, 31 of the 105 cases occurred within one to seven days but most of these occurred in the latter half of the first postoperative week. Pulmonary embolism tended to occur in the second week (40 patients) or later (23 patients in the second to fourth week), even as late as the fifth week (4 patients), despite early ambulation.¹⁸

TABLE III
RESULTS: CLINICAL MANIFESTATIONS AND PATHOLOGIC-PHYSIOLOGY OF
PULMONARY EMBOLISM

Signs and symptoms	Nos.	Pathologic-physiology
Massive and single	98	
Preliminary non-fatal	7	
Dyspnoea		Hypoxia, autonomic reflexes
Substernal chest pain		Reduction of coronary blood flow
Tachycardia		Reflex
Anxiety, Syncope, Convulsions		Cerebral ischaemia
Abnormal E.C.G.		Right ventricular strain
Shock		Decreased cardiac output
Right side cardiac failure		Mechanical, reflex block of pulmonary circulation
Fever		Tissue necrosis
Sudden death		Decrease in cardiac output, acute pulmonary hypertension

(a) *Pulmonary embolism.* The clinical manifestations of pulmonary embolism are protean.^{1,11,15} Table III represents these signs and symptoms in approximate order of importance and frequency. Most individuals first develop symptoms related to pulmonary embolism followed by those due to infarction.

(b) *Pulmonary infarction.* The salient signs and symptoms of pulmonary infarction are pleuritic chest pain, X-ray densities, fever, hemoptysis, cough, dyspnoea, tachycardia, elevated leukocyte count, and E.S.R.

(c) *Suggestive of pulmonary thromboembolism.* The signs and symptoms suggestive of pulmonary thromboembolism were unexplained fever; fever not responding to chemotherapy; increased severity of congestive heart failure, paroxysmal arrhythmia, tachycardia, digitalis toxicity, and mercury fast oedema in patients with congestive heart failure; unexplained "bloody" pleural effusion; lung abscess on X-ray; and unexplained leukocytosis.

(d) *Differential Diagnosis.* There are no specific physical signs by which pulmonary infarction can be differentiated from other pulmonary diseases associated with consolidation of the parenchyma.⁶ Moreover, the signs and symptoms may

closely simulate other disease processes involving the lungs, heart, abdominal organs, or the central nervous system. Differentiating a pulmonary infarct in the postoperative period from pneumonia, atelectasis, or pleural effusion may be very difficult. Many cases of pulmonary embolism closely resemble myocardial infarction, angina pectoris, or congestive heart failure. Cyanosis is uncommon in myocardial infarction unless cardiac failure supervenes.¹⁶ Recently, Robin¹⁷ has suggested a physiologic approach to the differential diagnosis in a patient with suspected pulmonary embolism by simultaneous measurement of arterial and endtidal carbon-dioxide tensions. In the absence of pulmonary infarction, a difference of less than 5 mm. Hg implied either no embolism or an embolus occluding less than the equivalent of a lobar branch of the pulmonary artery. In the absence of emphysema, a large difference indicated pulmonary vascular occlusion.

DISCUSSION

Pulmonary embolism presents a definite problem to the anaesthetist. This is apparent from the relatively high incidence of death from pulmonary embolism in autopsy-proved, postoperative patients. Many problems remain unsolved. Fundamentally, the mechanism of the thromboembolic phenomenon awaits clarification. Until this is possible, our crude knowledge that the factors of venous stasis, trauma to blood vessel walls, and physicochemical alterations of blood constituents can contribute to thrombopulmonary embolic states must suffice.

Questions arise as to what role, if any, anaesthetic agents and techniques play. Can their known alterations on blood coagulation, cardiac output, systemic arterial blood pressure, pulmonary arterial blood pressure, venous flow, tone and return, predispose to postoperative pulmonary embolism?

It is known¹⁸ that in the postoperative period there is an increase in platelet count and adhesiveness, in fibrinogen, and in prothrombin activity. The peak figures coincide with the time of maximum incidence of thrombosis. Sharnoff¹⁹ has suggested that a stressful situation such as anaesthesia and/or surgery produces hypercoagulability through the following mechanism. There is a disintegration of an increased number of megakaryocytes in the lung capillaries. This produces a sudden, marked increase in circulating platelets and hence a transient blood hypercoagulability, setting the stage for such a thromboembolic complication as pulmonary embolism.

Gernsmyer and co-workers²⁰ measured brachial and pulmonary artery pressures simultaneously in fifteen healthy persons during consciousness, phenothiazine sleep, and barbiturate anaesthesia. The influence of adrenaline, effortil, noradrenaline, acetylcholine, histamine, tetrazole, pressure upon the eyes, and release of pressure upon the carotid sinus were examined. The behaviour of arterial pressures during change of posture and withdrawal of blood and following infusion of Ringer's solution were observed. Contrary to brachial artery pressures, only minor changes of pulmonary artery pressures occurred due to these drugs and manoeuvres. Changes in blood volume caused pressure differences of the same magnitude in both arterial systems.

Should spinal anaesthesia be indicated or contra-indicated in these patients? Thirty-four of the 105 patients (30.4 per cent) in our series received spinal or peridural anaesthesia. Is intermittent positive pressure ventilation deleterious, especially in the presence of a reduced blood volume? This is implied by the experimental work of Gerst and co-workers.²¹ They studied the effects of haemorrhage on pulmonary circulation in dogs and demonstrated that with intermittent positive pressure ventilation, reduction of pulmonary blood flow may lead to complete closure of portions of the pulmonary bed. Following restoration of blood flow, there was some delay before these vessels again reopened. Could this phenomenon predispose to primary pulmonary artery thrombosis or set the stage for pulmonary infarction in the thromboembolic prone patient?

How significant are brief periods of hypotension, arrhythmia, hypoxia, and hypercarbia as precipitating factors in thromboembolism? Twenty-seven of the 105 patients (25.7 per cent) had one or more episodes of significant hypotension during anaesthesia. Eleven had atrial fibrillation and 13 previous myocardial infarctions.

Most of these questions are at present not objectively answerable directly from this review or from a perusal of the sparse prevailing relevant literature. Certainly theoretical consideration and indirect evidence indicate caution and a need for awareness of the factors and problems of the embolic-prone individual. The need for expert anaesthesia and the avoidance of any possible precipitating factor is clearly defined.

Certain facts *can* be concluded.

CONCLUSIONS: FACTORS INFLUENCING THE CONDUCT OF ANAESTHESIA

Since each episode of pulmonary embolism exposes the individual to a mortality risk and some patients with massive or repeated pulmonary emboli die in spite of treatment, the ultimate control of the disease will require its prevention. For this purpose there is need for more accurate means of predicting those individuals who will develop venous thrombi and subsequent embolization, and a method to prevent their formation in the postoperative period. The present means for predicting susceptible individuals are crude, for all patients with known predisposing diseases must be suspected as candidates for pulmonary embolism.

TABLE IV
CONCLUSIONS: PRE-ANAESTHETIC CONSIDERATIONS

(1) Predisposing states
(2) Phlebothrombosis
(3) Pre-Anaesthetic sedation

Pre-anaesthetic Considerations (Table IV)

(a) *Prevention of pulmonary embolism before operation.*

(1) Attend to medical and surgical predisposing states. This is well exemplified in a recent series involving elderly patients with fractured hips.²² One hundred

and fifty patients were given phenendione soon after admission and always prior to operation; 150 were not (control series). Pulmonary embolism occurred in no patient under the current influence of the anticoagulant; but in the control series, embolism developed in 18 per cent of cases and fatal embolism developed in 10 per cent of the patients.

(2) Look for already existing thrombosis in the lower limbs. Thrombophlebitis, when fully developed, can be easily recognized by the classical signs of pain, heat, redness, calf tenderness, and distention of superficial veins. One of the early signs of the disease is an increased size of the leg, detected by measurement of the circumference of the calf area. Awareness of the physical signs of incipient thrombophlebitis and a high index of suspicion toward pulmonary embolism will allow the anaesthetist to suspect tentatively many more patients with these conditions.

(3) Adequate pre-anaesthetic medication to remove anxiety and fear, since these factors predispose and have been found to increase coagulability in blood.¹⁸

TABLE V
CONCLUSIONS: ANAESTHETIC CONSIDERATIONS

(1) Normotension
(2) Cardiac Arrhythmias
(3) Posture
(4) No I.V. into lower limb veins
(5) Venous flow rate

Anaesthetic Considerations (Table V)

- (1) Rapid, quiet induction.
- (2) Adequate oxygenation and removal of carbon dioxide, patent airway, high flow oxygen.
- (3) Avoidance of exertion, straining, or "bucking."
- (4) Maintenance of normotension, since 27 of the 105 patients reviewed had one or more episodes of hypotension.
- (5) Maintenance of normovolaemia.
- (6) Non-toxic anaesthetic agents not irritable to myocardium.
- (7) Control of cardiac arrhythmias and cardiac decompensation.
- (8) ECG available.
- (9) Care in posturing, pressure points on veins, avoidance of unnecessary pressure on veins of the lower extremities.
- (10) A major cause of intimal damage is eliminated by avoiding intravenous administration of fluids in lower limb veins. Eight of the 105 patients (7.6 per cent) had received intravenous fluids into leg veins. In each instance, autopsy-proven thrombophlebitis and phlebothrombosis occurred and was the most likely source of the fatal pulmonary embolus. However, when this location is absolutely necessary, the routine use of 10 mg. of heparin sodium in each litre of fluid administered is of definite value in minimizing superficial and deep venous thrombosis.²³
- (11) Use of elastic stockings, pressure inflated suits, or elasto-crêpe bandages

on the lower extremities in order to increase the rate of flow through the veins by decreasing their calibre. Wilkins and Stanton²⁴ have observed a significant reduction in the occurrence of pulmonary embolism in medical patients by this latter method. They point out that it is important that the stockings fit snugly and be maintained in the proper position. If allowed to wrinkle and to slip downward, they will obstruct rather than augment venous blood flow. McLachlin and McLachlin²⁵ have used electrical stimulation to maintain calf vein flow during surgery in the curarized patient, since they had demonstrated by cineradiography stasis in calf veins during inactivity.

(12) Rapid, quiet emergence.

TABLE VI
CONCLUSIONS: POST-ANAESTHETIC CONSIDERATIONS

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(1) Mobilization
(2) Hydration
(3) Anticoagulants
(4) Venous ligation
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Post-Anaesthetic Considerations (Table VI)

(a) *Prevention after operation.*

(1) Early mobilization of lower extremities. The value of early ambulation is not proven, for in some studies the incidence of pulmonary embolism is unchanged.²⁶

(2) Avoid dehydration.

(3) Anticoagulants (chiefly heparin and dicumarol) indicated¹⁸ prophylactically in patients with (i) existing thrombophlebitis or phlebothrombosis of the leg veins; (ii) clinically diagnosed non-fatal pulmonary embolism; (iii) when immobilization is inevitable; (iv) congestive heart failure in emergency operations; (v) past history of thromboembolism; (vi) family history of thromboembolism.

(4) Surgical ligation of the vena cava, or less often of the femoral vein, has been widely employed to prevent pulmonary embolism in patients with thrombophlebitis of the leg veins or to prevent additional emboli in patients with non-fatal pulmonary embolism. Specific indications are:⁶ (i) when thrombi in the leg veins continue to cause pulmonary embolism in spite of properly regulated anticoagulant therapy; (ii) when anticoagulants are contra-indicated by the risk of bleeding, chiefly from lesions of the central nervous system, gastrointestinal tract, or post-transurethral prostate resection; (iii) when the patient cannot or will not co-operate with prolonged management of the anticoagulant regimen.

(b) *Treatment of pulmonary embolism.* Prompt and adequate supportive measures may be life saving for the patient with an acute pulmonary embolus.

(1) Oxygen to prevent hypoxia.

(2) Vasopressor drugs, to combat shock.

(3) Opiate, to relieve pain and apprehension.

(4) Correct underlying disease.

(5) Supportive therapy, (i) atropine; (ii) serotonin antagonists?

(6) Heparin given initially and continued until hypoprothrombinaemia is induced by one of the coumarin drugs reaches the optimum range. Maintenance of

prothrombin level in the therapeutic range should be continued for several weeks after full ambulation is achieved and all evidence of thrombophlebitis has subsided. In some cases, particularly those with multiple pulmonary emboli, pulmonary hypertension, and cor pulmonale, anticoagulants should be given for the remainder of the patient's life. Lifelong treatment is also required for patients with rheumatic heart disease who develop atrial thrombi and have multiple attacks of pulmonary embolism.⁶

(7) Surgical ligation of the femoral veins or vena cava, and occasionally pulmonary artery embolectomy.

SUMMARY

The relatively high incidence in a general hospital of autopsy-proven pulmonary embolism as a cause of death in the postoperative patient has been noted. A brief description of some of the main physiologic-pathologic factors involved in the pathogenesis and pathology of pulmonary embolism, with particular emphasis on their clinical implications especially where they pertain to the field of anaesthesia, has been given. Some of the problems which may confront the anaesthetist in dealing with patients prone to develop this condition have been outlined. Factors influencing the conduct of anaesthesia are discussed.

RÉSUMÉ

Les auteurs ont étudié 105 cas d'embolie pulmonaire, prouvée à l'autopsie, survenus à l'Hôpital Général de Vancouver durant les quatre années s'écoulant du 1^{er} juillet 1955 au 30 juin 1959. Chez 103 des 105 malades, l'embolie a été méconnue. On ne peut obtenir la preuve d'une embolie pulmonaire qu'à l'autopsie.

Dans les poumons, l'embolus peut être de l'air, de la graisse, du liquide amniotique, de la moëlle osseuse, des débris de néoplasme ou des objets de l'extérieur comme des balles. Cependant, ce que nous trouvons plus fréquemment et qui, du point de vue clinique, prend le plus d'importance comme embolus: ce sont les caillots (101 malades dans cette série). Les sites habituels des thrombi veineux qui se dirigent vers les poumons sont les veines des extrémités inférieures, les cavités droites du coeur et les veines du bassin.

Les facteurs prédisposant à la thrombose et à l'embolie pulmonaire sont (1) la stase veineuse, (2) la blessure des parois vasculaires et (3) les modifications physico-chimiques des constituants du sang.

Il n'existe pas de signes physiques spécifiques qui nous permettent de différencier un infarctus pulmonaire des autres maladies qui entraînent la consolidation du parenchyme. Après une opération, un infarctus pulmonaire peut devenir impossible à différencier d'une pneumonie, d'une atélectasie, d'un épanchement pleural, d'un infarctus du myocarde, d'une angine de poitrine ou d'une congestion par défaillance cardiaque.

Alors, la question se pose, quelle est la part de responsabilité, s'il en existe, qui revient aux agents et aux techniques anesthésiques? L'on sait, qu'au cours des suites opératoires, il survient une augmentation de la viscosité et du nombre des plaquettes et une plus grande activité du fibrinogène et de la prothrombine. On a

émis l'opinion (19) que cela était une réponse à l'agression que causaient l'anesthésie et la chirurgie.

On est d'avis que la fréquence de l'embolie pulmonaire post-opératoire peut être modifiée selon l'attention que l'on porte aux facteurs qui peuvent engendrer des thromboses intravasculaires. Il faut examiner le malade pour dépister précocement les signes de thrombophlébite. Des traitements aux anticoagulants peuvent être indiqués. Au cours de l'anesthésie, il faut insister pour que l'induction soit rapide, douce, que la ventilation soit toujours adéquate, que le volume sanguin et la tension artérielle soient maintenus, qu'on ne fasse usage que des agents les moins toxiques, qu'on dépiste et qu'on traite précocement les arythmies et les décompensations cardiaques et, enfin, qu'on surveille la position sur la table. S'il est possible de la faire, éviter d'administrer les fluides intra-veineux dans les veines des membres inférieurs et éviter toute compression sur les veines.

Au cours des suites opératoires, la prévention des embolies peut se faire en faisant la mobilisation précoce des extrémités, une hydratation adéquate et un usage judicieux des anticoagulants. Il peut devenir nécessaire de pratiquer la ligature chirurgicale de la veine cave ou de la veine fémorale.

Lorsque l'embolie pulmonaire est survenue, il devient salubre de prendre des mesures adéquates de traitement et, cela, promptement. Ce traitement doit inclure d'abord l'usage de l'oxygène pour prévenir l'hypoxie, des vasopresseurs pour lutter contre le choc, des sédatifs pour traiter la douleur et toute autre médication de support. Ensuite, il faut songer au traitement des causes de l'embolie.

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