PULMONARY EMBOLISM AND INFARCTION

BY

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It is generally admitted that pulmonary embolism and infarction should be regarded as major circulatory emergencies, and, although these conditions are still more often than not unsuspected or in doubt until post-mortem examination, there is fortunately good reason to assume that their clinical features have in recent years become more clearly defined, and that in consequence the percentage of correct diagnoses has increased materially. Although, however, the essential basis of our knowledge concerning pulmonary embolism and infarction is derived from necropsy studies, considerable advances have now been achieved in the fields of clinical medicine and experimental research, which, in conjunction, have provided evidence of a thoroughly practical and reliable character.

Incidence of Pulmonary Embolism

It cannot be denied, on the other hand, that difficulties in diagnosis frequently arise, and that for this reason—also incidentally, as was pointed out by Barnes (1937), owing to restricted post-mortem examinations—accurate statistics cannot yet be obtained of the mortality rate from pulmonary embolism. It is possible, however, to form some idea of the incidence of the condition from the statistical records that have from time to time been collected. In 567 consecutive necropsies Belt (1934) recorded a mortality rate of 6.5 per cent. from pulmonary embolism; in McCartney's series of 14,419 cases, which included deaths from medical causes and also post-operative, traumatic, and post-partum fatalities, the incidence of pulmonary embolism was 2.72 per cent.; and a very similar figure—namely, 2.07 per cent.—was noted by Collins (1936) in an analysis of 10,940 unselected consecutive necropsies at Los Angeles County Hospital.

For several obvious reasons the above figures admit of only an approximate estimate of the incidence of pulmonary embolism: the condition may be silent or relatively asymptomatic in a large number of cases; it has often been incorrectly diagnosed as coronary occlusion, the clinical picture of the two disabilities being in point of fact very similar; and it is fair to assume that in a large percentage of patients pulmonary embolism is unrecognized owing to limitations in the facilities for post-mortem examinations.

Aetiological Factors

In general terms pulmonary embolism may be regarded as a disability chiefly affecting people at or past middle life, and, although in the large majority of cases it is a post-operative complication, there are also certain other outstanding causes, including various forms of cardiovascular disease—for example, congestive heart failure, coronary occlusion, thrombophlebitis, etc.—and the associated shock and trauma following accidents.

A large variety of factors are concerned in the formation of the thrombus from which the embolus originates, and the more important of these can best be exemplified

by reference to typical post-operative cases. In such it is possible to trace primary factors and contributory causes. The former include local trauma of the tissues, blood vessels, etc., and the presence of organisms; the latter group comprises several morbid developments as follows: (1) Slowing of the blood stream, induced partly by recumbency and diminished muscle action, also partly by constricting bandages and post-operative immobility and by the shallow respiration which impairs aspiration from the great veins of the chest and abdomen. (2) Chemical and physical changes in the blood—for example, dehydration with concentration of the stream and an increase in the fibrinogen, the calcium content, and the platelet count. (3) Localized areas of injury in the vascular endothelium.

More often than not the primary thrombosis occurs in the external iliac, the femoral, or the saphenous veins; but certain other vessels—namely, the inferior vena cava and the pulmonary and internal iliac veins—may be responsible for the condition, as also may the heart itself in the advanced stages of myocardial failure. It is common knowledge that intracardiac thrombosis is a potential development in the decompensation process of heart disease, and such a condition is also frequently responsible for thrombus formation in the extracardiac circuit, the high incidence of the latter complication being well exemplified in a recent analysis by Belt (1934), who found that of eighty-three patients with congestive failure thirty-six developed venous thrombosis and twenty-five of these showed evidence of pulmonary embolism.

Diagnosis

The clinical aspects of pulmonary embolism are singularly complex in that their range of severity varies from the mild and relatively symptomless cases to those in which the signs prior to a long protracted illness or sudden death are unmistakable.

Numerous ingenious experiments have been devised with a view to assessing the morbid effects of embolic obstruction in the pulmonary circuit, and those of Cohnheim (1889) are deserving of special mention. He took simultaneous records of the pressure in the right auricle and the femoral artery, having previously applied a ligature to the pulmonary artery: no appreciable change occurred in the femoral or jugular curves even when the pulmonary artery was constricted to a considerable extent, but further tightening of the ligature brought about a sudden drop in the arterial pressure, with an equally sudden rise in the venous manometer reading, and death ensued as the result of the gradual removal of blood from the arterial circuit.

Later researches (Dunn, 1920; Gibbon and Churchill, 1936; Gibbon, Hopkinson, and Churchill, 1932; Haggart and Walker, 1923; Mann, 1917) have amply confirmed Cohnheim's deductions. Gibbon and his colleagues (1932) were of the opinion that pulmonary artery obstruction up

to 60 per cent. of its cross-sectional area had no appreciable effect on the arterial and venous blood pressures, but that occlusions of from 60 to 85 per cent. were productive of a reduced cardiac output and a rise in the venous pressure, and that the obstruction was fatal when 85 to 100 per cent. of the artery was occluded. These conclusions have been widely approved and, as was recently noted by Horn and his colleagues (1939), they emphasize the extreme degree (? 80 per cent. of the lumen or more) of obstruction that must exist in the pulmonary circuit to effect a fatal reduction in the systemic blood pressure.

The above findings more especially concern embolic obstruction of the main pulmonary artery or its major branches, and the clinical picture of such an accident is moderately distinctive. In a certain number of cases the event is immediately fatal; in others a characteristic series of signs and symptoms may be observed for varying periods before death, the patient being suddenly seized with urgent breathlessness, faintness, and feelings of alarmingly severe substernal oppression which tend to persist in spite of treatment. The physical examination discloses the shock syndrome in its entirety: characteristic signs include pallor, sweating, lividity, and dilated pupils; the pulse is rapid and soft and the blood pressure considerably lowered; the respiratory rate is accelerated and its excursion usually much diminished; collapse, often ushered in by uncontrollable vomiting, deepens, and unconsciousness as a general rule preludes the fatal issue.

Massive Pulmonary Embolism

The terminal phases of massive pulmonary embolism, though at times persisting for some days, are usually more rapidly progressive, as in the following case.

A middle-aged woman was admitted to hospital suffering from an extreme degree of congestive heart failure secondary to chronic rheumatic carditis. The heart was considerably enlarged; there were valvular defects in the form of mitral stenosis and tricuspid incompetence, and the rhythm was noted to be that of an uncontrolled auricular fibrillation. X-ray examination confirmed the cardiac enlargement, with aneurysmal dilatation of the left auricle, enlargement of the pulmonary conus, and bilateral pulmonary congestion. The patient made what appeared to be a perfectly satisfactory recovery following two weeks of orthodox treatment, but two days later she developed urgent signs of acute circulatory failure, the immediate sequel to a somewhat strenuous action of the bowels. Outstanding initial symptoms included severe pain across the front of the chest and an extreme degree of breathlessness; the skin was cold and moist, the face pallid, and the lips and extremities deeply cyanosed; the pulse rate was a grossly irregular 140 and the blood pressure approximately 90/40; the heart sounds were faint at all areas; the respiratory excursion was shallow and fine crepitations were audible over the lungs. The condition became rapidly worse in spite of treatment. A short period of restlessness supervened prior to unconsciousness, and death occurred approximately two hours after the onset of the seizure.

The post-mortem examination revealed massive embolization of the pulmonary conus with extensions into its main branches; the right auricle contained a large brittle mural clot which showed obvious signs of recent fragmentation and was evidently responsible for embolic obstruction of the entire pulmonary circuit.

In contradistinction to the rapidly fatal cases it must be clearly recognized that with medium-sized and small pulmonary emboli a certain number of patients survive the initial shock of the accident, and these in due course may later develop signs of pulmonary infarction and varying degrees of myocardial ischaemia.

As judged by necropsy evidence in a large number of cases small pulmonary emboli are subclinical developments. Others—more particularly those patients suffering

from chronic circulatory affections, in whom there is always a risk of thrombosis in the pelvic or other large veins—may present signs significant enough to warrant a diagnosis: typical examples are those patients who, having reached a perfectly satisfactory convalescence, suddenly and for no apparent reason develop urgent symptoms, including restlessness, thoracic oppression, orthopnoea, tachycardia, and varying degrees of collapse. In such cases a guarded prognosis is essential, for although complete recovery from the initial seizure may ultimately ensue there is always the possibility of serious recurrences developing.

Differential Diagnosis of Pulmonary Embolism and Coronary Thrombosis

A further practical consideration is the similarity which characterizes the early stages of pulmonary embolism and coronary thrombosis, the cardinal signs being so singularly alike in the two conditions that their differential diagnosis is often an intricate problem. The clinical phenomena common to both lesions comprise the following imposing list: uncontrollable pain in the chest, tachycardia, rapid respiration, pallor, cyanosis, and a soft and frequently imperceptible pulse; added to these one usually finds a falling blood pressure, varying degrees of shock with syncopal tendencies, sweating, vomiting, etc., and cardiographic signs typical of myocardial ischaemia.

It is obvious from the above that additional evidence must be forthcoming for the differential diagnosis of pulmonary embolism and coronary thrombosis. The past history of the patient and the circumstances leading up to the onset of the illness will often furnish valuable confirmatory details: previously existing heart disease, an exhausting period of decompensation, and the clinical phenomena suggestive of long-standing hypertension or a history of effort angina would all tend to favour the development of coronary thrombosis. On the other hand, one might reasonably suspect the occurrence of pulmonary embolism if the acute seizure is a sequel to a recent operation or accident, either of which conditions may be responsible for primary thrombotic foci in the venous trunks; moreover, the pain of pulmonary embolism is usually referred to the side of the chest rather than to the substernal region, though as a general rule there may be no obvious clinical evidence of pulmonary infarction in the early stages of the illness. Certain other features peculiar to pulmonary embolism include extreme grades of cyanosis and, as exemplified in the following case, urgent degrees of breathlessness associated with shallow respiration, the discomfort in the side being intensified by any attempt to increase the depth of the breathing.

A man aged 63 had a series of injections for varicose veins. A septic focus developed at the site of the fifth injection, and the patient was then admitted to a nursing home. The leg wound gradually healed under treatment, but convalescence was delayed by recurring "heart attacks" (four to five in number) which were characterized by the acute onset of urgent breathlessness, severe pain in the chest, faintness, collapse, and feelings of indigestion. Following the heart attacks the patient gradually developed congestive heart failure, and the objective signs three months later were as follows: heart enlarged to the right and to the left; apex impulse in the fifth space four and a half inches from the mid-line; rhythm regular except for an occasional premature contraction; blowing systolic murmur at the apex region; pulse 100, regular except for an occasional intermission; vessels normal for age; blood pressure 130/90; a moderate degree of jugular stasis when recumbent; slight oedema of both ankles; right hydrothorax; liver enlarged and tender. Electrocardiogram: T waves flattened in Leads I and II; prominent Q waves, deformed R-T segments, and sharply

inverted T waves in Lead III; S waves slurred and exaggerated in depth in Lead IV R.

Comment.—A review of the history and the clinical features of this case suggest that the so-called "heart attacks" were in point of fact attacks of pulmonary embolization, and in spite of the absence of evidence of gross pulmonary infarction the cardiographic abnormalities were regarded as confirmatory of this diagnosis.

Pulmonary Infarction

Apart from cases of massive embolization in which pulmonary oedema occurs rather than haemorrhagic consolidation, the incidence of true infarction with moderate-sized emboli is relatively small. Certain conditions, however, including chronic cardiac disease, post-operative invalidism, septic wounds, etc., appear to be essentially favourable for the formation of pulmonary infarcts, the responsible factor being passive hyperaemia in the lungs, and under such conditions a backward flow of blood stagnates in the vessels and tissues of the area peripheral to the obstructed arterial trunk. The infarct so produced is usually conical in shape, and a fibrinous deposit covers the visceral pleura of its base, which projects slightly above the surrounding surface.

The diagnosis of pulmonary infarction is chiefly based on the clinical picture, partly also on physical signs. In an average case a slightly raised temperature for a few days and a relatively rapid pulse rate may be the only indications that a focus of phlebitis and venous thrombosis which may be responsible in due course for embolization in the pulmonary circuit, and, later, for a haemorrhagic infarct, is in process of formation. Early indications of the latter are as a rule forthcoming within twenty-four hours of the embolic seizure: the temperature and the pulse rate rise abruptly, the respiration quickens, and the symptoms of shock and mental anxiety are materially intensified. Pain, exaggerated by deep breathing, is another early symptom, the underlying cause being acute pleurisy in the region of the infarct. As, moreover, the large majority of pulmonary infarcts develop in the lower lobes (the right more often than the left) the diaphragmatic type of pleurisy is relatively infrequent, and pain in such circumstances may be referred to the neck and the shoulder via a viscerocutaneous reflex, the diaphragm and the phrenic nerve being embryological developments from the cervical segments. It is further noteworthy that in certain cases of pulmonary embolism with infarction the pain may be clinically indicative of myocardial ischaemia, and, although it is nowadays recognized that such a condition may be induced by pulmo-coronary reflexes (Scherf and Boyd, 1939), it can be readily appreciated how closely the clinical picture of pulmonary embolism may simulate that of coronary occlusion.

It remains to mention the irritative and unproductive cough that as a rule develops on the second or the third day following the infarction, also the possibility of haemoptysis, which, though formerly considered one of the clinical signs of pulmonary infarct, occurs, in point of fact, in a small minority of cases and is no longer regarded as an essential diagnostic feature (Hampton and Wharton, 1920; Scherf and Boyd, 1939).

The physical signs of pulmonary infarction are rarely distinctive—more often than not the examination is entirely negative; on the other hand, a friction rub may be audible on the second or third day, there may be a circumscribed area of dullness with rales and altered breath sounds, and there may be diminished expansion on the side of the lesion.

X-ray examination is often a valuable aid in the diagnosis, and although it must be admitted that quite large

infarcts may escape radiological investigation, certain characteristic manifestations are frequently noted: a clouding in the region of the costo-phrenic angle may be observed within the first twenty-four hours; the hilar shadows on the side of the infarct may be accentuated; there may also be a moderately well defined area of pulmonary consolidation, which for a few days will tend to increase and then to diminish gradually in size and density.

Investigation with the Electrocardiograph

The above-mentioned clinical picture of pulmonary embolism and infarction should as a general rule be supplemented by electrocardiographic investigation, which in recent years has acquired an approved diagnostic value. McGinn and White (1935) found that pulmonary emboli in experimental rabbits and cats induced certain changes of rhythm, including sino-auricular tachycardia, auricular and ventricular fibrillation, also auriculo-ventricular dissociation and, with complete occlusion of the pulmonary artery, inversion of the T waves. In explanation of these changes the authors suggested asphyxia as a likely cause or, alternatively, dilatation of the heart. Confirmatory evidence of myocardial embarrassment in patients suffering from pulmonary embolism is also forthcoming. Barnes (1936) described electrocardiograms with characteristic abnormalities as follows: (1) A deep S wave and T waves of low origin in Lead I. (2) Diphasic T waves and depression of the R-T segments in Lead II. (3) Elevation of the R-T segments, inversion of the T waves, and abnormally deep Q waves in Lead III.

Love and his colleagues (1938) noted somewhat similar electrocardiographic signs, including depression of the S-T segments in Leads I and II, flattening or inversion of the T waves in Lead II, and an abnormally deep Q wave, also inversion of the T waves, in Lead III. These signs they attributed to dilatation of the right ventricle, and, incidentally, it is obvious that the curves of cases of pulmonary embolism closely resemble those of myocardial infarction. It is not surprising, therefore, that at times it may be extremely difficult to differentiate between the two conditions: the cardiographic evidence alone is insufficient, for, as Horn and others (1939) have recently emphasized, the characteristic curves in cases of pulmonary embolism are often identical with those from patients with infarction of the posterior wall of the heart, and in such circumstances serial curves will be essential to demonstrate the progressive changes typical of coronary occlusion as opposed to the pulmonary embolism records in which these changes may not occur. It is obvious from the above that accuracy in diagnosis will necessitate careful correlation of all the evidence available from the patient's history, the examination findings, and the electrocardiograms, and in practice one must always be prepared to recognize the possibility of pulmonary embolization if the clinical picture of an assumed case of coronary occlusion happens to be to any extent atypical (Averbuck, 1934). It is essential, moreover, that one should have in mind a clear conception of the intrinsic cardiac manifestations which characterize the syndrome of pulmonary embolism. These include the development of (a) the so-called acute cor pulmonale and (b) acute ischaemic myocardial damage.

Acute Cor Pulmonale

The acute cor pulmonale was first described by Paul White (1935) as being a characteristic cardiac development following pulmonary embolism. His observations were based upon four cases in which the presenting symptoms signified right heart embarrassment. The first case was that of a patient recovering from an operation

who suddenly developed acute substernal distress with breathlessness and collapse. The pulse rate was 130 and the blood pressure 90/70; there was pallor and a moderate degree of cyanosis. Further signs of particular interest included visible and palpable systolic pulsation in the second space at the left sternal margin, a to-and-fro friction rub to the left of the sternum in the second and third spaces, and accentuation of the second sound at the pulmonary area. The condition was first thought to be one of coronary thrombosis, but this diagnosis was changed later to pulmonary embolism with acute cor pulmonale. Of the other three cases, one occurred following a sprained leg, another after an attack of phlebitis, and the third as a sequel to an operation, this last case being confirmed by radiological examination and by cardiographic peculiarities, including S waves of exaggerated depth in Lead I, low-voltage T waves in Lead II, and deep Q waves and inverted T waves in Lead III.

In assessing the above cases the author concluded that if a pulmonary embolism is massive enough to cause dilatation of the right heart the initial shock syndrome may prelude the development later of acute cor pulmonale, a condition recognizable clinically by the following signs: (1) an area of prominence and pulsation in the second and third spaces to the left of the sternum, also a systolic murmur, a to-and-fro friction rub, and an accentuated second sound at the pulmonary area; (2) dilatation and exaggerated pulsation in the jugular veins; (3) gallop rhythm; (4) fever and leucocytosis within a few hours of the onset of the illness; and (5) the later development of a cough, possibly with blood-stained sputum, pleural pain and friction, and signs of consolidation which may or may not be capable of radiological demonstration.

Myocardial Ischaemia

It is generally agreed that myocardial ischaemia must be regarded as an integral factor in the syndrome of pulmonary embolism, for not only is its symptom-complex the exact counterpart of that obtaining in frank cases of myocardial infarction the sequel to coronary occlusion, but its characteristic cardiogram is essentially similar to that recorded in cases of posterior basal myocardial ischaemia; further, as was pointed out by Horn and his colleagues (1939), sudden death following multiple small emboli in relatively few branches of the pulmonary artery can more reasonably be ascribed to a cardiac pathology than to significant interference with the pulmonary circulation.

Several theories have been advanced to explain the presence of acute myocardial ischaemia in pulmonary embolization, the more important being shock, anoxaemia, and exaggerated pulmo-coronary nervous reflexes.

Shock.—Some degree of circulatory shock is invariably present in patients suffering from occlusion of the pulmonary circuit, and, having in mind its significant clinical features, which include a decline in the blood pressure, a diminution in the cardiac output, and a reduced flow in the coronary vessels, it is reasonable to assume that a condition of shock may be responsible *per se* for the development of myocardial ischaemia. It should further be noted that the trend of modern opinion in regard to the aetiology of the circulatory and cardiac manifestations of pulmonary embolism is distinctly favourable to the shock-syndrome theory, which, in the more severe cases with urgent degrees of heart failure, explains also their comparative freedom from symptoms of acute cor pulmonale.

Anoxaemia.—It is obvious that varying grades of anoxaemia are to be expected as the result of embolic interference with the pulmonary circulation, and in its more severe forms the condition may be productive of myocardial ischaemia; moreover, it has been pointed out by Gibbon and Churchill (1936) that, although the blood pressure does not fall even with

occlusion of 85 per cent. of the pulmonary vascular bed, there is distinct oxygen unsaturation of the arterial blood when more than 40 per cent. of the pulmonary circuit is occluded.

Pulmo-coronary Nervous Reflexes.—It has been conclusively demonstrated that experimental pulmonary emboli not large enough to cause significant reduction in the pulmonary blood flow may be responsible for myocardial injury, and this, according to certain authorities, is the direct sequel to reflex vasoconstriction of the coronary vessels. Scherf and Schönbrunner (1937) were of the opinion that pulmonary embolization originated strong stimuli in the lungs and pulmo-coronary nervous reflexes which induced vasoconstriction in the coronary vessels and myocardial ischaemia secondary thereto; further, it has been suggested that, as pulmonary embolization more particularly augments the load on the right ventricle, it is in this chamber that the more significant effects of myocardial ischaemia are likely to be especially severe (Scherf and Boyd, 1939).

The above-mentioned nervous theory has been to some extent discounted by Horn and his colleagues (1939), their contention being that, even assuming a diminution of coronary flow by vagal constriction, such an effect would be materially modified by the coexisting fall in blood pressure, the increased heart rate, the reduced cardiac output, and the anoxaemia, apart from which they emphasize the absence of typical inhibition symptoms—for example, slowing, heart-block, and ventricular standstill—in cases of pulmonary embolization. Otherwise, these authors stress the shock syndrome as being the primary cause of acute myocardial ischaemia in cases of pulmonary embolism, and in their view the ischaemic manifestations are more likely to occur if there is cardiac hypertrophy or coronary narrowing, also if life is adequately prolonged after the initial embolism. Further investigations have confirmed these views, and a recent article by Friedberg and Horn (1939) on the subject of myocardial infarction without coronary thrombosis records ischaemic necrosis in twelve cases of pulmonary embolism. The myocardial lesions were chiefly located in the left ventricle and its papillary muscles, and the coronary vessels showed varying degrees of thickening and narrowing. It was the opinion of these authors that shock and asphyxia were primarily responsible for the myocardial damage, and coronary spasm via vagal reflexes was, they thought, possibly a subsidiary factor.

REFERENCES

- Averbeck, S. H. (1934). *Amer. J. med. Sci.*, **187**, 391.
 Barnes, A. R. (1936). *Proc. Mayo Clin.*, **11**, 11.
 — (1937). *J. Amer. med. Ass.*, **108**, 1347.
 Belt, T. H. (1934). *Amer. J. Path.*, **10**, 129.
 Cohnheim, J. F. (1889). *Lectures on General Pathology*, 1, 54, London, New Sydenham Society.
 Collins, D. C. (1936). *Amer. J. Surg.*, **33**, 210.
 Dunn, J. S. (1920). *Quart. J. Med.*, **13**, 129.
 Friedberg, C. K., and Horn, H. (1939). *J. Amer. med. Ass.*, **112**, 1675.
 Gibbon, J. H., jun., and Churchill, E. D. (1936). *Ann. Surg.*, **104**, 811.
 — Hopkinson, M., and Churchill, E. D. (1932). *J. clin. Invest.*, **11**, 543.
 Haggart, G. E., and Walker, A. M. (1923). *Arch. Surg.*, **6**, 764.
 Hampton, H. H., and Wharton, L. R. (1920). *Johns Hopk. Hosp. Bull.*, **31**, 95.
 Horn, H., Dack, S., and Friedberg, C. K. (1939). *Arch. intern. Med.*, **64**, 296.
 Love, W. S., jun., Brugler, G. W., and Winslow, N. (1938). *Ann. intern. Med.*, **11**, 2109.
 McGinn, S., and White, P. D. (1935). *J. Amer. med. Ass.*, **104**, 1473.
 Mann, F. C. (1917). *J. exp. Med.*, **26**, 387.
 Scherf, D., and Schönbrunner, E. (1937). *Klin. Wschr.*, **16**, 340.
 — and Boyd, L. J. (1939). *Cardiovascular Diseases*, St. Louis and London.
 White, P. D. (1935). *Ann. intern. Med.*, **9**, 115.

P. JOURNEAULT (*Thèse de Paris*, 1940, No. 265) records an outbreak of sixteen cases of poliomyelitis which occurred in October and November, 1938, in the Indre department of France. The ages of the patients ranged from 18 months to 17 years. Apart from the first case, which occurred in an infant, all the children attacked attended the same school. There were two examples of familial cases—namely, the first in two cousins living on the same farm, and the second in a brother and sister, who both died of ascending paralysis. There is no evidence of the disease having been conveyed by animals. Two patients died, in nine the paralysees became permanent, and five made a complete recovery.