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Pulmonary Embolism

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The high rate of morbidity and mortality for which pulmonary embolism is responsible, is clearly revealed by a study of the incidence of thromboembolism\(^1\) and emphasizes its great importance. Venous thrombosis in the deep veins of the legs, the most common cause of pulmonary embolism, has been demonstrated at autopsy in 50 per cent of all patients who had been confined to bed; the number of medical and surgical patients were equal.\(^2\) Pulmonary embolism was found in 10 per cent of all autopsies, and was considered to be the cause of death in 3 per cent of all autopsied patients.\(^3\) The clinical incidence of venous thrombosis and pulmonary embolism, however, is considerably less than the above figures would indicate, namely 0.5 per cent to 1.6 per cent of postoperative patients, 1 per cent of general hospital admissions, and 1.2 per cent of postpartum patients.\(^1,4,6\)

It is essential, in discussing pulmonary embolism, to have a clear understanding of the meaning of the various terms commonly employed in dealing with this subject. Pulmonary embolism refers to the migration of gaseous or particulate matter from any portion of the cardiovascular system peripheral to the pulmonary artery, and its lodgement in the pulmonary arterial tree. In this paper the discussion will be limited to the migration and lodgement of aseptic blood clots (bland emboli). Thus, the emboli may come from the valves or chambers of the right heart, or the vast venous channels leading to the right heart. Pulmonary thrombosis is the erection in situ of a thrombus in the pulmonary vascular tree, and although the end result may be the same as when pulmonary embolism occurs, it represents a different entity, and is not included in our discussion.

Local circulatory disturbances, as well as abnormal reflexes, consequent to pulmonary embolism, may result in atelectasis, edema, hemorrhage, inflammation, and necrosis of the lung parenchyma and pleura. Resolution and complete restitution to normal may take place if only the first four processes occur (preinfarction), but fibrosis will be the end result if there is destruction of pulmonary parenchyma (infarction).

Another possible consequence of pulmonary embolism is the acute cor pulmonale. This term is applied to a group of clinical, roentgenologic, and electrocardiographic findings which embrace the following: a prominent pulsation in the second and third intercostal spaces to the left of the sternum; dilatation and pulsation of the jugular veins; cyanosis; accentuation of the pulmonic second sound; at the pulmonic valve area, a loud systolic murmur, sounds resembling a pericardial friction rub, a gallop rhythm, and a palpable shock corresponding to closure of the pulmonic valve; and dilatation and overactivity of the pulmonary artery and conus. The characteristic electrocardiographic changes of acute cor pulmonale will be discussed below. This entire syndrome may be obscured by the rapid development of peripheral vascular collapse, or right heart failure may supervene.

Pulmonary embolism, then, may or may not be followed by pulmonary infarction (or preinfarction), and/or acute cor pulmonale. Many other manifestations consequent to pulmonary embolism commonly occur, and these will be discussed below. Pulmonary infarction and
acute cor pulmonale occur in the absence of pulmonary embolism, and therefore, are not pathognomonic of the latter. Nevertheless, the diagnosis of pulmonary embolism is made largely on the basis of symptoms, signs, and laboratory findings associated with pulmonary infarction and acute cor pulmonale. The acute cor pulmonale, in addition to providing valuable diagnostic signs, indicates grave functional abnormalities, while pulmonary infarction, except when extensive, is of little importance save for the diagnostic signs which are furnished by it.

ETIOLOGY

A free floating or detachable clot in the vascular system distal to the pulmonary artery is the one condition essential for pulmonary embolism. Theoretically, then, the source of embolism may be the chambers and valves of the right side of the heart or any part of the extensive venous channels draining into it. Actually, the great majority of emboli come from the deep veins of the legs, a few come from the pelvic plexus of veins, or from the right side of the heart, and the remainder, which are extremely rare, originate in the large veins of the upper extremities.

The mechanism responsible for the intra-vascular formation of blood clots is poorly understood. The preponderance of thromboembolism in bed-ridden and postoperative patients, and under conditions in which injury to the vessel wall may be sustained (mechanical trauma, infection) emphasizes the importance of two of the factors which are related to the clotting process: slowing of the blood stream, and injury to the vessel wall. The occurrence of thromboembolism in patients with polycythemia or other hematologic abnormalities, after the administration of certain drugs, and following rapid diuresis, has led to the notion that changes in blood composition play a part in venous thrombosis. In spite of extensive investigation of this subject, little is actually known concerning it.1

The two outstanding facts in relation to the etiology of pulmonary embolism are its pre-

ponderance in bed-ridden patients and its negligible incidence, apart from obstetric cases, in patients under 30 years of age. Contrary to previously held views, most cases occur in nonsurgical patients with a notably high incidence in those with heart disease. Even in those with heart disease the heart itself is not often the source of the emboli.

Pulmonary embolism is uncommon in apparently healthy, ambulatory individuals. In such individuals it results from "idiopathic thrombophlebitis," a condition which is distinguished by the following features: it occurs almost without exception in males, in contradistinction to the slight predominance of males in the entire group of thromboembolism; two-thirds of the patients have recurrent episodes of phlebitis; about one-third of the patients develop pulmonary embolism; and one-tenth of the patients eventually display evidence of malignant tumors, polycythemia, or thromboangiitis obliterans.4

PATHLOGIC PHYSIOLOGY

Many of the phenomena which are observed in pulmonary embolism can be attributed directly to obstruction of blood flow in the pulmonary arterial system. The sudden vascular obstruction is immediately followed by local disturbances in the pulmonary circulation, a sharp rise in right ventricular pressure, and a drop in left ventricular pressure; the latter may result in coronary failure. Pulmonary obstruction, therefore, plays a direct part in the development of pulmonary infarction, the syndrome of acute cor pulmonale, peripheral vascular collapse, and certain of the cardiac disorders which are occasionally associated with pulmonary embolism. However, clinicopathologic correlation between the number of clinical episodes and the number of emboli which can be recognized at autopsy is very imperfect, clearly indicating that many emboli are "silent," and suggesting that some of the clinical manifestations are consequent to reflexes originating in inflamed veins or in arteries lodging emboli. These reflexes involve the pulmonary vasculature, the bronchi, the diaphragm, the coronary arteries, the neurogenic mechanism of the heart, and the peripheral vascular system. Anoxia, which is
frequently a striking feature of pulmonary embolism, can be explained on the basis of some of these reflexes as well as on such pulmonary abnormalities as atelectasis, infarction, and congestion.

The lodgment of a clot in a pulmonary artery, therefore, produces local disturbances in pulmonary circulation, pulmonary hypertension, a lowering of systemic pressure, abnormal reflexes, and anoxia, and these elements provide the basis for all the phenomena observed in pulmonary embolism. The particular functional and structural alterations which follow pulmonary embolism will depend on the proportionate role of these elements, which are closely interrelated, and upon the following factors: the caliber of the vessels occluded, the extent of propagation of the emboli within these vessels, and the pre-embolic state of the heart, lungs, and circulation.

**The Clinical Picture**

The numerous clinical manifestations observed in pulmonary embolism develop as a result of the complex interplay of the various elements mentioned in the preceding paragraph. Pain is related to local disturbances in pulmonary circulation, to pleural involvement, and to impairment of coronary circulation. Dyspnea has a manifold origin, stemming from bronchospasm or vasospasm, disturbances in pulmonary circulation, immobility or diminished respiratory excursion of the diaphragm, atelectasis and/or pulmonary infarction, anoxia, and impairment of cardiac function. Anoxia is manifested clinically by cyanosis. Hyperbilirubinemia may occur when anoxia, pulmonary infarction, and hepatic congestion coexist. Pulmonary hypertension, anoxia, and coronary failure, are responsible for the abnormal cardiac signs, including all the manifestations of acute cor pulmonale and congestive heart failure. Some of the clinical phenomena which have been attributed, at least in part, to abnormal reflexes are dyspnea, asthmatic breathing, pulmonary edema, syncope, atelectasis, and peripheral vascular collapse. Pulmonary preinfarction and infarction are closely related to the circulatory disturbances resulting from pulmonary obstruction.

Dyspnea, chest pain, and cough are the most frequent symptoms, and fever, tachycardia, abnormal pulmonary signs, and peripheral vascular collapse are the most common physical findings. Cyanosis, hemoptysis, syncope, and the various manifestations of acute cor pulmonale are less commonly observed. Jaundice, coma, sudden weakness, convulsions, nausea, vomiting and hiccup are occasional findings.

These manifestations occur singly, or in various combinations. A characteristic feature is their intermittent appearance so that the clinical course may consist of a series of episodes with intervening silent or relatively silent periods. The manifestations may be the same in different episodes, or there may be no resemblance between one episode and another. Contrary to the observations of others, we have been impressed by the frequency and multiplicity of symptoms and signs, and if these are properly appraised, sudden unexpected death from pulmonary embolism should be a much rarer experience than it is. For example, a brief syncopal attack, or a short paroxysm of auricular fibrillation may be the sole warning, hours or days before sudden death. Since early diagnosis of thromboembolism is essential for the institution of therapeutic measures to avoid fatalities, the prompt recognition and proper interpretation of such developments is important.

Chest pain is the most common single manifestation of pulmonary embolism. It occurs in about 75 per cent of the cases. Pleuritic pain was noted in 54 and anginal pain in 26, of 108 patients with pulmonary embolism recently studied. Although pleuritic pain was a complaint in one-half of the patients, a pleural friction rub was observed in only 10 per cent of the group, and pleural effusion was but seldom recognized. However, small amounts of fluid may accumulate in one or both pleural cavities, and rarely, recurring pleural effusions of large size may dominate the clinical picture. The fluid is often sanguineous, but otherwise does not display any characteristic features.

The anginal type of pain may closely
simulate either angina pectoris or acute myocardial infarction, although certain differences, referred to later, can usually be discerned. Its occurrence does not depend on the presence of pre-existing heart disease, and there is no predilection for males or the older age groups as is true in coronary heart disease.

Dyspnea is noted by almost half of the patients, its incidence being exceeded only by pain. It may be mild or severe, and wheezing respiration or frank pulmonary edema may occur; the latter is not uncommon. A characteristic feature of pulmonary embolism is severe dyspnea without obvious evidence of pulmonary or heart disease.

Cough is almost as common as dyspnea, occurring in over one-third of the patients, and hemoptysis is evident in one-fourth of the cases.

Abnormal signs, as mentioned above, are extremely common. Fever occurs in about two-thirds and tachycardia in over one-half of all patients with pulmonary embolism. There is no characteristic febrile curve, except that sharp spikes in temperature are common, and fever is usually present at the time clinical manifestations are first noted. Sustained fever up to 103 F. or 104 F. for days or a week or more may be observed, with gradual fall to normal. Occasionally fever is the only recognizable manifestation of pulmonary embolism, the patient presenting the problem of fever of unknown origin. A remarkable feature, and one in striking contrast to the great incidence of fever, is the rarity of shaking chill in the absence of complicating sepsis.

Pulmonary signs are observed in well over half of the patients. They are due to atelectasis, preinfarction, infarction and pleural effusion, and embrace localized areas of dullness, crepitant rales and bronchial breathing. These signs may be found anywhere in solitary or multiple areas, but are most common at the right base. They may disappear completely in hours or days, or may persist for a week or longer.

Sudden vascular collapse is one of the characteristic features of pulmonary embolism. It may be the first indication of trouble, antedating by hours or days other manifestations of thromboembolism. There may be a single attack of transient or sustained vascular collapse, or repeated episodes may occur. The transient attacks resemble ordinary syncope. In some cases vascular collapse is associated with, or may precede or follow pulmonary edema, chest pain, the advent of pulmonary signs, or paroxysmal rapid heart action. Occasionally, a pronounced, temporary rise in blood pressure is associated with anginal pain.

Some of the most characteristic, though less common physical signs involve the heart and pulmonary artery, and were referred to previously as the acute cor pulmonale. A prominent pulsation, due to dilatation and overactivity of the pulmonary artery and conus, may be visible or palpable in the second and third intercostal spaces to the left of the sternum, and dilatation and pulsation of the jugular veins, and cyanosis, may be noted. Auscultation at the pulmonic valve area may disclose marked accentuation of the second heart sound, a loud systolic murmur, sounds resembling a pericardial friction rub, and a pronounced protodiastolic gallop rhythm. A shock corresponding to closure of the pulmonic valve may be palpable. These signs appear suddenly, but may be transient if peripheral vascular collapse or right heart failure supervene.10

Paroxysmal auricular fibrillation is an occasional complication of pulmonary embolism, and, like vascular collapse, may be the first indication of trouble, antedating by hours or days other manifestations of thromboembolism. Paroxysmal auricular tachycardia and paroxysmal auricular flutter occur less frequently. High grade A-V block and paroxysmal ventricular tachycardia have not been observed by the writer in uncomplicated instances of pulmonary embolism.

Thus, the "typical" clinical picture of pulmonary embolism will be characterized by chest pain, dyspnea, cough, fever, pulmonary signs, and tachycardia. Syncope, hemoptysis, and the various manifestations of acute cor pulmonale will be observed in some of the cases. The clinical course will be distinguished by the episodic appearance of these manifestations, separated by silent intervals. However,
the variety and changing combinations of the many symptoms and signs frequently impart a remarkably variegated, and at times, bizarre character to the clinical picture. The clinical picture in many cases, therefore, does not conform to the textbook description of pulmonary embolism, but simulates many other disorders. The more common of these are angina pectoris, acute myocardial infarction, simple pleurisy, pleurisy with effusion, tuberculosis, pneumonia, acute heart failure, asthma, tumor, diseases of the central nervous system, and psychoneurosis.

**Laboratory Observations**

The electrocardiogram frequently displays features which are helpful in the diagnosis of pulmonary embolism, and should be obtained whenever this condition is suspected. If tracings are taken immediately, and repeated daily, or after each clinical episode, until the diagnosis is definitely established or excluded, transient electrocardiographic changes will be observed in about three-fourths of the cases. The pattern of acute cor pulmonale is the most characteristic of these, and is noted in one half of the cases. Its main features are large S deflections in lead I, prominent Q and inverted T waves in lead III, and in some of the cases, inverted T waves in the right sided precordial leads. The sudden appearance and rapid evolution of these changes, and the rather rapid return to normal, distinguishes these tracings, and helps to differentiate them from examples of posterior myocardial infarction. In addition, the QRS complex in lead aVF is normal, except in rare instances, whereas in posterior myocardial infarction an abnormal Q wave is frequently noted. Another electrocardiographic change of diagnostic importance is the sudden appearance of transient, incomplete right bundle branch block. Finally, in many cases the only abnormality noted is transient inversion of the T waves in the right sided precordial leads. Although of considerable diagnostic significance, these abnormalities are not pathognomonic of pulmonary embolism and are observed in other conditions.

The usefulness of the electrocardiogram as a diagnostic aid is limited by the fact that changes characteristic or suggestive of pulmonary embolism do not always occur. This deficiency is especially common in the presence of heart disease which alters the electrocardiogram, as, for example, acute myocardial infarction. When pulmonary embolism complicates acute myocardial infarction, or vice versa, electrocardiograms will display the features characteristic of acute myocardial infarction, rather than those which can be recognized as indicating pulmonary embolism.

Roentgenologic study may disclose highly significant signs, the most common being areas of plate-like atelectasis, and truncated shadows corresponding to areas of preinfarction or infarction. These are better detected by fluoroscopy than by ordinary films. Fluoroscopy also allows the demonstration of dilatation and overactivity of the pulmonary artery and conus, and abnormal behavior of the diaphragm, characteristic features of pulmonary embolism which might otherwise remain undisclosed. The diaphragm on the involved side is often high, and may exhibit diminished or absent respiratory excursions. Occasionally one may observe an occluded pulmonary artery and the avascular pulmonary shadow representing the bloodless lung it once irrigated. The avascularity imparts an appearance of increased translucency to the portion of lung parenchyma affected, so that the picture of localized pulmonary emphysema is simulated. During the acute stage the pulmonary artery lodging an embolus is surrounded by a hazy irregular shadow due to edema of the adjacent tissues.

As the acute inflammatory reaction subsides, the shadow of the occluded pulmonary artery becomes more clearly distinct, and eventually is abruptly demarcated from the surrounding structures, giving the appearance of an amputated hilar shadow.

Leukocytosis occurs in about 70 per cent of the patients. The elevation in white cell count is usually only moderate, with a slight shift to the left, even when extensive pulmonary infarction is present. Leukocytosis may persist for days at a time, or may appear and disappear without apparent reason. Leukocytosis may be noted when other signs of thromboembolism are absent.
The sedimentation rate is increased, at times markedly so.

Hyperbilirubinemia occurs in about half of the cases.

**Diagnosis**

The diagnosis of pulmonary embolism rests on two groups of facts, those pertaining to etiology, and those embracing the numerous symptoms, signs and laboratory findings which comprise the clinical picture described in a preceding section. In many instances the clinical and laboratory phenomena are so characteristic, that there is no difficulty in making the diagnosis. The diagnosis should be clearly evident when an elderly, bedridden patient suddenly develops dyspnea, cough, and pleuritic pain, and examination reveals a sharp rise in temperature, pulmonary consolidation, and leukocytosis. The signs may be less characteristic, perhaps a small area of dullness and crepitant rales, or highly suggestive, such as hemoptyis and a pleuritic friction rub. Or the diagnosis may appear evident because the various features which distinguish acute cor pulmonale are observed, or pulmonary infarcts or an occluded pulmonary artery and related phenomena are demonstrated roentgenographically, or the changing electrocardiographic patterns indicative of pulmonary embolism are noted. These phenomena are so characteristic of pulmonary embolism that they may be considered diagnostic. In some cases the diagnosis is strongly suggested, not so much by the special character of the clinical features, as by the clinical course, i.e., the explosive and episodic appearance of various manifestations separated by silent intervals.

On the other hand, the diagnosis may be missed when bizarre combinations of symptoms and signs occur, or when there is only an isolated symptom or sign, as is so often the case, at least during part of the clinical course. Furthermore, the clinical phenomena which occur may be the uncommon and less characteristic ones; these lack diagnostic importance unless their significance is enhanced by pertinent etiologic factors. For example, paroxysms of auricular fibrillation, or brief syncopal attacks, occur under such diverse conditions that consideration of pulmonary embolism as a possible cause will be necessary only when they occur in individuals who are likely candidates for thromboembolism, that is, in those past middle age who have been confined to bed, and those who have sustained recent leg trauma or infection. In such cases, the presence of deep venous thrombosis in the lower extremities, the most common immediate cause of pulmonary embolism, may be the most useful clue to embolism as the explanation of these phenomena. The necessity of careful and repeated examination of the limbs, when attempting to establish a diagnosis of pulmonary embolism, is evident. Tenderness in the plantar veins of the foot, or in the calf muscles is an early sign. Tenderness along the course of the great veins on the inner aspect of the thighs, swollen and tender inguinal lymph nodes, and pitting edema, are later developments. However, thrombophlebitis in the lower extremities may exist without producing any signs or symptoms, and venography, properly executed, may reveal its presence. If no evidence of phlebitis is found, some other site of origin of the embolus may be looked for. It cannot be emphasized too strongly that embolism should never be excluded merely because phlebitis cannot be demonstrated. In fact, the diagnosis of pulmonary embolism must frequently be made without definite proof of the existence of phlebitis.

The diagnostic problems in this field are considerable, and errors both of omission and commission are not infrequent; failure to make the diagnosis is the more serious of these. A high index of suspicion is the first necessary step for correct diagnosis, since remarkably little may be apparent to suggest the diagnosis of pulmonary embolism. Once the condition is thought of, however, thorough elicitation of symptoms and signs, careful roentgenologic and electrocardiographic study, and examination of the extremities for evidences of phlebitis, may reveal signs of diagnostic significance which otherwise might have escaped recognition. Pulmonary embolism must be suspected in every elderly, bedridden patient in whom the clinical course is unfavorable, or who develops chest pain of anginal or pleuritic type, or acute dyspnea. It is necessary to
consider embolism whenever a patient with heart failure does not respond to treatment in the expected manner, or a diagnosis of angina pectoris, acute myocardial infarction, dissecting aneurysm, pneumonia, or "infectious" pleurisy is entertained but not established. Furthermore, embolism must be considered whenever patients who are likely candidates for thromboembolism display any of the following phenomena: unexplained vascular collapse, unexplained syncope, paroxysmal auricular fibrillation, hemoptysis, unexplained fever, pulmonary edema especially when not readily explained by the underlying disease, cyanosis, and jaundice. Deep cyanosis, acute dyspnea, and pulmonary edema, in the absence of obvious pulmonary or heart disease, are strongly suggestive of pulmonary embolism.

The greatest difficulty in diagnosis is encountered in patients who have anginal pain, thus raising the question of angina pectoris or acute myocardial infarction. In spite of the similarity in many of the manifestations of pulmonary embolism and coronary disease, differences exist which make possible the differential diagnosis. When pulmonary embolism is the cause of anginal pain there may be distinct pleuritic pain in addition, or the anginal pain may be intensified by inspiration, a feature which is not observed in angina pectoris or at the onset of acute myocardial infarction. Syncope is common in pulmonary embolism, and particularly distinguishing is its occurrence prior to the onset of pain. On the other hand, syncope is uncommon in coronary disease, especially prior to the occurrence of pain. Paroxysmal auricular fibrillation occurs in both conditions, but when it precedes pain it is more likely to be due to pulmonary embolism than to acute myocardial infarction. Tachycardia and a pronounced fall in blood pressure are the rule early in the course of pulmonary embolism whereas at the onset of acute coronary disease, bradycardia is common, and, as a rule, blood pressure changes are not striking; indeed, not infrequently the blood pressure rises simultaneously with the onset of pain in coronary disease. Fever, leukocytosis, and an increased sedimentation rate are commonly present at the time clinical manifestations are first noted in pulmonary embolism, but are rarely observed in the first 24 hours in acute myocardial infarction. Paroxysmal ventricular tachycardia and high grade A-V heart block are fairly common complications of acute myocardial infarction, but do not occur in pulmonary embolism. Evidence of pericarditis excludes the diagnosis of pulmonary embolism, and pleurisy rules out uncomplicated acute myocardial infarction. Finally, electrocardiographic and x-ray studies expertly interpreted, are helpful.

**Prognosis**

Pulmonary embolism is one of the important causes of morbidity and mortality in postoperative patients, and in bedridden nonsurgical patients past middle age. While recovery frequently occurs, the threat of sudden death is ever present, and the mortality rate rises sharply with each embolism when recurrent episodes occur. It is a common cause of sudden and unexpected death, although the element of surprise, judging from our experience, is due to failure to appreciate some of the early warning signs. Grave disturbances involving the heart, lungs and circulation occur, but if a fatal issue is avoided, complete recovery may be anticipated almost without exception. In the rare instances in which repeated embolization occurs over a period of years, cardiac enlargement and finally, chronic congestive failure, ensue. The features are those of chronic cor pulmonale.

**Treatment**

Since pulmonary embolism is most commonly the consequence of deep venous thrombosis in the lower extremities, its incidence could be materially reduced by the prevention of thrombophlebitis. The numerous methods and procedures which are practiced with this end in view testify to the importance which is widely attributed to this etiologic factor, and to the difficulty in preventing venous thrombosis. Early ambulation of surgical and other patients, active and passive movements of the legs, massage, wiggling of the toes, leg binders of one sort or another, and avoidance of pressure on the soft parts of the limbs, are some of the measures employed. Prophylactic vein
ligation prior to surgery in elderly patients has not been demonstrated to have appreciably reduced the incidence of pulmonary embolism, but is believed by some observers to be a worthwhile precaution. More recently anticoagulants have been administered prophylactically, mostly to patients with acute myocardial infarction and congestive heart failure, with impressive results.

The treatment of pulmonary embolism is still the subject of some controversy. It cannot be denied that many patients recover without having had specific therapy, even after multiple embolic episodes, or that death occasionally occurs in some cases despite early diagnosis and prompt and vigorous treatment. Nevertheless, the mortality rate can be reduced by treatment, although no single known form of therapy can assure recovery in every case. Treatment by oxygen inhalation, morphine, atropine, papaverine, digitalis, antibiotics, and plasma or blood though purely supportive and symptomatic, is of considerable importance. The prompt institution of measures to promote the comfort of the patient and support the circulation may be an urgent necessity, and takes precedence over other therapy. Pain, dyspnea, vascular collapse, cyanosis, and paroxysmal rapid heart action are the most important indications for the various therapeutic measures mentioned above. Oxygen is useful when there is cyanosis, dyspnea, or vascular collapse, and morphine is of value for its sedative and analgesic effect, and for the control of dyspnea. The combined use of papaverine and atropine may have a strikingly beneficial effect on dyspnea. Plasma or blood appears to be helpful in the presence of vascular collapse. Paroxysmal auricular fibrillation and paroxysmal auricular tachycardia should be treated with digitalis, which otherwise is rarely of any use in pulmonary embolism. Antibiotics are frequently given to prevent pulmonary infection, but their value is dubious unless there is clear cut evidence of infection.

Surgical interruption of the large venous channels of the lower extremities or of the inferior vena cava, or anticoagulant therapy is employed as soon as the diagnosis of embolism or phlebitis is made, in order to forestall the discharge of a first or a subsequent embolus. There is some question as to the relative merits of heparin and dicumarol or similar substances. In view of the necessity of injecting heparin intravenously it would seem desirable to use it in addition to dicumarol only to initiate therapy when an immediate anticoagulant effect is desired, and then to continue treatment with dicumarol alone once the prothrombin activity is suitably depressed. Repeated intravenous injections may be difficult technically, and damage to veins may, at times, assume serious importance; heparin injected by any other than the intravenous route is unreliable and may cause pain, swelling, hematomata, and fever. The sublingual route remains to be evaluated. However, heparin has many advantages and may be used alone, especially when dicumarol is contraindicated, or when laboratory facilities for accurate prothrombin time determinations are not available.

Agreement concerning the relative merits of, and the indications for, vein ligation and anticoagulants has not been reached. Each method has advantages and potentialities not possessed by the other. Anticoagulants possess the following advantages: they are usually effective, when properly administered, regardless of the primary seat of thrombosis; they are said to inhibit propagation of clots in diseased veins or of emboli lodged in the pulmonary vessels; they avoid the disadvantages of a surgical procedure, especially in poor risk patients; and they obviate the late effects of vein ligation.

The advantages of vein ligation are: the alleged greater effectiveness in preventing embolism; avoidance of the harmful and even dangerous effects of anticoagulants; its applicability when anticoagulants are contraindicated, as in patients with bleeding diatheses, renal, and liver disease, and in the presence of conditions predisposing to serious hemorrhage, such as active peptic ulcer and ulcerative colitis; the simplicity and brevity of management after it is performed, in contrast to the difficulty of controlling the action of anticoagulants and the troublesome daily tests required when dicumarol or similar substances are used; avoidance of the need for special laboratory facilities, often lacking, and of the
danger involved in delaying emergency surgery required in patients who are receiving anticoagulants.

The following outline has proved useful as a general plan of treatment. Anticoagulants are administered: (1) prophylactically in all conditions in which there is a predisposition to phlebitis, providing surgery is not contemplated; patients with acute myocardial infarction, and those with congestive heart failure confined to bed fall into this group; (2) for the treatment of thrombophlebitis if surgery is not contemplated; in this group will be patients with acute myocardial infarction, congestive heart failure, and other nonsurgical diseases, and postoperative and obstetrical patients in whom the danger of hemorrhage is past; (3) in all patients with phlebitis, including those with pulmonary embolism, in whom vein ligation would be a prohibitive risk; (4) in patients with pulmonary embolism, in whom the seat of venous thrombosis is inaccessible to surgery, or when the evidence is reasonably certain that the embol comes from the heart: (5) when emboli continue to occur despite vein ligation; and (6) when a diagnosis of thromboembolism is suspected, but cannot be established with certainty.

Vein ligation is indicated: (1) for the prevention of pulmonary embolism in elderly patients who are about to undergo major surgery; (2) in all patients with phlebitis and/or pulmonary embolism if surgery is contemplated; (3) for all patients with thrombophlebitis and/or pulmonary embolism in whom anticoagulant therapy is contraindicated; and (4) in patients in whom pulmonary emboli continue to occur, despite apparently adequate anticoagulant therapy.

**Summary**

The incidence and importance of bland pulmonary embolism as a cause of morbidity and mortality have been emphasized. The pathologic physiology, the clinical picture, the laboratory findings, the diagnosis, and the treatment have been discussed. Venous thrombosis in the lower extremities is the most common immediate cause of pulmonary embolism, but clinical evidence of its presence is frequently lacking. It is difficult to prevent venous thrombosis in spite of the employment of numerous prophylactic measures. Although the diagnosis of pulmonary embolism is easy in some cases, it may be impossible in others. Statistical proof of the effectiveness of treatment is difficult to obtain, but clinical experience appears to indicate that the aforementioned therapeutic procedures are worthwhile. It is evident that many important problems relating to thromboembolism remain unsolved.

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