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# Pulmonary thromboembolism : a study of 46 autopsied cases

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# PULMONARY THROMBOEMBOLISM

## A STUDY OF 46 AUTOPSIED CASES

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## INTRODUCTION

Embolic occlusion of pulmonary arteries has long been considered a major cause of death and has been exten-sively studied for many years. It is the purpose of this paper to discuss various aspects of this disease (such as incidence, prophylaxis, and treatment) and to present a series of cases of proven pulmonary embolism with reference to the characteristics of the illness and the factors which promote it.

## INCIDENCE

The incidence of pulmonary embolism depends on the nature of the primary illness, age of the patient, and many other factors. These figures will vary a great deal in different surveys.

In a review of autopsies at Michael Reese and Chicago Memorial Hospitals (1), covering a period of 17 years, 56 cases of massive pulmonary embolism were found--an autopsy incidence of one per cent. In only three of these cases was a correct diagnosis made before death. In seven cases, there had been previously known thrombophlebitis.

At Charity Hospital, New Orleans (2), over a 13 year period, there were 32,254 deaths. During this time, a third of the deaths were submitted for post-mortem examination. There was an incidence of .057 per cent fatal pulmonary embolism per hospital admission and an incidence of four per cent of autopsies performed. Thirty-seven children had developed pulmonary thromboembolism in this series--the majority following suppurative phlebitis of cavernous or lateral sinuses.

An autopsy series at Massachusetts General Hospital (3) showed small incidental emboli present in approximately five per cent of autopsies, with massive emboli found in 1.86 to 3.5 per cent. This figure was dependent upon the period studied.

At Columbus, Ohio, State Hospital (4) over a four year period, in a series of 512 autopsies, an incidence of 25.7 per cent pulmonary emboli has been reported. Of these, 55.2 per cent were of the massive type.

In 178,252 operations performed on the European continent, 2,874 patients developed venous thrombosis of the extremities--an incidence of 1.61 per cent. Of those with thrombophlebitis, one-sixth subsequently suffered one or more episodes of embolism (5).

Among 567 autopsies conducted at Toronto General

Hospital (6), ten percent were found to have some type of pulmonary embolism.

These statistics give an idea of the nature of this universal problem. For years, a pulmonary embolism often went unrecognized because the physician performing the autopsy was inexperienced or unaware of the possibility that an embolus was present. Thus it was not reported (6). In addition, pre-autopsy embolming sometimes obscures the diagnosis. Simple postmortem clots may not be easily distinguished grossly from embolus if it has had contact with embalming fluid. The true embolus may then be missed (4).

## DIAGNOSIS

The diagnosis of pulmonary embolism may be easily made or may prove to be quite difficult--especially if one must rely on clinical signs and symptoms alone (7).

Pulmonary emboli are usually divided as to size into three types. The first is the massive pulmonary embolus, which usually lodges itself in the pulmonary artery and perhaps in the right heart as well--and may extend to the right and left main pulmonary vessels. This condition is characterized by sudden shock and by almost instantaneous death, unless the clot is quickly

broken and distributed throughout the lung fields. Most of the acute and severe eymptoms--such as chest pain, cyanosis, and severe dyspnea--can be attributed to this type of embolus.

The second type of embolus occludes the medium sized (secondary or tertiary) pulmonary arteries. Though it is often fatal, it does not often give the picture of acute shock.(8). The emboli are usually of smaller caliber than in massive embolism and therefore lodge in the medium sized pulmonary arteries (9). However, chest pain (usually pleuritic or anginal in type), cyanosis, and dyspnea may still be seen; and with infarction, there may be localizing signs of consolidation or pleural effusion over the lungs.

The third type of embolism--and one which may be quite obscure clinically and may often go undiagnosed or misdiagnosed prior to autopsy--is that of multiple minute emboli scattered throughout the substance of the lung. Death may occur following this complicationwith the autopsy picture often likened to an arteritis or atherosclerosis of the vessel walls (10). Multiple small infarcts are often seen (11). Clinically, then, there may be a picture of chronic right heart failure with polycythemia (12), dyspnea, and cyanosis (13). This condition may be misdiag-nosed as mitral stenosis without murmur or some unusual

form of congenital heart disease (14).

In pulmonary embolism, the clots are usually found curled up and/or packed in the pulmonary circulation; but they retain the contour of the vessels in which they originate. Common sources of emboli are veins in the legs, pelvic veins, mesenteric and portal veins (15), and the chambers of the heart (16). Thrombophlebitis or phlebothrombosis is often associated (17). For example, swelling, cyanosis, pain or tenderness of the lower extremities is often the only warning that pulmonary embolism is imminent. But thrombophlebitis may not be clinically recognizable until after embolism has taken place (18). Chest pain is usually listed as the most common complaint if there has been embolism. Respiratory manifestations are listed as the second most common complaint. Of these, cyanosis, dyspnea, cough, tachypnea, hemoptysis, and pleural friction rub are the most common. There are usually signs of inflammation, such as fever, (which is not necessarily high) and cardiovascular manifestations; tachycardia, fall in blood pressure, cold clammy skin, apprehension, arrhythmias, prominent pulsation in the second and third intercostal spaces to the left of the sternum, distended neck veins, rise in blood pressure, palpitation, systolic pulmonary murmur (19) with sounds resembling a pericardial

friction rub, accentuation of pulmonic second sound, and pulmonic gallop rhythm (20).

There may be cerebral signs such as coma, sudden weakness, effort syncope (21), incontinence, dizziness, convulsions--and miscellaneous symptoms, such as nausea, vomiting, jaundice (22, 23). epigastric distress, hi cups, muscular aches and pains (24), and abdominal pain (25).

The electrocardiogram may be an aid to diagnosis. However, most cases of massive pulmonary emboli succumb before electrocardiographic studies can be carried out. Nevertheless, when electrocardiograms can be taken, a characteristic pattern is often seen. One sometimes finds a right heart pattern with axis deviation and other signs of acute cor pulmonale. Differentiation from coronary thrombosis can usually be made (26). There may be a right bundle branch block (27). Though this picture is thought to be typical, only 11.1 per cent of a series of patients at Charity Hospital in New Orleans, with proved pulmomary embolism, showed these characteristic changes in electrocardiogram. At Massachusetts General Hospital, 20 per cent of those who had electrocardiograms taken showed acute cor pulmonale (16).

Another aid to diagnosis, especially when there are infarcts present, is the use of X-ray. One often finds

prominent hilar are s (28)--and with occlusion--avascular pulmonary fields (29). The heart shadow is sometimes considerably increased in size. The infarcts may have the appearance of pleural thickening rather than showing actual areas of consolidation. Infarcts are frequently fusiform in shape. At peripheries of the lobes they are classically triangular or wedge-shaped (30). When there has been hemoptysis, one may find areas of homogeneous density attributed to intrapulmonary hemorrhage (31). The residual of an old pulmonary infarction shows on the X-ray film as band-shaped or wed e-shaped shadows radiating from hilum to periphery (29).

## TREATMENT

Treatment of pulmonary embolism now centers around its prevention. In massive embolism, the Trendelenberg operation, or embolectomy, has been occasionally performed, but strictly as a heroic measure. Its use has been disappointing--carrying with it 93.2 per cent mortality (32).

As soon as pulmonary embolism has been diagnosed, one should give supportive therapy which is designed to combat shock. There is no evidence that antibiotics are of value. Pleural effusions, as they develop, should

be aspirated to allay dyspnea. Hemoptysis is rarely extensive enough to warrant treatment. Oxygen may be given. Papaverine and atropine were formerly administered routinely be various physicians as it was felt these drugs contributed to the relaxation of the pulmonary bed (33).

In massive pulmonary embolism, any treatment designed to prevent further occurrence is usually of no avail. But with the appearance of smaller emboli in the lung vessels, producing a less severe clinical picture, it is important that prophylaxis be attempted--thus pre-venting further embolism, which may be even more crippling, or fatal.

At the present time, there are two major courses of treatment available to accomplish this purpose.

The first is venous ligation. Assuming that the thrombotic process is limited to the veins in the lower extremities, ligation of these veins will prevent further embolism. This is usually accomplished through an incision over the fossa ovalis ith ligation of the superficial femoral vein just before it joins the deep femoral vein. If the latter is not also involved by an inflammatory process, it will carry collateral venous circulation following the ligation. The saphenous veins also contri-bute to collateral flow (34). When thrombophlebitis is found to involve the common femoral or iliac veins,

ligation of the common iliac may be necessary (35). Even this procedure may fail to prevent embolization if there is unsuspected thrombosis in other pelvic plexuses (36). Occasionally the vena cava itself is tied off.

A number of clinicians feel that ligation of the veins in the extremity where the patient has symptoms of inflammation is a futile procedure. They consider thrombophlebitis alone as never responsible for embolism--but instead blame phlebothrombosis, where the clots are not attached to inflamed vessel walls and thus more easily are set free in the venous circulation. They therefore advocate the ligation of the veins in the extremity not showing evidence of thrombophlebitis, despite the fact there may be no symptoms in that leg (37). Routine autopsy examination of calf veins of patients confined to bed for varying lengths of time showed thrombi somewhere in these vessels in 5.2 per cent of cases (38). Some groups have routinely ligated the veins of both extremities with the onset of the first symptom and as soon as diagnosis could be made (39). They felt the patient was then free from the threat of subsequent embolism. It is believed that the great saphenous vein only rarely is implicated in thrombophlebitis or pulmonary embolism (34).

The other primary preventative measure is anticoagu-lant therapy. This is accomplished by the use of heparin (5), or administration of dicumarol. The former drug, because of its rapid anticoagulant effect, is given right away and administered simultaneously with dicumarol until the latter, whose effect is delayed for several days, can be given alone and maintain anticoagulant effects (36). Anticoagulant therapy must be continued at effective levels for 14 to 28 days until all deep clots have organized and endothelialized. There is a certain amount of danger in the administration of these drugs. Bleeding and clotting times must be watched closely until the thrombotic process--which may be temorary--subsides (40).

Occasionally, a patient receives anticoagulant drugs and in addition undergoes venous ligation. Many have found the use of sympathetic block, which reduces vasospasm and thus perhaps any thrombotic process, quite valuable usually as an additional procedure (41). The time-honored treatment of phlebitis in the legs was immobilization and elevation of the involved extremity. It was felt that leg elevation promoted lymphatic drainage and thus prevented the formation of phlegmasia alba dolens. Immobilization of the limb was thought to be necessary if the inflammation were to subside (42). In

addition, early ambulation following surgery, with exercises for all bedridden patients, has been advocated.

Various factors may predispose to venous thrombosis and thus to embolism. Among them are blood dyscrasia (41), muscle injury (34), sprained ankles, fractures, the vasospasm during cold weather, injections of hemorrhoids, anesthesia, toxins, obesity, dehydration, increasing age, operations, use of tobacco, and application of excess cold or heat to extremities (17). In one study, it was found that the incidence of fatal pulmonary embolism was highest after certain operations--notably hernia repair, operations on the uterus, urinary bladder and gall bladder (43), splenectomy, resection of intes-tines and stomach, other intestinal operations (44), and prostatectomy (45). Heart disease may also predis-pose to development of this condition (46, 47).

Precipitating factors of embolism may also include such mechanical influences as straining at the stool (48), active or passive physical exertion, the milking action of a large enema, or getting out of bed for the first time after an operation. In addition, embolism may occur at the time of removal of a femoral vein catheter (49).

## EXPERIMENTAL STUDIES

Numerous investigators have tried to reproduce pul-monary emboli in various experimental animals. Many materials have been used--among them, split peas, clotted and macerated blood clots, fibrin clot, barium sulfate, solutions, oily suspensions of charcoal, lycopodium spores, cotton, glass beads (50), paraffin, grains of rice, tapioca, and beads of enamel (51, 52, 53). These substances would be introduced in the animal's venous system, usually per cannula, passing to the lungs and lodging in the pulmonary arteries, producing varying degrees of circulatory impairment, anoxia, and infarction of lung tissue.

Investigators then speculated as to the actual mechanism of death and continued experiments in an effort to discover the factors responsible. It was found that emboli could cause three different clinical conditions in animals and that sudden death usually resulted from massive embolism with lodgment in the pulmonary artery or its major branches.(54). Much research has attributed sudden death to neurocirculatory disturbances of a reflex nature (55, 56, 57, 58). However, others feel that animal experiments show only a mechanical factor present and that death is ona basis of anoxia after blockage of the pulmonary circulation (59). Some investigators

believe both mechanical and reflex factors operate to produce death (60).

Experimental studies have shown a predilection of smaller emboli for the right lung and for the lower lobes of each lung. But the right lung is the larger of the two and thus receives more than its share of blood from the pulmonary artery. It is felt that the lower lobes are more commonly the victim of embolism because their blood supply is more direct than the blood supply to other lobes, and not because of the effect of gravity (61). Experiments have also shown that massive but non-fatal pulmonary embolism may fail to produce infarction of the lung, presumably because collateral circulation is adequate. (62).

The effects of multiple small sized emboli in the experimental animal have also been studied. Microscopically, the areas of embolization tend to produce local lesions in the arterial walls, including thickening of proliferation of the endothelium and various changes in the intima and media. These changes are similar to the effects of arteriosclerosis and atherosclerosis (63, 64, 65, 66, 67).

## PROGNOSIS

Of those surviving an acute attack of pulmonary embolism, many will die later of other causes, with embolism as only a contributing factor. Many recover completely, having no recurrence of either venous thrombosis or embolism. Others may be subject to recurrent attacks of both and may later die of diseases which seem to predis-pose to thrombotic episodes such as polycythemia, leukemia, and carcinoma--particularly of the visceral type (68).

Many patients survive, but are victims of chronic venous insufficiency of the legs. They may have ulcerations, induration, chronic cellulitis, and extensive pigmentation (69). Life may be maintained for years after recurrent embolization if adequate collateral circulation can be established, utilizing such channels as bronchial arteries (70). After some time, the emboli undergo organization, which may be complete often with recanalization (71).

## MATERIAL AND METHODS

To further view this problem, a statistical study was made of 837 autopsies at Methodist Hospital, Omaha, Nebraska. Included in this series were all autopsies performed on persons 15 years of age and over, divided into groups according to age (Table I). During a ten year period (1946-1956), there were 487 males and 350 females autopsied at the hospital. In all cases, the cardiac cavities and all ramifications of pulmonary arteries were examined for gross and microscopic evidence of thromboembolism; and lung tissue was also searched for infarction. If there was evidence of embolism, the pathologist performing the autopsy routinely examined inferior vena cavae, iliac veins, and their tributaries and "milked" the femoral veins. In no cases were the veins below the inguinal ligament actually opened and examined.

No thrombus was considered embolic unless, in the opinion of the pathologist, it was obviously not conforming to the lumen of the pulmonary vessel, or loosely attached to the embolic site. In all cases, the thrombus was examined microscopically and found to be of typical ante-mortem type, showing platelet layers, lines

TABLE I

| Age Group | Total Cases | Cases with Pulmonary Embolism | | | |
|---|---|---|---|---|---|
| | | Massive Embolism | Other Emboli | Total Embolism | % with Emboli |
| 15-29 | 43 | 1 | 1 | 2 | 4.7 |
| 30-39 | 37 | 0 | 0 | 0 | 0 |
| 40-49 | 104 | 2 | 1 | 3 | 2.9 |
| 50-59 | 168 | 3 | 4 | 7 | 4.2 |
| 60-69 | 229 | 6 | 8 | 14 | 6.1 |
| 70-79 | 181 | 9 | 4 | 13 | 7.2 |
| 80-99 | 76 | 6 | 1 | 7 | 9.2 |
| TOTAL | 837 | 27 | 19 | 46 | |

Table showing number of autopsies in each of seven age groups represented in this study, number of massive and other type pulmonary emboli occurring in each age group, and percentage of emboli in each age group.

of Zahn and/or evidences of early organization. All other types of pulmonary embolism were excluded from this study--i.e., tumor embolism, fat embolism, etc. When embolus was found to occlude the pulmonary trunk and/or its main branches, it was considered as massive pulmonary embolism and the cause of death. When embolus was discovered in the main branches of each pulmonary artery or in smaller ramifications, it was considetered as an embolus of medium type and as a contributing factor to death or an incidental finding at autopsy.

## RESULTS

A total of 46 patients were found to have pulmonary thromboembolism. This represents an overall incidence of 5.5 per cent--massive pulmonary embolism accounting for 3.2 per cent of the total and embolism of arteries of smaller caliber accounting for 2.3 per cent of the total.

Twenty-seven of the 46 patients, or 58.7 per cent, were found to have massive pulmonary embolism. Eighteen patients, or 39.1 per cent, had embolism of medium-sized arteries; and in one patient, the emboli were found limited to small-sized arteries. Four of those with emboli of medium-sized arteries also had emboli in smaller-sized

vessels. Some of the cases dying of massive pulmonary embolism had emboli in medium-sized arteries as well as the pulmonary conus and its bifurcation.

It was found that 33 of the 46 patients, or 71.7 per cent, were listed as medical patients during their illness. The remaining 13 patients, or 28.3 per cent, had had recent surgery and thus were listed primarily as surgical patients. Of those patients dying of massive pulmonary embolism, 11, or 40.7 per cent, had had previous surgery. Of those patients showing embolism other than the massive type, three, or 15.8 per cent, had had previous surgery.

When considering the surgical patients as a group, one finds that of 13 patients showing pulmonary thromboembolism at autopsy, 84.6 per cent were of the massive type. In contrast, only 6.0 per cent of the 33 medical patients showing pulmonary thromboembolism at autopsy were of the massive type.

During the patients' illness, peripheral thrombo-phlebitis had been diagnosed in six of the 27 patients (22.2 per cent) with massive pulmonary embolism--but in only two patients (10.5 per cent) of the 19 patients with other types of embolism. The overall incidence of throm-bophlebitis prior to embolism was 17.4 per cent. In

only three of the eight cases where thrombophlebitis had been diagnosed prior to death, could clot be demonstrated at autopsy in either the iliac or other pelvic veins, the inferior vena cava, or produced by "milking" the femo-ral veins.

Various degrees of infarction were noted in 24 of the 46 patients, or 52.2 per cent. Massive pulmonary embolism did not produce massive pulmonary infarction in any case. In one-third of the cases with massive pul-monary infarction, small, usually wedge-shaped infarctions were noted, possibly from previous minor pulmonary em-bolism. However, pulmonary infarctions were found in 79.0 per cent of patients with types of embolism other than massive.

The patients were all studied with reference to their primary illness, i.e., the illness for which they were hospitalized (Table II). It was found that 16 of the 46 patients, or 34.8 per cent, were suffering from neoplastic disease of some type. This included 12 cases of carcinoma, three cases of brain tumor, and one case of sarcoma. There were three cases of lung carcinoma, two cases each of ovarian carcinoma and stomach carcinoma, and one case each of carcinoma of the prostate, endometrium, cervix, and pancreas. In addition, there was one case of undiffer-

TABLE II

| Primary Diagnosis | Number | % |
|---|---|---|
| Neoplastic Disease<br>Carcinoma, 12 cases; Brain Tumor, 3, Sarcoma, 1. | 16 | 34.8 |
| Cardiac Disease<br>Myocardial Infarction, 5 cases; Congestive Heart Failure, 3; Hypertensive Cardiovascular Disease 1; Arteriosclerotic Heart Disease 1; Coronary Insufficiency, 1. | 11 | 24.0 |
| Cerebrovascular Accident | 5 | 10.9 |
| Fracture<br>Femur, 3 cases; Ankle, 1; Thoracic & Lumbar Vertebrae, 1. | 5 | 10.9 |
| Miscellaneous<br>Ulcerative Colitis, 1 case; Cholecystitis, 1; Leiomyoma of Uterus, 1; Pneumonia, 1; Vesicular Calculi, 1; Strangulated Hernia, 1; Intestinal Obstruction, 1; Bronchial Asthma, 1; Diabetes, 1. | 9 | 19.5 |
| TOTAL | 46 | 100.0 |

**Table giving the primary diagnosis and classification of 46 cases of pulmonary embolism and showing the number and percentage of cases in each classification.**

entiated carcinoma. The brain tumors included one meningioma, one glioma, and one glioblastoma multiforme. The sarcoma was a case of leiomyosarcoma of the uterus.

Eleven of the 16 patients with neoplastic disease in this series showed massive pulmonary embolism at autopsy; while the other five patients showed embolism of medium or small caliber vessels. Neoplastic disease as the major illness constituted 40.7 per cent of those dying of massive pulmonary embolism and 25.3 per cent of those showing less severe degrees of embolism.

Infarcts resulting from pulmonary embolism were found in eight of the 16 patients with neoplastic disease, or an incidence of 50 per cent. A possible source of embolism was found at autopsy in seven of the 16 patients, or in 43.8 per cent (Table III). The one patient in 46 who was demonstrated to have emboli limited to small-sized vessels was a patient whose primary diagnosis was carcinoma of the pancreas.

Eleven of the 46 cases (24.0 per cent) had some type of cardiac disease as their primary diagnosis. Of these, five were diagnosed as having myocardial infarction, three with congestive heart failure of undetermined origin, one with hypertensive cardiovascular disease, one with coronary insufficiency, and one with

TABLE III

| Patients with Neoplastic Disease | | | Overall % Entire Series |
|---|---|---|---|
| Additional Findings | Number | % | |
| Massive Pulmonary Embolism | 11 | 68.8 | 58.7 |
| Embolism Other Than Massive | 5 | 31.2 | 41.3 |
| Producing Pulmonary Infarction | 8 | 50.0 | 52.2 |
| Appendicular or Mural Clot Found | 2 | 12.5 | 15.2 |
| Other Possible Source for Emboli Found | 5 | 31.2 | 28.3 |
| Total Possible Source for Embolism | 7 | 43.8 | 43.5 |

Table analyzing additional findings present in patients whose primary illness was some type of neoplastic disease, and comparison with entire series of 46 cases.

arteriosclerotic heart disease. When considering the five cases of myocardial infarction as a separate group, one finds that none showed massive pulmonary embolism at autopsy. All had emboli of medium-sized vessels, or medium and small-sized vessels. Of the other six cardiac cases, three showed emboli of medium-sized arteries, and three showed embolism of the massive type.

In considering the cardiac group as a whole, eight of the 11 patients had pulmonary infarction as a result of the embolism.

Appendicular or mural clot was found in the heart in four of the eleven cases and peripheral clot in three of the 11 cases. Thus seven of the 11 cardiac cases were found to have a possible source for embolism (Table IV).

In five cases of the 46, or 10.9 per cent, bone fracture was the primary diagnosis. Three had fractured femurs, one had fractured ankle with cast, and one patient had compression fractures of thoracic and lumbar vertebrae. All five cases were found to have massive pulmonary embolism; and three of the five had clinical evidence of thrombophlebitis of the legs prior to death. A possible source for embolus was found at autopsy in only one of the five cases (Table V).

TABLE IV

| Patients With Cardiac Disease | | | Overall % Entire Series |
|---|---|---|---|
| Additional Findings | Number | % | |
| Massive Pulmonary Embolism | 3 | 27.3 | 58.7 |
| Embolism Other Than Massive | 8 | 72.7 | 41.3 |
| Producing Pulmonary Infarction | 8 | 72.7 | 52.2 |
| Appendicular of Mural Clot Found | 4 | 36.3 | 15.2 |
| Other Possible Source for Emboli Found | 3 | 27.3 | 28.3 |
| Total Possible Source for Embolism | 7 | 63.6 | 43.5 |

**Table analyzing additional findings present in patients whose primary illness was some type of cardiac disease, and comparison with entire series of 46 cases.**

TABLE V

| Patients with Fractures<br>Additional Findings | Number | % | Overall % Entire Series |
|---|---|---|---|
| Massive Pulmonary Embolism | 5 | 100.0 | 58.7 |
| Embolism Other Than Massive | 0 | 0 | 41.3 |
| Producing Pulmonary Infarction | 2 | 40.0 | 52.2 |
| Total Possible Source for Embolism | 1 | 20.0 | 43.5 |
| Diagnosed Before Death | 3 | 60.0 | 19.6 |
| Thrombophlebitis Diagnosed During Illness | 3 | 60.0 | 17.4 |

**Table analyzing additional findings present in patients whose primary illness was some type of fracture, and comparison with entire series of 46 cases.**

Cerebrovascular accident was listed as the primary illness in five of the 46 cases (10.9 per cent). Precise information is available in only one case where autopsy permit included the cranium; and cerebral hemorrhage was found. In the other four (where there was no head post-mortem), the patients were debilitated or bedfast for long periods of time prior to hospitalization and sub- sequent death. Two of the five had massive pulmonary embolism; and the other three showed embolism of lesser degree. Four of the five cases showed emboli-produced infarction at autopsy. None of the five had embolism or peripheral phlebitis diagnosed prior to death. A possible source of emboli was found in two patients at autopsy, however. One of these patients showed appen-dicular clot in the heart, possibly resulting from auricular fibril tion; the other had clot in peripheral veins (Table VI).

Of the 27 patients with massive pulmonary embolism, 15 succumbed within 25 minutes after acute symptoms de-veloped; in 12, death was delayed. Of those dying sudden-ly, four had collapsed while straining at stool or getting out of bed for the first time after surgery or debilitating illness.

Of the total group of 46 patients, a possible source of emboli was demonstrated at autopsy in 20 cases, or

TABLE VI

| Patients with Cerebrovascular Accident | | | Overall % Entire Series |
|---|---|---|---|
| Additional Findings | Number | % | |
| Massive Pulmonary Embolism | 2 | 40.0 | 58.7 |
| Embolism Other Than Massive | 3 | 60.0 | 41.3 |
| Producing Pulmonary Infarction | 4 | 80.0 | 52.2 |
| Total Possible Source for Embolism | 2 | 40.0 | 43.5 |
| Diagnosed Before Death | 0 | 0 | 19.6 |
| Thrombophlebitis Diagnosed During Illness | 0 | 0 | 17.4 |

Table analyzing additional findings present in patients whose primary illness was some type of cerebrovascular accident, and comparison with entire series of 46 cases.

43,5 per cent. Seven had antemortem thrombus in the heart (mural or appendicular) and 13 were found to have clot fragments in inferior vena cavae, pelvic and iliac veins, or were produced by "milking" the femoral veins.

The incidence of pulmonary thromboembolism increased with the age of the patient as shown in Table I. Thus in the age group 80 years and above, 9.2 per cent of those autopsied were found to have embolism of some type. In this age group, 7.9 per cent died of massive pulmonary embolism.

## DISCUSSION

It is interesting to compare this series of embolism with other similar series. This group of cases is in general comparable to the series at Charity Hospital, New Orleans (2), where fetal pulmonary embolism was found to occur in four per cent of autopsies performed (all age groups included). At Michael Reese and Chicago Memorial Hospital (1), there was an incidence of one per cent. At Massachusetts General Hospital (3), the in-cidence varied between 1.86 and 3.5 per cent massive pulmonary embolism.

Small incidental embolism with or without infarction was less common in this series than in that reported at

the Massachusetts General Hospital--0.6 per cent compared with 5.0 per cent (3).

In reviewing our cases, it is quite obvious that debilitating illnesses were a prominent factor in the development of thrombophlebitis and/or embolism. Including all cases of neoplastic disease in this series (15 cases) and adding the five cases of cerebrovascular accident, five cases of fracture, three cases of congestive heart failure, and those additional cases recuperating after surgery or myocardial infarction (confined to bed), we have accounted for 42 or the 46 cases, or 91.3 per cent.

Small infarcts produced by possible previous small emboli were present in one-third of the cases of massive pulmonary embolism. Patients with massive pulmonary embolism all succumbed before massive infarction had time to develop. Therefore, the cause of death was massive embolism, not massive infarction. Perhaps the one-third mentioned were the victims of previous small non-fatal embolic episodes.

If this was the case, then prophylactic treatment after the first episode might have aborted a tragic and sudden death. In those six cases of massive pulmonary embolism where thrombophlebitis of the legs had been diag-

nosed prior to embolism, some type of prophylaxis might have also been effective in avoiding death. However, in no case was venous ligation performed or anticoagulants administered.

Only six of the 27 cases of massive pulmonary embolism were correctly diagnosed as such before death or at time of death. Because massive pulmonary embolism is so often clinically indistinguishable from some other conditions (notably myocardial infarction), and because such a large percentage of the cases in this series actually died "slowly" (without acute onset or symptoms ), it is understandable why so few of the patients had embolism diagnosed prior to death.

It is interesting to consider the role played by the fibrillating or otherwise damaged heart in the production of pulmonary emboli. Clot may then form along the infarcted walls or in the auricular appendages. When such clots originate in the left heart and break loose from their moorings, a clinical picture of peripheral embolism develops--either to brain, extremity, coronary artery, or to viscera. These usually produce infarction of the area of tissue deprived of its blood supply. When such clots form in the right heart and become detached, they pass to the pulmonary arteries. The

size of the vessel occluded depends upon the size of the clot set free, producing pulmonary embolism. This may or may not be followed by pulmonary infarction. In this series, this source for embolism was seen in seven of the 46 cases. As was mentioned, three of these cases followed myocardial infarction. In an additional case, auricular fibrillation was a clinical diagnosis--though the patient's primary diagnosis was cerebrovascular accident. One other case had been diagnosed as having congestive heart failure of unknown cause. It is not known if auricular fibrillation was present; but there was an appendicular clot present.

As is usually the case in autopsy series presenting the problem of pulmonary embolism, a possible source for emboli was found in only a relatively small portion of patients. This may in part be attributed to limitations of autopsy, since leg veins cannot usually be examined.

As is shown in Table I, there appears to be a rising incidence of pulmonary embolism with increasing age. However, with increasing age, there was also increasing tendency to confinement to bed and generalized debility which could also explain predilection for older age groups. Of the 76 patients in the 80 and over age group, seven showed pulmonary embolism. Six of these seven were of the massive

type. Thus in this older age gro p, the incidence of massive pulmonary embolism was 7.9 per cent, more than twice the overall incidence.

## SUMMARY

The problem of pulmonary thromboembolism is one well recognized as a major cause of de th and as a much feared complication to both medical and surgical patients. Its incidence in various autopsy series varies between eight and ten per cent. Massive pulmonary embolism varies among series between one and five per cent.

Pulmonary emboli are usually divided into three types--massive embolism, embolism of medium-sized pulmonary arteries and embolism of small-sized pulmonary arteries. The clinical diagnosis may prove easy or quite difficult. Most common symptoms are chest pain and respiratory com-plaints. The most common signs are generalized inflamma-tion, cardiovascular manifestations, cerebral signs and other miscellaneous symptoms. The electrocardiogram and X-ray may be helpful.

Treatment now centers around prevention, with close attention given to any signs of thrombophlebitis. Once diagnosed, supportive therapy, with administration of oxygen, is usually warranted. E mbolectomy, performed

on those afflicted with massive pulmonary embolism, has proved disappointing. Prophylaxis may consist of ligation of veins of lower extremities and the use of anticoagulants. Such factors as trauma to the extremity, blood dyscrasia, and dehydration, precursors to thrombophlebitis and phlebothrombo is, may predispose to pulmonary embolism. The pulmonary embolism seems to occur most commonly following surgical procedures as well as with concomitant heart disease. Mechanical factors, such as straining at stool, will occasionally precipitate the dislodgment of clot, which then is carried to the lungs.

The cause of death may be due to simple anoxia or to neurocirculatory disorders, according to experimental data. The mechanism of development of infarcts has also been studied extensively. Many different materials have been introduced into the venous circulations of experimental animals; and investigators have reproduced all types of embolism.

Patients surviving pulmonary embolism may later die of other causes or may subsequently suffer from additional episodes, some of them fatal. A number of patients appear to recover completely.

A study was made of 837 autopsies at Methodist Hospital, Omaha, Nebraska, encompassing a ten-year period

(1946-1955). Forty-six of these patients were found to have pulmonary thromboembolism at time of postmortem examination. Twenty-seven of these 46 were of the massive type, while the other 19 cases were of lesser degree--either embolism of medium-sized arteries, small-sized arteries, or a combination of the two conditions. Infarction produced by embolism was found in 24 of the 46 patients. It was found that 13 of the 46 had had recent surgery, while 33 were medical patients. The embolism was diagnosed before death in only nine cases. There was clinically demonstrable thrombophlebitis of peripheral veins in eight cases. In 20 cases, a possi-ble source for embolism was found at autopsy, either in peripheral veins or as mural or appendicular clot in the heart. Fifteen patients had as their primary illness, neoplastic disease; eleven, cardiac disease; five, frac- ture, and five, cerebrovascular accident. Debilitating illness thus appeared to be a major precursor.

## CONCLUSIONS

In a series of 837 autopsies at Nebraska Methodist Hospital, Omaha, from 1946 to 1955, 46 cases of pulmonary thromboembolism were found. Of these, massive embolism predominated. Although embolism-produced pulmonary in-

farction was more common in medical patients than in surgical patients, massive pulmonary embolism was more common if the patients had had recent surgery.

Though 5.5 per cent of the autopsies showed some type of pulmonary embolism, only a relatively small per cent of these had been diagnosed as such before death, had had antecedent diagnosed thrombophlebitis, or could be shown to have a source for embolism at autopsy.

Some of the deaths in this series might have benefitted from prophylaxis after an earlier, non-fatal embolus or with treatment of peripheral thrombophlebitis.

Among other factors, neoplastic disease, cardiac disease, fracture or cerebrovascular accident, seemed to predispose to the development of pulmonary embolism.

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