Pulmonary Emboli*
A Factor in the Etiology and Pathogenesis of Pulmonary Emphysema

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Pulmonary embolism may be attributed to foreign objects, fat, oil, air, and other unusual conditions; however, the usual contributing factor is related to cardiovascular thrombosis, of which the common and frequent cause is venous thrombosis.

Pulmonary embolism and its effects cannot be understood without considering venous thrombosis, the common source of the embolus. The expression “venous thrombosis” is used in order to avoid controversy over the terms thrombophlebitis and phlebothrombosis. Thrombophlebitis indicates one end of a disease spectrum where infection is evident and embolus rarely occurs; phlebothrombosis, the other end of the spectrum, reveals little, if any, infection but is associated with a relatively high frequency of emboli. There is every grade to be found between these two extremes of the condition. A relatively small piece or the whole intravenous thrombus may break loose and be filtered out of the blood stream by the lungs. Every conceivable type of embolus could occur, from a huge one filling the main pulmonary artery to an embolus of microscopic size.

It is impossible to cite the incidence of venous thrombosis. In one group of patients it is easy to establish a positive diagnosis. There is another group in which the disease is not considered because of the silent nature of the process. The silent type defies a prediction of incidence, but embolism to the lung cannot be understood without seriously considering the silent type of venous thrombosis.

The results of the pulmonary embolism can be as variable as the embolus or emboli that lodge in the lung, depending upon the size, frequency, and presence or absence of infection. The results also depend upon the age and general health of the patient and upon the presence of concomitant disease. The symptoms of an embolus to the lung may be death in a few minutes after the occurrence or they may be so minimal that diagnosis cannot be made. The effects of pulmonary embolus may be sudden death. If death does not occur, there may be lung tissue destruction such as cavity formation, abscess, bronchopleural fistula, and/or scar tissue. Complete recovery with no demonstrable after-effects is possible. There are many well-known and well-documented sequelae of pulmonary embolism. Other conditions may occur that are not recognized. Perhaps effects now beyond imagination are yet to be described.

Materials of the Study
The discussion and conclusions reached herein are derived from a study of old necropsy material and reports, a study of medical records of pulmonary embolism at Church Home and Hospital from 1953 to 1959, inclusive, a study of selected patients, and a perusal of pertinent literature.

It is unnecessary to describe death occurring a few minutes after massive pulmonary embolism. The hospital records, necropsy reports, and literature are replete with this condition.

Case Reports

Case 1
White man, age 76, admitted to a hospital October 22, 1951. The diagnosis was right pleural effusion. On December 18, 1951 he became dyspneic and complained of left chest pain. The following is quoted from the records: “—extremities negative.” Death occurred December 26, 1951. Necropsy revealed neurilemmoma in the right posterior mediastinum with small right
FIGURE 1: Photograph shows hilum of left lung of Case 1. A large coiled embolus—A; in the left pulmonary artery—B; bronchus—C.

There was an embolus of the left pulmonary artery (Fig. 1). The extremities were not examined and the source of the embolus was not recorded in the necropsy report.

FIGURE 2: Photograph of hilum of left lung of Case 2 showing old pulmonary embolus—A; intermediate pulmonary embolus—B; a new fresh embolus—C.
CASE 2

Negro man, age 39, was admitted with hemoptysis to a hospital March 29, 1955. A diagnosis of upper respiratory infection was made. Onset of the illness occurred one month prior to admission. On admission, physical examination revealed normal upper and lower extremities, except for bilateral pitting edema. The lungs were normal, but the liver was palpable four fingers below the costal margin. On April 1, 1955, a diagnosis of thrombophlebitis of the external jugular vein was made. He died April 4, 1955. The necropsy revealed thrombosis of the veins of the upper extremities and neck. There was hypertrophy and dilatation of the upper right auricle and ventricle, and multiple old and new pulmonary emboli. In Fig. 2, cut surface of the hilum reveals old as well as fresh emboli to the pulmonary artery. Fig. 3 shows the pulmonary artery with anterior aspect removed, revealing the extensive thrombus. The fresh thrombus that occurred distal to a solid old thrombus in the upper left-hand branch can be noted. Dissection of a branch of the pulmonary artery is seen in Fig. 4. The old Y-shaped thrombus indicates propagation from the larger clot located at the bifurcation of the pulmonary artery. It is obvious that a clot of this shape does not occur as an embolus. Examination revealed an old embolism with a new embolus which caused death. It showed propagation of the clots, both new and old, distal to an occlusion of the pulmonary artery. The patient also had right heart failure and pulmonary hypertension.

CASE 3

Negro man, age 45, was discharged from a hospital July 23, 1954 with a diagnosis of "(1) infection of lung due to embolus, (2) thrombophlebitis, left leg, (3) enlargement of the heart due to cause unknown." He was readmitted March 28, 1955 because of dyspnea. He had a progressively deteriorating course and died July 25, 1955. There was no acute episode during the hospitalization. At necropsy, an old occlusion of the right and left iliac veins was found revealing the organization of thrombus and some recanalization: "The left jugular vein was thrombosed throughout. Cor pulmonale was advanced." The lungs revealed an old organized thrombus upon which propagation and formation of a new clot occurred (Fig. 5).

CASE 4

Negro man, age 28, was admitted to a hospital September 17, 1953 and died about 24 hours later. There was a history of illness beginning two years previously. He lost weight; about six months after onset, he became short of breath. One year after onset, he expectorated blood. He was treated as a cardiac patient. In March, 1953, he suffered a "right-sided stroke." One month prior to admission there was swelling of both legs, which became worse the day before admission. The necropsy revealed "No thrombus in femoral or iliac veins." (There was no further description of the venous system). Diffuse hypertrophy of the heart was noted, "—which was apparently relatively greater in the ventricles than in the auricles. Heart valves were normal." There were "—well-developed mural thrombi. These mural thrombi filled about one-third of the left ventricle and about one-fifth of the right ventricle." The lungs revealed, among other abnormalities "—large, irregular scars which deformed and shrunk the lower part of the lobe," as shown in Fig. 6. The pulmonary emboli had their origin in the right ventricle.

CASE 5

White man, age 67, was discharged from the hospital September 18, 1953, with a diagnosis of "—cor pulmonale, bronchial asthma, and pulmonary emphysema." He did well until three weeks prior to admission when an increase in dyspnea and ankle edema occurred. Physical examination revealed a chronically ill, cyanotic,
dyspneic patient. In the lungs there were fine moist rales at the bases posteriorly and "—rhonchi were heard throughout the chest. The heart appeared normal. The liver was enlarged, and the legs showed considerable edema. He was readmitted to the hospital and gradually became worse. An acute episode occurred 24 hours before death. He died November 12, 1954.

Necropsy examination revealed "—the lungs severely emphysematous. Almost the entire upper lobes of each lung stand out as a mass of huge blebs. The remainder of the lungs felt coarse and contained small blebs—. The right ventricle was greatly enlarged and greatly hypertrophied, and the left ventricle was relatively small. In the stem of the pulmonary artery and extending to the arteries of each lung was a large aneurysm-like dilatation nearly filled with lamellated hyalin fibrin." Fig. 7 reveals the emphysema and the lamellated organized thrombus in the major pulmonary arteries.

CASE 6
White woman, age 40, was discharged from a hospital August 7, 1957. The diagnosis was pulmonary emphysema with pneumonitis and right heart failure. Chest x-ray film of March 27, 1957 is shown in Fig. 8. A chest x-ray film dated September 15, 1959 revealed considerable increase in the pulmonary emphysema, but little change in the heart (Fig. 8). She was readmitted to the hospital September 9, 1959, at which time she reported that her dyspnea began about three years ago and recently became worse and that it was associated with ankle edema. A series of unfortunate complications ensued and she died October 7, 1959. The necropsy revealed definite pulmonary emphysema, hypertrophy of the right
ventricle and "— a peptic ulcer of the greater curvature of the stomach with massive hemorrhage into the stomach and upper gastrointestinal tract." The pulmonary arteries were injected rather than studied grossly or microscopically. Fig. 9 shows the prepared left lung specimen obtained by injecting the pulmonary artery. The prepared specimen of the right lung was essentially the same. (A similarity in the size of the pulmonary artery can be seen in Cases 5, 6 and 7).

CASE 7

White woman, age 38, was examined on May 21, 1964. Her father and a paternal aunt were said to have died of pulmonary emphysema. A chest x-ray film taken in September, 1960 was interpreted as normal. A routine chest x-ray film on May 12, 1964 (Fig. 10), revealed large pulmonary arteries. There were minor emphysematous changes in the apical regions on both sides not reproducible by photographs. She had no symptom except slight exertional dyspnea with some cough and less than one teaspoon of tenacious clear sputum a day. Physical examination proved essentially normal except for an anterior cardiac thrust and a pulmonic second sound greater than the aortic second sound. The
pulse rate was 80 and the blood pressure 110/60. "Cardiac catheterization was compatible with pronounced pulmonary hypertension associated with a marked increase in total pulmonary resistance, with no evidence of an intracardiac shunt." The cinephotofluorographic examination revealed considerable reduction in size of the arteries entering the apical regions on both sides. On April 29, 1965 a pulmonary scintiscan showed a slightly diminished uptake in the upper lobe of the left lung medially (Fig. 11).

A survey was made of all pulmonary embolisms that occurred at Church Home and Hospital from 1953 to 1959 inclusive. The starting point was selected because original chest roentgenograms were available from 1953. The end point was chosen in order that an arbitrary minimum of six years should elapse from the onset of pulmonary embolism. There were 35,346 admissions. Pulmonary embolism was diagnosed in 94 cases. A total of 31 patients died in the hospital and 17 necropsies were obtained on this group. The time interval from onset to death was a few seconds in four patients to three weeks in one. There were 63 patients who recovered and were discharged from the hospital. Of these, 48 patients had a definite diagnosis of cardiac disease made before the suspected embolic episode. After a study of the hospital charts and the x-ray films it was impossible to be definite about the presence of pulmonary emboli in these patients; therefore, the study was not carried further in this group. In 15 patients there was a surgical, traumatic, or noncardiac diagnosis made before the suspected pulmonary embolism. A study of the hospital records and the chest roentgenograms did not substantiate the diagnosis in five of them; the remaining ten appeared to have had pulmonary embolism. Four of these ten died after leaving the hospital. The cause of death could not be determined. The remaining six of the ten patients who did have pulmonary embolism were contacted; all are free of symptoms and apparently well. Three of the six have had recent chest roentgenograms and pulmonary scintiscans and all are free of demonstrable changes or residuals from the embolic episode. The remaining three refused to undergo the examination.

![Figure 8: Chest roentgenograms of Case 6. A—was taken March 27, 1957. It reveals the large pulmonary arteries bilaterally and the bullous emphysema in lower lung fields. B—was taken September 15, 1959. It reveals increase in size of pulmonary arteries and an increase in the bullous emphysema of both lower lung fields.](http://journal.publications.chestnet.org/pdfaccess.ashx?url=/data/journals/chest/21432/ on 06/21/2017)
FIGURE 10: Posteroanterior and lateral views of chest roentgenograms of Case 7 which reveal large pulmonary arteries. These may be compared with Fig. 8 and 9 of Case 6.

DISCUSSION

The incidence of pulmonary embolism is difficult to discuss accurately. In the study of 35,346 admissions, the diagnosis was made in 94 instances and 31 of the patients died in the hospital. However, only 17 of these were confirmed by necropsy. In the literature the incidence is reported in from 1.5 to 25 per cent of the cases as a routine necropsy finding. It averages as high as 25 per cent in a necropsy series done upon patients in a custodial institution. Pulmonary embolism is estimated to cause 2 to 3 per cent of all deaths and accounts for 30,000 deaths a year in the United States. Elfman believes it causes 5 to 7 per cent of all deaths from coronary artery thrombosis, 5 to 7 per cent of all postpartum deaths, and 50 per cent following pelvic surgery. Pulmonary embolism occurs more frequently after the age of 40 and more frequently in the obese. He is of the opinion that it occurs three times more frequently in the medical patient than it does in the surgical patient. In the Church Home and Hospital series, pulmonary embolism was diagnosed approximately three times more frequently in the medical patient as compared to the surgical patient.
It is obvious that the incidence depends upon an accurate diagnosis and the clinical diagnosis is always open to question.

The diagnosis of pulmonary embolism is rather difficult to make in an accurate manner,1, even in the event of sudden death. In the past, the diagnostic error ranged from 33 to 89 per cent, according to Gorham.2 Perhaps the only infallible conclusion is that arrived at by necropsy or operation. Since surgery using cardiopulmonary bypass is becoming more common,3 it is even more important that accurate diagnosis be made. The theory that there may be time for the surgical removal of the large pulmonary embolism before death is observed in the small series from Church Home and Hospital where the period from embolism to death was seconds to three weeks, and in Case 1 about seven days. The time interval from emolization to death is vividly reported by Gorham.4 In 100 cases of massive pulmonary embolism, the time was 41 per cent in ten minutes or less, 3 per cent in 15 minutes, 22 per cent in 15 minutes to two hours, 8 per cent in two to 12 hours, 21 per cent from 12 hours to 14 days, and in 5 per cent the time interval could not be determined. Case 1 illustrates an interval of seven days between the occurrence of the embolism and death. It reveals that death may be related to disease that existed before the embolism occurred. If the right lung had been normal, the patient most likely would have survived the embolism.

Many pathologic conditions can occur after pulmonary embolism ranging from sudden death to complete recovery without sequela or demonstrable ill effect.6,9,10 Death may occur within a few seconds or it may be a slow downhill course requiring three weeks, as shown by a study of the hospital records. Death may occur only after repeated embolic episodes11 that may follow at intervals of time separated by at least one month as in Case 2, and by episodes over a two-year period as shown by Case 4. Death may occur by late propagation of a clot or by thrombus formation upon an old organized pulmonic embolus as revealed in Cases 2 and 3. Death may

**Figure 11:** Photograph of pulmonary scintiscan of Case 7.
result from pulmonary hypertension with or without lung changes as revealed by Cases 2 and 5, and the report of Rosenberg and others. As illustrated by the cases reported and by the literature, there may occur pulmonary embolism, or organization of the embolus, with fibrosis and/or recanalization. There may be infarction of the lung with fibrotic scar, breakdown of the lung tissue with bronchopleural fistula, lung abscess, or cavitation. After pulmonary embolism, recovery may be complete without demonstrable sequel or organic defects as demonstrated by three of the Church Home and Hospital patients.

Pulmonary hypertension is a disease of questionable etiology. The report of Rosenberg indicates that in six of nine cases studied at necropsy, there were changes compatible with multiple pulmonary emboli. This report is convincing even though routine necropsy revealed a high percentage of patients with pulmonary emboli.

When suspected embolism occurs or when a definite clinical diagnosis is made and the patient recovers, there can be speculation as to the sequela and/or complete recovery. When recovery is complete with no injury to the lung, perhaps it is the result of resorption of the clot. By pulmonary arteriography, Fred and associates demonstrated resolution of pulmonary thromboemboli in seven patients in as short a period as one week. Robb and co-workers believe perfusion is necessary for resorption of the micro emboli. Robertson and colleagues indicate that resorption of the clots occurred uniformly in animals when the portal system was experimentally filled with blood clots. The vascular arrangements of the lung and liver are in some ways similar since the liver has a large venous supply from the portal vein and an arterial supply through the hepatic artery. These two intermingle in the sinusoids of the liver and drain by way of the hepatic veins into the inferior vena cava. The lungs receive a large venous supply of blood by the pulmonary artery and a supply of arterial blood from the bronchial arteries. The two intermingle in the pulmonary capillary bed and are drained from the lung by the pulmonary veins. The complete resorption of the embolus, when it does occur, may be the result of the unique vascular supply. It is obvious that a functioning double blood supply prevents infarction of the lung with each embolus. Many writers aptly point out that lung embolization is not synonymous with lung infarction.

Pulmonary emphysema may be found in the presence of conclusive evidence of pulmonary embolism, as shown by necropsy reports and illustrated in Case 5. Perhaps it can be considered a factor in the pathogenesis of pulmonary emphysema. It is possible that the presence of pulmonary emphysema was coincidental and pulmonary emphysema may have been present before the embolization occurred. The same reasoning can be applied to the cause of pulmonary hypertension.

When there are so many degrees of tissue reaction in pulmonary embolism ranging from complete recovery to tissue destruction, as illustrated by bronchopleural fistula, cavitation or scar formation, it seems probable that a degree of injury may result in precisely the proper amount and proper distribution to cause pulmonary emphysema. It is easier to conceive of localized emphysema resulting from embolization than it is to believe generalized emphysema might occur in this manner. Crenshaw produced (localized) pulmonary emphysema in the horse through destruction and/or obstruction of the pulmonary capillary bed by injection of materials through the bronchial artery. Pulmonary emphysema and pulmonary emboli have been observed and described in the past. Cudkowicz and Armstrong in describing an emphysematous lung stated: "Serial sections taken from these lobes showed on histological examination that the pulmonary artery branches were occluded by organized thrombi and intimal thickening and that the enlarged vasa vasorum in
these adventitia communicated with the new channels within the thrombosed pulmonary artery lumina."

Ryan found evidence of pulmonary embolism or thrombosis significantly higher in a group of 66 patients with longstanding severe emphysema than in a series representing the general hospital population of similar age, but without pulmonary disease. Kernan and associates, in a study of 125 necropsies in patients with pulmonary emphysema and a control group of 40 patients, found no statistical difference in embolization between the two groups. Nicholson reported necropsy results in 16 patients with severe pulmonary emphysema and in this group eight were found to have pulmonary embolic disease. A study of a necropsy series, regardless of the type of disease, has revealed 1.53 to 25 per cent with pulmonary emboli.

If destruction of the pulmonary capillary bed is the cause rather than the effect of pulmonary emphysema, it seems reasonable that gradual further destruction of the capillary bed can be caused by repeated small pulmonary artery emboli in exactly the proper degree or severity. Pneumonitis of virus or pyogenic etiology may cause destruction of areas of the pulmonary capillary bed; however, it is well known that pneumococcal pneumonia characteristically does not destroy the pulmonary capillary bed. The patient with pulmonary emphysema often becomes permanently worse (more dyspnea) after an attack of pneumonitis. Ryan suspects the attack may be an embolus and not infection or pneumonitis.

In Cases 5, 6, and 7, the history of venous thrombosis was absent. However, this is not uncommon even though pulmonary embolism is found at necropsy. Case 5 revealed a tremendous enlargement of the pulmonary artery and is this respect it resembles Cases 6 and 7. Cases 5 and 6 definitely showed pulmonary emphysema. There is every reason to believe that there is beginning pulmonary emphysema in the upper lobe of Case 7. Only time will prove whether or not fully developed pulmonary emphysema will occur before pulmonary hypertension takes the patient's life. It is difficult to attribute a diffuse disease of the lung to a localized assault such as embolization, even with repeated episodes. Perhaps pulmonary emboli superimposed on diffuse generalized emphysema may be the cause for bullae formation. This formation in a lung with generalized pulmonary emphysema causes an area of more complete tissue destruction; generalized pulmonary emphysema indicates that no area of the lung is free of airway obstruction. It appears logical that the proper interference with the pulmonary capillary bed by an embolus may cause localized pulmonary emphysema, lobar or even unilateral emphysema. Since the etiology of generalized pulmonary emphysema is unknown, perhaps more intensive study should be made of the embolic dispersoids described by Schreiber.

**SUMMARY**

Pulmonary embolism occurs in from 1.5 to 25 per cent of routine necropsies and it is often found in the absence of a history of venous thrombosis. Pulmonary embolism is difficult to diagnose accurately without necropsy or operative evidence of emboli. It appears that death may occur suddenly, slowly, or not until repeated episodes of embolism occur and then death may be in part the result of pre-existing disease. There may be complete recovery after pulmonary emboli without demonstrable evidence of sequel. Many conditions may develop between death and complete recovery. The clinical course and pathogenesis of pulmonary emphysema are influenced by pulmonary emboli. Pulmonary emboli may be the cause of localized, lobar, or unilateral pulmonary emphysema. Pulmonary emboli may also be the cause of bullae in generalized pulmonary emphysema.

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**RESUMEN**

La embolia pulmonar se observa en el 1.5 a 25 por ciento de las autopsias y frecuentemente
CIGARETTE SMOKING AND IN VITRO THROMBOSIS OF HUMAN BLOOD

In 24 of 60 habitual smokers, the in vitro thrombosis formation time of the blood was decreased soon after cigarette smoking. In 23 individuals, it was unchanged, and in three, it increased. The average change was statistically highly significant. Other data indicated that the findings after smoking are not due to the motional effects of the experimental procedure itself, but are probably the result of smoking. It is suggested that the increased thrombotic tendency is mediated via the nicotine-induced release of epinephrine. It is further suggested that this hyperthrombotic state is a major etiologic factor in the increased incidence of acute myocardial infarction in habitual smokers.


MYOCARDIAL INFARCTION IN YOUNG PERSONS

Of 80 patients with myocardial infarction, age up to 40 years, in 36 the disease ran a severe course (in 16 patients sudden death supervened, ten died in the hospital within the first 24 hours, two on the 10th and 23rd days of the disease). An abdominal form of myocardial infarction was encountered in six cases, in five there was a painless type infarction, in two, a combined form. In one patient, myocardial infarction ran a course resembling a severe attack of bronchial asthma.


TRACHEOESOPHAGEAL FISTULA

Two cases of tracheoesophageal fistula as a result of nonpenetrating chest trauma are reported. Review of the literature reveals 15 other cases. The injury has been noted in only young adult men. Steering wheel trauma has been the mechanism of injury in the majority of instances. Mediastinal and/or subcutaneous emphysema have been present in the majority of cases. The fistula characteristically became symptomatic only after three to five days. In no instance did the fistula heal spontaneously. Surgical repair was attempted in 14 patients and resulted in cure in 13.