PULMONARY EMBOLISM
INCIDENCE AND SIGNIFICANCE

Abe Towbin, M.D., Columbus, Ohio

Pulmonary embolism becomes an increasingly important problem as the extent of its incidence becomes unveiled. Although the subject of much study, the incidence of pulmonary embolism has remained a matter of uncertainty and disagreement. Pulmonary embolism is reported by some as being infrequent; it may, in fact, represent one of the most important forms of terminal illness, one of the commonest causes of death in the population at large. The diagnosis of pulmonary embolism is difficult and equivocal. The disease is usually portrayed as being of sporadic occurrence; although this conception is deeply rooted in medical opinion, it is open to question. To obtain an exact measure of the incidence of fatal pulmonary embolism in the general population, two conditions must be fulfilled: the evaluation must be based on autopsy examinations and a high percentage of the deaths in a given community over a period of years must be examined. The disagreement in the literature regarding the incidence of pulmonary embolism stems from the fact that it has been difficult to provide circumstances in which these conditions could be fulfilled.

POSSIBLE APPROACHES TO PROBLEMS

Studies of pulmonary embolism in the past, despite the variable factors encountered and despite the difficulties in obtaining comprehensive data, have contributed important information. The incidence of pulmonary embolism continues to be studied intensely in many clinics. In previous surveys of thromboembolic disease of the lung, recourse has generally been had to three avenues of investigation: vital statistics, clinical studies of cases diagnosed in the hospital, and general hospital autopsy studies. These methods, because of their inherent limitations, do not provide conclusive cross-sectional data of the incidence of pulmonary embolism in the general population. In pursuit of this problem, a fourth method, the autopsy study of persons in custodial institutions, is offered in the present work.

Vital Statistics.—Vital statistics, as generally registered, are unacceptable as an indicator of the incidence of pulmonary embolism because of inevitable errors in deathbed diagnosis and inadequate number of autopsies. Members of the older age group, in large proportion, remain at home during their terminal illness; at death, which is often ascribed to “natural causes,” autopsy is not performed. Definite information regarding the nature and incidence of terminal illness is buried with the remains and lost forever. A survey of vital statistics shows that the diagnosis of pulmonary embolism is rarely made by physicians in deaths occurring at home. In the vital statistics of the city of Columbus, Ohio, in 1951, 3,958 deaths representing all ages were registered; of these deaths, slightly over one-half, 2,133, occurred in hospitals. Pulmonary embolism was diagnosed in 62 cases, or 2.91% of hospital deaths. In deaths that occurred at home, the diagnosis was considered in 0.76% of cases; these vital statistics indicate that the diagnosis of pulmonary embolism was made only one-fourth as often in home deaths as in hospital deaths. Significantly, most of the hospital cases of pulmonary embolism occurred in medical patients; few were surgical. In most cases the nature of the terminal illness was unrecognized clinically, the diagnosis being established only after autopsy. It is likely that the fourfold difference in frequency of fatal pulmonary embolism registered in these vital statistics reflects discrepancies in diagnosis rather than a true difference in incidence of pulmonary embolism in hospitalized and nonhospitalized patients. These data derived from the vital statistics emphasize that in medical practice there is a general unawareness of the frequency of pulmonary embolism.

Clinical Surveys.—Clinical surveys, the second method of analyzing the incidence of pulmonary embolism, have been made of patients with pulmonary disease admitted to general hospitals. In these studies the diagnosis of pulmonary embolism is generally based on physical signs and symptoms, radiological and electrocardiographic changes, and autopsy findings in available cases. In most clinical studies, the number of cases of fatal and nonfatal pulmonary embolism diagnosed on the ward is compared to the total hospital admissions. Such surveys provide significant presumptive data regarding the rela-
The incidence of pulmonary embolism in hospital practice. Short, studying pulmonary embolism in a general hospital, stressed the incidence of pulmonary embolism in medical patients; he concluded that thromboembolic disease of the lung may, in fact, be the commonest serious acute pulmonary disease in modern general hospital practice. In the study by Short the incidence of thromboembolic disease was higher than that of lobar pneumonia. The attitude of the past that pulmonary embolism is a disease limited largely to the postoperative period is deep rooted in medical thinking. This conception is wrong. Embolism in medical patients, though less dramatic than in surgical cases, is of frequent occurrence. Carlotti and co-workers studied the incidence of fatal and nonfatal pulmonary embolism in patients treated at Massachusetts General Hospital between 1936 and 1945. The diagnosis of pulmonary embolism was made in 0.6% of patients on the medical service and 0.24% on the surgical service.

Evaluation of the incidence of pulmonary embolism by clinical means is subject to errors arising from mistakes in clinical diagnosis. The clinical delineation of pulmonary embolism by roentgenologic and other clinical methods is often inconclusive; pulmonary embolism is mimicked by coronary occlusion and pneumonia and other pulmonary disease, and is often so diagnosed. On the other hand, cases with all the clinical signs and symptoms of pulmonary embolism may, in fact, be some other disorder. Although clinical surveys of pulmonary embolism in general hospital services are not an absolute index, such studies are of considerable significance; these studies emphasize the high incidence of nonfatal pulmonary embolism. As the frequency of pulmonary embolism becomes more widely realized clinically, vigilance is increased and diagnostic error is reduced; accordingly, data from clinical studies become more meaningful.

**Autopsy Series in General Hospitals.**—The third important means of studying pulmonary embolism is by analysis of autopsy series in general hospitals. These studies tend to be more definitive than analyses based on clinical findings. Considerable impetus has been given to the investigation of thromboembolic disease by recent advances in anticoagulant and surgical treatment. This problem has come under close scrutiny in medical as well as in surgical clinics. Many studies deal with the incidence of postoperative pulmonary embolism; the prevention of this complication is still a challenge to the surgeon. General hospital autopsy series, together with clinical studies, are of great importance in determining the relative changes in incidence of disease and in evaluating prophylactic and therapeutic measures in hospital practice.

**References**


Belt, in a study of 567 autopsies on adults at Toronto General Hospital, found pulmonary embolism in 56 cases, an incidence of 10%; in 37 cases the emboli were massive and accounted for death. Medical cases of pulmonary embolism predominated over surgical cases in a ratio of 40 to 16. Ochsner, DeBakey, DeCamp, and da Rocha reviewed the incidence of thromboembolism at Charity Hospital in New Orleans over a 12 year period beginning in 1937. In this large general hospital during that period 32,354 deaths occurred and 10,947 autopsies were performed. Death was attributed to pulmonary embolism in 476 cases; in 383 the diagnosis was confirmed at autopsy. These investigators pointed out that a progressive increase in venous thrombosis and its attendant sequelae occurred during this period of years. In 10,940 consecutive autopsies reviewed by Collins at Los Angeles County Hospital, the incidence of fatal pulmonary embolism was 2.07%. McCartney, studying the autopsy records of the department of pathology at the University of Minnesota in the 20 year period beginning in 1919, found that 2.67% of deaths were due to pulmonary embolism. Roe and Goldthwait studied the frequency of embolism at Massachusetts General Hospital for the five year period beginning in 1943; in 2,083 autopsies, pulmonary emboli of varying size were present in 9.75% of cases; in 4.42% embolism was extensive and accounted for death; cases with massive embolism showed a steady and appreciable increase during the period of study. DeBakey, in a recent collective study compiled from reports in the literature, found that 10,497 cases of fatal pulmonary embolism had been reported in 374,844 autopsies, an average incidence of 2.8%.

Studies based on autopsy series in general hospitals suffer from the serious distortion caused by selectivity and restriction of patients admitted. The census of general hospitals in most communities does not accurately reflect the incidence of terminal illness in the aged. The population of a general hospital is, to a large degree, made up of patients of the younger age group with acute illness. Pulmonary embolism is predominantly a disease afflicting patients in the later decades of life. Since members of the older age group often do not seek hospitalization during terminal illness, critical data dealing with this segment of fatal illness most pertinent in evaluation of pulmonary embolism are not included in the autopsy statistics registered in a general hospital.

In most communities only a fraction of the general population is studied at autopsy. Even in the hospital there is a natural tendency among physicians to secure autopsy information only in cases of special academic interest with special emphasis on fatal illness in the younger age group. Consequently, with older patients, even those who are hospitalized, often little effort is made at the time of death to obtain permission for autopsy. In the aged patient with cardiorespiratory symptoms the cause of death is often, by routine, catalogued as arteriosclerotic heart disease or bronchopneumonia. Herein lies the source of considerable error. Every death, whether of immediate singular medical interest or not, merits autopsy investigation to determine the nature of terminal illness.

To obtain consistently valid data of the incidence pattern of fatal illness in the general population, autopsies must be performed in a high percentage of the persons...
who die in a given community. If admission of aged persons with terminal illness is restricted and if the autopsy percentage is low, autopsy data from a general hospital cease to reflect the incidence of fatal illness in the community.

Autopsy Series in Custodial Institutions.—In contrast to the relatively low incidence of pulmonary embolism reported in general hospitals, Moran,8 in a five year study of deaths at Pittsburgh City Home and Hospital, observed pulmonary emboli in 23.1% of autopsies; 6.8% of deaths in this custodial institution were due to massive pulmonary embolism. Custodial institutions provide unique access to information regarding the general incidence of terminal illness. If a high autopsy percentage is available, data obtained from autopsy studies in a custodial institution tend to reflect the pattern of terminal illness in the general population more closely than statistics from a general hospital.

The present study was carried out in the large institutionalized population of Columbus State Hospital in a period extending over four years. Autopsy studies were available in a majority of deaths. Although all adult age ranges are represented in the census of the institution, and although psychiatric patients are treated here, the population is composed in large measure of older persons who, lacking family ties, require simple maintenance and custodial care. Physical illness observed clinically in this group is representative of that occurring in a cross section of the adult population in a general community of comparable size. Accordingly, autopsy studies of terminal illness in this institutional community provide a key to the incidence pattern of terminal illness in the average adult population. This study, as initiated in 1949, was formulated to define the nature and incidence of all types of fatal illness occurring in this population; however, attention became sharply focused on the problem of pulmonary embolism during the course of the investigation because of the frequent and unheralded incidence of thromboembolic lesions in the lung discovered at autopsy.

METHOD OF THIS STUDY

Facilities became available in the present study to survey the incidence of pulmonary embolism in an institutional population equivalent to a community of about 2,500 persons. This investigation was carried on in the period between Sept. 1, 1949, and Jan. 1, 1954, a period of four years and four months, at Columbus State Hospital in Columbus, Ohio. In this time 881 deaths occurred. Postmortem examinations were performed in 512 cases, or 58%.

The ages at death in the cases in which autopsy was performed ranged from 22 to 94 years; most deaths, as in any community, were in adults of advanced years. The number of deaths in each age group is shown in table 1; for comparison, the number of deaths that occurred in each adult age group in the surrounding city of Columbus during 1951 is noted. The distribution by ages in the two populations compared here is parallel. The age group between 60 and 69 years makes up 22.7% of deaths in Columbus and 24.7% of cases in the autopsy series. In 46.4% of deaths in the city the age was 70 years or over; similarly, 48% of the deaths in the autopsy series occurred in persons of 70 years or over. The autopsy series thus reflects closely the age distribution of adult deaths occurring in the general population in this region.

The plan of investigation as initiated in 1949 represented a concerted effort to define more exactly the nature of terminal illness in this institutional community. In carrying out this investigative program two principles were emphasized: first, to obtain a valid cross section of fatal illness occurring in the population, efforts were made to obtain autopsy permission in each death regardless of the apparent medical importance of the case; second, the postmortem routine was standardized. In a study such as this, autopsy must be done not only in a high percentage of cases but in a carefully regulated and vigilant manner. Technical procedure at autopsy must be carefully controlled in studying the pathology of thromboembolic disease and in evaluating its incidence. The postmortem examination should be done soon after death; with passage of time, tissue enzymes are liberated, and adherent thrombi or emboli may become loosened by local autolytic action.

<table>
<thead>
<tr>
<th>Age, Yr.</th>
<th>Autopsy Series</th>
<th>Columbus, Ohio, 1951</th>
</tr>
</thead>
<tbody>
<tr>
<td>No.</td>
<td>%</td>
<td>No.</td>
</tr>
<tr>
<td>20-29</td>
<td>13</td>
<td>49</td>
</tr>
<tr>
<td>30-39</td>
<td>36</td>
<td>121</td>
</tr>
<tr>
<td>40-49</td>
<td>45</td>
<td>313</td>
</tr>
<tr>
<td>50-59</td>
<td>60</td>
<td>661</td>
</tr>
<tr>
<td>60-69</td>
<td>120</td>
<td>829</td>
</tr>
<tr>
<td>70 and over</td>
<td>246</td>
<td>1,166</td>
</tr>
<tr>
<td>Total</td>
<td>512</td>
<td>3,658</td>
</tr>
</tbody>
</table>

It is requisite that autopsy be performed on unembalmed bodies. Arterial irrigation considerably complicates the problem of analyzing blood clots. The stream of embalming fluid, introduced under pressure, may bring about artefactual dislodgment or impaction of intravascular clots. The embalming solution converts a simple postmortem clot to a mottled gray-red friable mass resembling an embolus; a recent embolus may be so altered that its true nature at autopsy remains a matter of doubt. In the present study effort was made to perform autopsies as soon as possible after death, day or night, on unembalmed bodies; during the period of this study 95% of autopsies were performed on unembalmed bodies. In 65% of cases the autopsy was done within five hours after death. In this study 88% of the autopsies were performed by me, the remainder by other pathologists. In both groups of cases the incidence of thromboembolic lesions observed was similar; accordingly it is felt that variations in autopsy technique and observation were held to a minimum.

In evaluating the findings in this study, note was made of the patient's mental status prior to death. Although a majority of the population in the institution required only simple maintenance, a review of the clinical records revealed that there was in 30% of cases a degree of active mental disturbance seemingly out of proportion to the

natural infirmities of age. These cases, evenly distributed through groups with and without pulmonary embolism, did not appear to alter the general significance of the study.

In the course of the investigation the autopsy percentage in the institution rose. During the last four months of 1949, 49% of persons who died were examined at autopsy; in 1950, 54%; and in 1951, 67%. The autopsies represented by this increase were largely in those cases that are diagnosed at the bedside as terminal bronchopneumonia or arteriosclerotic heart disease, cases that are sometimes called "chronies" or less flattering names. As the number of autopsy permissions in these cases increased in proportion, an unanticipated change in the incidence pattern of fatal illness as observed in the autopsy room became evident. Pulmonary embolism, though a common finding at autopsy in other years, showed a striking increase. This sharp rise in incidence of thromboembolic disease coincided with the period in which the autopsy percentage rose and occurred after the practice of embalming bodies before autopsy was discontinued.

When pulmonary arteries were occluded by adherent clot, it is likely that in some instances the process began as an embolus and grew by appositional thrombosis and that in some instances the occlusion originated in situ as a thrombus. The resulting closure of the pulmonary artery, the effect pertinent to the present study, whether embolic or thrombotic, would be largely the same, an ischemia of the lung tissue. In analyzing an antemortem clot in a pulmonary artery it is often difficult to distinguish between embolus and thrombus. Ceelen,\textsuperscript{10} in reviewing this problem, found that most researchers, including Virchow, held that most antemortem clots in the branches of the pulmonary arteries are embolic. Consistent with this, in the present report such lesions will generally be referred to as embolic.

In analyzing the emboli in the pulmonary arteries, three groups of cases, based on the extent of vascular occlusion, could be defined. Arterial occlusion was classified as massive, medium, and small, according to the size of the occluded artery. Massive embolism was the diagnosis applied at autopsy if one or more of the main lobar arteries was occluded by an antemortem clot. Usually in these cases the presence of a characteristic, coiled, friable, laminated embolus presented no problem in autopsy diagnosis. Occlusion was classified as medium if the largest artery occluded was 5 to 10 mm. in diameter; these are arteries that are located mainly in the intermediate third of the lung field. Involved arteries of less than 5 mm. in diameter, such as those located in the peripheral zone of the lung, were classified as small artery occlusion.

**RESULTS**

The original investigation had not been designed specifically as a study of thromboembolic disease; however, the high incidence of pulmonary embolism discovered at this time proved to be a most significant aspect of the data. In the first year 29% of the 90 cases at autopsy revealed thromboembolic lesions of some degree in the lung. The incidence of thromboembolic disease in the lung for the entire period of study is indicated in table 2. Of the 512 cases studied at autopsy, thromboembolic lesions were present in 132, or 25.7%. In this series massive pulmonary embolism was the cause of death in 73 cases, or 14.2%. Occlusion occurred in arteries of medium caliber in 18, or 3.5% of cases. Arterial occlusion limited to the small branches in the periphery of the lung occurred in 41, or 8% of autopsies.

Well-established infarcts of the lung were noted in 60 autopsies, representing 45% of the cases in which there was embolic disease of the lung. In many instances, as will be noted later, rapid death did not permit development of definite infarction. As is well known, occlusion of an artery may not lead to infarction even after a prolonged period. Infarction in the lung is not likely to occur after impaction of the embolus unless there is antecedent embolization of the pulmonary circulation, as in chronic passive congestion, or unless there is coexistent parenchymal disease such as pneumonia or bronchiectasis.

The most frequent site of embolization in the lung was the right lower lobe; this lobe was involved in 61% of the cases in which there were thromboembolic lesions; usually there were concurrent emboli in other lobes. In 38% the left lower lobe arteries contained embolus; other lobes had a smaller number of emboli. The distribution of emboli noted here may be due to the anatomic structure of the pulmonary arterial tree. The artery to the right lower lobe lies in a more direct line with the current from the main pulmonary artery than do the slightly angulated branches to the other lobes; consequently, more emboli may be directed to the right lower lobe than to other sites.

The occurrence of pulmonary embolism in the present study is greater than generally reported; the incidence recorded in most previous studies is derived from a distinctly selected population. Whereas the present survey is based on terminal illness occurring in a wide cross section of adults in an institutional community, most other reports are derived from studies of deaths occurring in the more highly restricted population of general hospitals. The findings in the present study agree closely with those of Moran,\textsuperscript{9} who studied the general incidence of pulmonary embolism in a population similar to that of the present study. In Moran's study of 635 con-

---

secutive autopsies, emboli were observed in 147 cases, an incidence of 23.1%; in 43 instances, embolism of massive degree occurred.

The present study indicates that in the adult population pulmonary embolism increases sharply with age. The number of cases in which autopsy was performed and the incidence of pulmonary thromboembolic lesions as related to age groups is recorded in Table 2. Two hundred forty-six deaths occurred in persons more than 70 years old; 83 of these cases, or 34%, showed thromboembolic lesions in the lung at autopsy. Massive pulmonary embolism was the direct cause of death in 46, or about one-fifth, of the persons in this portion of the population who came to autopsy.

**CLINICAL PATTERNS OF PULMONARY EMBOLISM**

In considering this series of cases from a clinical point of view, it became evident that three definite clinical patterns can be associated with the process of pulmonary embolism: sudden death, a subacute course, and a chronic pattern. These three clinical forms are detailed in Table 3. The clinical effects evoked by thromboembolic disease of the lung may be varied and confusing. Although the division of cases presented here is empirical and there is necessarily an overlapping of one group with another, this classification permits a panoramic view of the clinical guises of pulmonary embolism observed in this study.

Sudden death occurred in 24, or 18%, of the patients in this study who had thromboembolic lesions in the lung. Clinically, these cases demonstrated the textbook picture of sudden, unexpected death; however, at the bedside these were often diagnosed as coronary occlusion. Autopsy showed that 18 of this group had large, coiled, loosely impacted emboli in one or more of the lobar arteries.

In six instances of sudden death, emboli in medium-sized pulmonary arteries constituted the principal finding at autopsy. The clinical and experimental studies of de Takats and Jesser have emphasized that patients may die from a small embolus obstructing an insignificant area of the lung; it is felt that a widespread radiation of autonomic reflexes occurs during pulmonary embolism and that this may contribute to the cause of death. It is well known that in the leg, embolic occlusion of a relatively small artery may cause rapid blanching of the entire limb; massive spasm, initiated at the site of the impacted embolus, sweeps up and down the arterial tree; and the entire extremity is rendered anoxic. Similarly, the impaction of an embolus, large or small, in a pulmonary artery may evoke spasm through the entire pulmonary arterial tree. This spasm, if severe, would account for sudden anoxic death.

The subacute clinical pattern of pulmonary embolism was observed in 55 cases; this represents 42% of deaths associated with pulmonary embolism and 11% of deaths occurring in all cases in which autopsy was performed in this study. In this group the period of terminal illness usually extended over a period varying from several days to a few weeks. This protracted terminal illness, accompanied by increasing respiratory symptoms, was usually interpreted at the bedside as bronchopneumonia. The cause of death as defined at autopsy usually came as a surprise to the clinician. This "quiet" form of pulmonary embolism is not widely realized in general practice. In 32 cases in which there was a subacute course clinically, massive adherent emboli, often associated with lung infarcts, were found at autopsy. These cases were particularly interesting clinically because of the deeply rooted textbook conception that massive pulmonary embolism usually causes sudden death; the present study indicates, on the contrary, that with massive embolism a terminal illness prolonged over several days is commoner than sudden death.

Chronic terminal illness was present clinically in 53, or 40%, of the patients with thromboembolic lesions in the lung. Well-attached emboli associated with lung infarcts of varying age were usually observed at autopsy. These findings indicated that the embolic process in these cases was chronic and recurrent and did not represent

---

**Table 3.—Clinical Patterns in 132 Patients with Thromboembolic Pulmonary Lesions Who Came to Autopsy**

<table>
<thead>
<tr>
<th>Clinical Type</th>
<th>No. of Cases</th>
<th>Length of Terminal Illness</th>
<th>Autopsy Findings *</th>
<th>Clinical Diagnosis *</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sudden death</td>
<td>24</td>
<td>Instant to several hours</td>
<td>Massive embolism in one or more lobar arteries</td>
<td>Coronary occlusion</td>
</tr>
<tr>
<td>Subacute course</td>
<td>55</td>
<td>1 to 7 days</td>
<td>Occlusion of large and medium-sized pulmonary arteries; early infarcts</td>
<td>Bronchopneumonia</td>
</tr>
<tr>
<td>Chronic pattern</td>
<td>53</td>
<td>Several weeks</td>
<td>Often only small arteries occluded; often arteries of all calibers occluded; infarcts of varying age</td>
<td>Often no pulmonary diagnosis made</td>
</tr>
</tbody>
</table>

* In most cases.

**Table 4.—Effect of Age, Sex, Race, and Body Weight on Incidence of Thromboembolic Disease of the Lung in 512 Autopsies**

<table>
<thead>
<tr>
<th>Average Age, Yr.</th>
<th>Males</th>
<th>Females</th>
<th>All Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Autopsies No.</td>
<td>No.</td>
<td>%</td>
<td>No.</td>
</tr>
<tr>
<td>All cases</td>
<td>512</td>
<td>63.7</td>
<td>65.9</td>
</tr>
<tr>
<td>With thromboembolic lesions</td>
<td>322</td>
<td>70.3</td>
<td>70.6</td>
</tr>
<tr>
<td>Without thromboembolic lesions</td>
<td>390</td>
<td>64.2</td>
<td>63.5</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Sex</th>
<th>Males</th>
<th>%</th>
<th>Females</th>
<th>%</th>
<th>All Patients</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>White</td>
<td>No.</td>
<td>%</td>
<td>No.</td>
<td>%</td>
<td>No.</td>
<td>%</td>
</tr>
<tr>
<td>Negro</td>
<td>461</td>
<td>90.0</td>
<td>51</td>
<td>10.0</td>
<td>117</td>
<td>25.5</td>
</tr>
<tr>
<td>Average Body Weight, Lb.</td>
<td>182</td>
<td>74.5</td>
<td>20</td>
<td>70.6</td>
<td>123</td>
<td></td>
</tr>
</tbody>
</table>

merely an agonal complication. In many instances only small-caliber arteries were occluded; however, in 22 cases in this group there was massive pulmonary artery occlusion; these were mainly cases of unjointed fracture of the femur in severely debilitated patients with large decubital ulcers. Femoral vein thromboli were usually evident.

Clinically, in patients with chronic syndrome of pulmonary embolism, death was generally associated with no sudden terminal change; in most instances the patients died quietly; often respiratory symptoms were remarkably minimal, pulmonary findings clinically being overshadowed by other major pathological processes such as renal or malignant disease.

FACTORS CONTRIBUTING TO PULMONARY EMBOLISM

Age and Sex.—As noted previously in table 2, the incidence of pulmonary embolism in the adult population increases with age. These findings coincide with the reports by Carlotti, Roe and Goldthwait, and others. The present study stresses particularly the great frequency of thromboembolic disease in the seventh and eighth decades; in the extremely aged, pulmonary embolism may, in fact, be the commonest direct cause of death. In the present study the cases of pulmonary embolism occurring in the later decades account for a much larger proportion of the total incidence than is evident in reports in the older literature. This difference may be related, in part, to the consistent rise in average longevity that has occurred in the general population. Since pulmonary embolism is largely a disease of old age and since the older age group makes up an increasingly larger proportion of the total population, a gradual rise in the total incidence of pulmonary embolism in a given community may be expected in the future.

Sex difference influenced the incidence of pulmonary embolism almost as much as the factor of aging. The incidence of thromboembolic disease was significantly greater in women than in men. As indicated in table 4, 33.6% of women and 20% of men showed thromboembolic lesions. This incidence is in agreement with the findings of Morgan, who, in a similar study, reported pulmonary embolism in 30.8% of women and 20.5% of men. The reason for the difference in incidence in the sexes is not readily evident. Phlebothrombosis, according to Hunter and his associates, occurs with almost the same frequency in men and women. In the present series the average age at death in both sexes was practically the same. The resolution of this problem, the cause of the difference in incidence of thrombotic disease in the two sexes, merits further investigation.

Besides age and sex differences, other factors relating to the cause of pulmonary embolism were explored during the course of this investigation. It is evident that many bodily mechanisms influence the onset, course, and final effect of thromboembolic disease in the lung. Three phases in the process present themselves for consideration: formation of the thrombus, detachment of the thrombus, and impaction of the embolic mass.

Formation of Thrombus.—A preexisting thrombus in a systemic vein is the prime cause of embolic disease of the lung. Parenthetically, it can be stated that the prevention of pulmonary embolism lies in the prevention of thrombosis of peripheral systemic veins. The building-up of a thrombus is related to alterations in the clotting mechanism of the blood, slowing of the blood flow, and local changes that may be present in the lining of blood vessels. It was not within the scope of this study to investigate the clotting mechanism of blood in the cases studied. Whether the chemical coagulability of the blood increases with age is not well defined; this should be further investigated. The older age group is, however, subject to many minor intercurrent illnesses that are known to increase coagulability of blood; this circumstance may play an important role in effecting a higher incidence of thrombosis and embolism in the older age group.

Detachment of Thrombus.—Early in this study attention was sharply directed to one clinical factor that strongly influenced the occurrence of pulmonary embolism. In many cases in older persons in relatively good health sudden massive embolism developed after a period of bed rest for a minor illness such as an upper respiratory infection; such patients were stricken fatally when ambulation was resumed. It is likely that stasis of the venous blood flow associated with enforced bed rest sets the stage for thrombosis; with the return to ambulation, detachment of loose, newly formed thrombi in the lower extremities results in fatal embolism. In some instances embolism occurred entirely without proclivities, sometimes during sleep, in persons previously apparently well.

Many cases of thromboembolic disease were initiated by inflammatory processes in the tissues of the lower extremities. Decubital ulcers often gave rise to thrombosis in extremital veins. In 19 cases, recent fracture of the femur led to femoral vein thrombosis and pulmonary embolism. Considering the entire series of cases with pulmonary embolism, relatively few showed clinical signs of venous thrombosis prior to death; femoral phlebothrombi, though present, were often silent before embolization. In 32 of the 132 cases of thromboembolic disease of the lung in this study, thrombi were visible in the proximal segment of the femoral vein at autopsy or could be expressed from the vein by "milking" the extremity. It is likely that a considerably larger number of thrombi were present; since dissection of the limbs was usually restricted in the autopsy permission, confirmation of suspected deep venous thrombosis often was not available. Hunter and associates studied phlebothrombosis in the lower extremities in 351 unselected autopsies. Thrombi were found in the deep veins of the leg in 52.7% of middle-aged and older persons who had to remain in bed for varying periods. Celen has stressed the frequency of pulmonary embolism in the presence of venous thrombosis: "In very careful dissections of the arteries of the lungs, in cases where there are thromboses in other parts of the body, there will be found emboli in the lungs in 75% of cases."

Impaction of Embolic Mass.—Impaction of the embolus is the event responsible for the initiation of the immediate clinical effects of the thromboembolic process. Correlation of the clinical course with the autopsy findings indicated that there is a wide variation in the effect produced by the impaction of an embolus in a pulmonary artery. As noted previously, often a relatively small embolus precipitated death. On the other hand, occlusion of a large portion of the pulmonary vascular bed was in some instances tolerated for long periods. There was often no reasonable explanation for this wide variation in clinical effect. It was noted, however, that if the functional reserve of the lungs or the heart had been reduced by antecedent disease and if congestive failure or other cardiorespiratory embarrassment was already present, the effect of pulmonary embolism tended to be intensified.

Other Factors.—Various other constitutional and environmental factors were considered in studying the occurrence of pulmonary embolism. In reference to race, 90% of the patients studied in this series were white and 10% were Negro. The incidence of pulmonary thromboembolic lesions in white patients as noted in table 4 was 25.5%: the incidence in Negro patients was only slightly greater, 29.4%.

Cardiac disease has been cited 12 as an important antecedent in thromboembolic disease. The circulatory stasis associated with congestive heart failure tends to favor the formation of extremal venous thrombi. Congestive heart failure of varying degree is common in patients of the older age group; in the present study it appeared evenly distributed in cases with and without pulmonary embolism. As noted previously, pulmonary embolism in patients with antecedent heart disease was less well tolerated than in other patients. Pulmonary embolism occurred slightly more frequently in patients with hypertension than in persons with normal blood pressure.

Obesity has been pointed out as a constitutional factor contributing to the development of thromboembolic disease, particularly during the postoperative state. 14 In the cross section of population in the present study neither the postoperative state nor obesity played an important role in influencing thromboembolic disease. Postoperative deaths were relatively few in the series studied. The average body weight for all persons who came to autopsy was 132 lb. (59.9 kg.); for the group with pulmonary embolism, 128 lb. (58.1 kg.). Only 3% of the persons, both with and without pulmonary embolism, were over 200 lb. (90.7 kg.) in weight.

Malignant tumors are sometimes considered to be a direct factor in causing thromboembolic disease. In this series of 512 autopsies there were 70 cases of malignant tumors; in 28 of these cases the disease was far advanced and there was extensive invasive growth and metastasis at the time of death. Pulmonary embolism was present in 33.3% of cases in which there were far-advanced malignant growths. Arterial occlusions in most instances occurred in vessels of small caliber. The number of neoplasms in the present study constitutes a small group; however, the results indicate that, although the incidence of pulmonary embolism in patients with malignant disease is high, it is not significantly greater than that of the older age group in general. Most malignant disease, like most pulmonary embolism, occurs in the older age group. The high incidence of thromboembolic disease reported in patients with malignant disease may indicate merely that embolism is common in the cancer age, not that it is actually related to the presence of cancer.

Climatic and seasonal changes have been suggested as being of some importance in influencing the incidence of pulmonary embolism. In Columbus, Ohio, the site of the present study, the weather changes occurring during the cycle of the seasons are moderate but distinct. The incidence of pulmonary embolism was not significantly influenced by seasonal changes. Most investigators who have studied the problem have observed a uniform occurrence of pulmonary embolism through the seasons of the year. 15 In the summer months thromboembolic lesions were found in 26% of patients who died and who came to autopsy, in autumn in 29%, in winter in 26%, and in spring in 31%.

SUMMARY AND CONCLUSIONS

Pulmonary embolism is of far wider occurrence than is generally realized; in the present study, it was one of the commonest direct causes of death in the aged. Its incidence will probably increase, since it is primarily a disease of old age, since the older age group is growing, and since many types of bacterial terminal illness are being controlled. In this study, three clinical patterns could be distinguished in cases of pulmonary embolism: sudden death, usually diagnosed as coronary occlusion, involving the major branches of the pulmonary arterial tree; a subacute form that usually resembled terminal bronchopneumonia, in which the large and medium-sized pulmonary arteries were affected; and the chronic clinical form usually incident to prolonged terminal illness, in which frequently only the small arteries were occluded. All three forms of the disease had frequently been wrongly diagnosed during life. Three factors strongly influence the occurrence of pulmonary embolism: age, sex, and periods of enforced bed rest. The greater frequency of incidence in women than in men is unexplained and should be the subject of further study.

The results of this study tend to dispel two textbook suppositions that are deeply rooted in medical thinking: first, that pulmonary embolism is mainly a postoperative complication, and, second, that it is characteristically a sudden and rapid form of death. The vast majority of cases occurred in medical patients, and only a small percentage of patients died suddenly. As the wide variation in its clinical picture becomes better recognized, and as the criteria for its diagnosis becomes clarified, pulmonary embolism will be correctly diagnosed more often, and more extensive prophylactic and therapeutic measures will be pursued.