5-1-1935

Problem of pulmonary embolism: report of thirty nine cases

Richard Birge
University of Nebraska Medical Center

Follow this and additional works at: https://digitalcommons.unmc.edu/mdtheses

Part of the Medical Education Commons

Recommended Citation

This Thesis is brought to you for free and open access by the Special Collections at DigitalCommons@UNMC. It has been accepted for inclusion in MD Theses by an authorized administrator of DigitalCommons@UNMC. For more information, please contact digitalcommons@unmc.edu.
THE PROBLEM OF PULMONARY EMBOLISM:
Report of Thirty-nine Cases

by

Richard Birge

Senior Thesis
University of Nebraska
College of Medicine
Omaha, Nebraska
1935
# TABLE OF CONTENTS

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>I. INTRODUCTORY</td>
<td>1</td>
</tr>
<tr>
<td>II. THE CLINICAL CASE</td>
<td></td>
</tr>
<tr>
<td>A. Symptoms</td>
<td>3</td>
</tr>
<tr>
<td>B. Diagnosis</td>
<td>7</td>
</tr>
<tr>
<td>III. MORBID ANATOMY</td>
<td></td>
</tr>
<tr>
<td>A. The Autopsy Findings</td>
<td>10</td>
</tr>
<tr>
<td>B. The Thrombus</td>
<td>12</td>
</tr>
<tr>
<td>C. The Embolus</td>
<td>15</td>
</tr>
<tr>
<td>D. The Pathological Background</td>
<td>17</td>
</tr>
<tr>
<td>1. Physical and Mechanical Factors Concerned in Thrombosis and Embolism</td>
<td>18</td>
</tr>
<tr>
<td>2. Biochemical Factors Concerned in Thrombosis and Embolism</td>
<td>22</td>
</tr>
<tr>
<td>3. The Role of Infection</td>
<td>29</td>
</tr>
<tr>
<td>IV. THE INCIDENCE OF PULMONARY EMBOLISM—CONSIDERATION OF CASE HISTORIES</td>
<td></td>
</tr>
<tr>
<td>A. General Considerations</td>
<td>33</td>
</tr>
<tr>
<td>B. Relation of Age to Pulmonary Embolism</td>
<td>34</td>
</tr>
<tr>
<td>C. Relation of Sex to Pulmonary Embolism</td>
<td>35</td>
</tr>
<tr>
<td>D. Relation of Race to Pulmonary Embolism</td>
<td>35</td>
</tr>
<tr>
<td>E. The Sources of Pulmonary Emboli</td>
<td>35</td>
</tr>
<tr>
<td>F. Relation of Pulmonary Embolism to the Primary Disease</td>
<td>36</td>
</tr>
<tr>
<td>G. Fatal Pulmonary Embolism</td>
<td>38</td>
</tr>
<tr>
<td>H. Postoperative and Post Partum Pulmonary Embolism</td>
<td>41</td>
</tr>
<tr>
<td>I. Relation of Heart Disease to Pulmonary Embolism</td>
<td>41</td>
</tr>
<tr>
<td>J. Pulmonary Embolism Complicating Septic Thrombosis</td>
<td>45</td>
</tr>
<tr>
<td>K. Relation of Therapy to Pulmonary Embolism</td>
<td>45</td>
</tr>
<tr>
<td>L. Presentation of Case Histories</td>
<td>46</td>
</tr>
<tr>
<td>V. NOTES ON THERAPEUTIS</td>
<td>92</td>
</tr>
<tr>
<td>VI. SUMMARY</td>
<td>95</td>
</tr>
<tr>
<td>VII. BIBLIOGRAPHY</td>
<td>96</td>
</tr>
</tbody>
</table>

480676
THE PROBLEM OF PULMONARY EMBOLISM:

Report of Thirty-nine Cases

INTRODUCTORY

The question of pulmonary embolism has become quite recently one of more than usual interest at the University Hospital. In a period of less than four months, during the latter part of 1934, six cases of fatal pulmonary embolism came to autopsy. There had been no cases of fatal pulmonary embolism during the first eight months of 1934, but one case in 1933, and two in 1932.

A review of these cases revealed nothing which might explain the increased incidence of fatal pulmonary embolism. It was, however, known to the writer that a quite large percentage of autopsies show evidence of pulmonary embolism, when both fatal and non-fatal cases are considered. It was recalled that, since the occurrence of pulmonary embolism depends upon the formation of primary thrombi in the systemic venous system or in the right heart, the amount of thrombus which might break loose and reach the pulmonary arterial system through the blood stream would be the essential factor determining the outcome of a given case. It seemed that one might consider the occurrence of thrombosis as the fundamental pathological change in these cases, and the embolic involvement of the lungs as incidental or accidental. If this conception were proper, less significance could be attached to an increase in the occurrence of fatal pulmonary embolism over a short period of time. The important problem
would be to determine whether the increase in fatal cases was actually accompanied by an increase in total cases of pulmonary embolism, or whether the increase depended only upon the fact that, in a small group of cases, larger than usual emboli had gained access to the pulmonary arteries.

University Hospital records for a three-year period ending December 31, 1934 reveal a smaller number of pulmonary emboli found at post-mortem examination during 1934 than during either of the two preceding years, although pulmonary embolism as the primary cause of death was more frequent in 1934. In the three-year period 309 autopsies were performed. In thirty-nine, the post-mortem diagnosis of pulmonary embolism or pulmonary infarction was made, and in nine, pulmonary embolism was found to be the primary cause of death. The percentage incidence was 12.6 per cent for total cases showing pulmonary embolism or infarction, and 2.9 per cent for cases of fatal pulmonary embolism.

This series of cases is too small for a critical study of the incidence of pulmonary embolism and of the more important factors related to its occurrence. It is of interest because it demonstrates the total incidence of pulmonary embolism cases at the University Hospital to be comparable to that of other hospitals and clinics where much larger series have been accumulated, and, most important of all, because it demonstrates no increase in total pulmonary embolism cases in 1934 corresponding to the increase in fatal pulmonary embolism cases during that year.

The thirty-nine autopsy cases seen in the University Hospital during 1932, 1933, and 1934 are summarized, and their essential features, in relation to the common finding of evidence of pulmonary embolism, are discussed in the following pages.
THE CLINICAL CASE

Symptoms

Pulmonary embolism may be so insignificant as to produce no symptoms whatsoever, or so massive as to result in death in a few minutes or hours. It occurs most frequently in middle-aged or elderly patients following some minor exertion to which the patient has been unaccustomed, as, for example, getting out of bed. The chief symptoms are dyspnea, cyanosis or pallor, often precordial or substernal pain, sweating and other evidences of shock, and sometimes anxiety with fear of impending disaster. The severity of the symptoms depends largely on the size and number of emboli and the resultant degree of embarrassment of the pulmonary circulation.

A sudden and unexpected onset of symptoms is characteristic. Death ensues within a short time if the common pulmonary artery is occluded or if multiple small emboli occlude a sufficient amount of the pulmonary arterial system. However, death is not immediate. Of the nine University Hospital cases (pages 48 to 58) in which pulmonary embolism was the immediate cause of death, the shortest period intervening between onset of symptoms and exitus was seven minutes in case 4 (page 51), and the longest period was two hours and twenty-five minutes in case 5 (page 53). At necropsy massive emboli were found in the common pulmonary artery, but, because of the length of survival, after the onset of symptoms, it is apparent that occlusion could not have been complete in any case. In this respect the experimental work of Haggart and Walker (26) on laboratory animals is of passing interest. They found that until from 52 to 66 per cent of the pulmonary circulation is cut off there is no significant variation of the circulatory condition of an animal, and that the end-point
(52 to 66 per cent) is sharply defined, and circulatory collapse is precipitated by minute increases in pulmonary arterial obstruction beyond the end-point.

Relatively small pulmonary emboli may cause sudden, sharp pain in the chest, producing signs of consolidation and perhaps a friction rub. The temperature rises, and the leucocyte count is usually found to be moderately increased. The respiration is shallow and rapid, due to the pain produced by deep breathing. After a short time cough may develop with expectoration of blood-streaked sputum. After a few days the symptoms may resolve and the patient completely recover. Case 14 (page 63), for example, complained on April 30, 1932 of sudden onset of pain, exaggerated by deep breathing, over the region of the liver; there was hemoptysis in small amounts for three days; and physical examination revealed an area of dullness over the right lower lobe. The symptoms of pulmonary embolism cleared up and the patient died a week later, a cardiac death. Necropsy revealed a large infarct in the right lower lobe.

There may be multiple and smaller emboli, followed by larger ones. Blood-tinged sputum is usually seen after the lodgement of the earlier emboli, and a patient may have apparently recovered when the process is repeated. On August 10, 1934, case 4 (page 51) complained of rather sharp pains over the precordium with only slight difficulty in breathing. On August 17 the patient had a severe pain in the right lower chest with radiation to the shoulder. Coarse rales were found in the lower right chest with diminished breath sounds. Following this occurrence the patient coughed considerably, with production of some blood-streaked sputum. On August 26 the patient had been sitting up in bed, suddenly screamed, collapsed, and died about seven minutes later.
A single massive pulmonary embolism may occur, with death resulting in a short time. A cholecystectomy and appendectomy had been performed on case 5 (page 53) on September 10, 1934. The patient progressed well until the fifth postoperative day when she suddenly sat up in bed, breathing rapidly and showing considerable cyanosis. She complained of no pain. She was given morphine, caffeine sodio-benzoate, and digalen, but she died two hours and twenty-five minutes after the onset of the symptoms. At autopsy a single ante-mortem thrombus was found in the common pulmonary artery. It was sixty centimeters in length and of practically uniform diameter, about one centimeter. There were no thrombi in the branches of the pulmonary arteries, and there were no infarcts in the lungs.

Infected ante-mortem blood clots may reach the pulmonary arterial system. They are usually multiple and small, and give rise to small infarcts which soon assume the characteristics of ordinary metastatic lung abscesses. Seven of the cases in this series (cases 27 to 33 inclusive, pages 79 to 85) showed this type of lung pathology. In all of the seven cases the primary thrombi were associated with definitely inflammatory processes. Since pulmonary emboli in these cases were small and caused little pulmonary circulatory embarrassment, they produced no demonstrable clinical symptomatology except that referable to the inflammatory processes.

On the other hand, a pulmonary infarct of considerable size may undergo secondary infection and degeneration. Case 36 (page 88) showed at autopsy gangrene, associated with pulmonary thrombosis, of the lower lobe of the left lung. There was a primary pelvic thrombosis which showed no evidence of being infected, and it may therefore be concluded that the gangrenous process in the lung was associated with secondary bacterial invasion. Dr. J. P. Tollman, Pathologist at the University Hospital,
confirms this interpretation in his report of the case, saying: "This is interpreted as being a pelvic thrombosis. Some of these thrombi became loosened and caused infarction of the left lower lobe of the lung. It subsequently became gangrenous." In such cases the symptomatology is that of the usual non-fatal case of pulmonary embolism, with the symptoms related to the gangrenous change in the lung developing in the course of a few days.

In summation of the symptomatology of pulmonary embolism, it may be well to quote Churchill (18), who says: "One of the best expositions of the signs and symptoms of pulmonary embolism is to be found in the paper of Giertz and Crafoord, based on a statistical analysis of the clinical picture presented by twenty-seven patients. In twenty-three instances the condition was correctly diagnosed before death. The symptoms observed were, in order of frequency, as follows: sudden onset of symptoms without any warning; high, soft, imperceptible pulse; marked pallor; unconsciousness; slight cyanosis; craving for air; dyspnea; altered respiration, superficial or deep; snatching or groaning; feeling of oppression, dread, anxiety, restlessness; pain, or stitch in chest, usually over precordium; "shock", cold perspiration; pulsations in veins of neck (the authors remark that this symptom is probably more frequent than was noted in the brief accounts available); waving arms about, wanting to get up. Violent vomiting, strabismus, dilated pupils, giddiness, and yawning also occasionally occur. The symptomatology is summarized as follows: 'In most instances it (massive pulmonary embolism) comes like a bolt from the blue with typical symptoms of which the most frequent are intensive pallor, loss of pulse and consciousness. Common symptoms are also oppression, craving for air, and a mild cyanosis with a typical venous pulsation above the clavicles.'"
PROBLEM OF PULMONARY EMBOLISM

Diagnosis

Pulmonary embolism is a much more frequent occurrence than is generally recognized. University Hospital autopsy reports over a three-year period reveal a total incidence of 12.6 per cent of pulmonary embolism cases in total autopsies performed. Belt (12) emphasizes in a recent paper that pulmonary embolism is much commoner than it is usually considered to be. He states: "Usually regarded as a postoperative event of relatively rare occurrence it proves, on the contrary to be a common autopsy finding, more often associated with medical than with surgical cases. The frequency with which it may be uncovered at autopsy is surprisingly high, as many pathologists have already pointed out (Lubarsh, Fahr, Henderson, Singer, Wertheimer, Dietrich, Benda, Ceelen, Axhausen, Putnoky, and Farkas). On our own service, under the direction of Prof. Oskar Klotz, we have demonstrated pulmonary emboli in about ten per cent of our routine autopsies."

Once the frequency of pulmonary embolism is recognized and the condition thought of in making a differential diagnosis, and once it is realized that pulmonary embolism occurs in medical as well as postoperative surgical cases, the diagnosis of pulmonary embolism will be made by the clinician in a large number of cases previously diagnosed only at autopsy. In this connection Bunn (16), in discussion of differentiation of pneumonia from pulmonary embolism, says that the chief error in a number of cases which were provisionally diagnosed as pneumonia was the failure to consider both pneumonia and pulmonary embolism as possibilities.

Hamburger and Saphir (28) also suggest that "in cases of sudden severe dyspnea, unexpected death following some slight exertion, acute severe right-sided chest pain, unexplained sudden death, consider, at least, pulmonary embolism either alone or in association with coronary thrombosis. As part of such consideration look particularly for the possible thrombotic source
of such embolic and evaluate the degree of cyanosis, increased right heart
dullness, sudden engorgement of the liver, as fitting into the picture of
acute right heart failure from pulmonary obstruction." The authors admit
that the differential diagnosis between pulmonary embolism and coronary
thrombosis may be difficult, but reiterate: "If the possibility of pul­
monary embolism is more frequently borne in mind as 'complicating or
simulating' coronary thrombosis, we feel the percentage of correct diag­
noses will be proportionately higher." Besides pneumonia and coronary
thrombosis, the chief conditions, according to Lord (17), with which
pulmonary embolism may be confused are postoperative shock, postoperative
concealed internal hemorrhage, and acute pneumothorax.

The fundamental phenomenon in cases of pulmonary embolism is the
thrombosis occurring either in the systemic venous system or in the right
heart. Clinically, however, evidence of a thrombotic process is usually
not elicited prior to the onset of symptoms of embolic manifestations,
excepting in cases, such as a lateral sinus thrombosis extending from a
mastoid infection, which are on a septic basis. In the group of thirty­
nine cases, there were seven cases of this frankly septic thrombotic type
(cases 27 to 33 inclusive, pages 79 to 85). Only two other cases (cases
8 and 18, pages 56 and 67) showed definite clinical evidence of thrombo­
phlebitis developing as a premonition of the embolism to follow.

McCartney (45) says in this respect: "Pulmonary embolism results from
thrombosis, but apparently most often occurs when symptoms of thrombosis
are absent. Conner (19) says, 'There is reason to believe that the
characteristic local signs of thrombophlebitis appear only after the
occlusion of the vein has been complete and after more or less periphlebitic
inflammation has been added. This may explain why embolism occurs when
signs of thrombophlebitis are absent rather than in cases of frank phlebitis.
A thrombus completely occluding the vessel would, perhaps not become de­
tached so easily as would the thrombus floating in the blood stream and
attached only over a relatively small area."

Consequently, if one is to predict the possible occurrence of a pul­
monary embolism in a clinical case, one must look elsewhere than for
evidence of thrombophlebitis. According to Rosenthal (61) the two most
important factors in the formation of thrombi, outside of colloidal,
chemical, or physical changes of the blood, are in order of importance,
heart and vessel changes, and infectious processes. This observation is
very definitely borne out by the group of cases under consideration. Twenty-
one were definitely associated with circulatory failure on a cardiac basis,
and at least eight were associated with infectious processes involving the
veins or the endocardium. These problems will be discussed in considerable
detail below; it is only essential to emphasize here that, although many
cases of pulmonary embolism are unpredictable, venous circulatory stasis
and septic thrombophlebitis are the chief forerunners of pulmonary embolic
accidents.
MORBID ANATOMY

The Autopsy Findings

McCartney (45) describes the chief post-mortem findings in a case of fatal pulmonary embolism so adequately and concisely that it may be well to cite the description:

"Cyanosis, which may have been pronounced at the time of death, usually has disappeared by the time the necropsy is performed. Edema of the subcutaneous tissues may or may not be demonstrable. Usually the right ventricle and auricle are found distended. If the heart is removed before the pulmonary artery and its two main branches are examined, the embolus may be overlooked. The embolus may be found obstructing the right or left pulmonary artery, or riding over the bifurcation, filling the pulmonary artery, or even extending back into the right ventricle. The embolus may be made up of many pieces of blood clot, or be a long folded or coiled mass. The external surface of such an embolus usually shows fine corrugations (the lines of Zahn) and has a red, white, or mottled appearance. If, instead of a single large embolus, there has been a shower of small emboli, these will be found in the smaller branches of the pulmonary arteries. Infarcts are not usually present."

He continues: "In delayed death the emboli may propagate in the pulmonary arteries and become adherent, so that it is sometimes difficult to distinguish between embolism and primary thrombosis of the pulmonary artery. The lungs may be normal or show edema and congestion. In slow deaths infarcts, bronchopneumonia, or in the case of infected emboli, abscesses may be present. The liver, spleen, and kidneys show acute passive congestion."
It is apparent, therefore, that the pathological findings in the pulmonary arterial system are the ante-mortem clots occluding the system and the evidences of secondary changes in the heart, lungs, and other organs. The other important findings relate to the underlying pathological conditions which may suggest an explanation for the occurrence of embolism. The pathologist consequently searches as carefully as he may for the thrombus or the former site of the thrombus, and also attempts to determine evidence of local trauma, infection, circulatory failure, and other factors which may explain the formation of the thrombus.

The source of the embolus in many cases is not found. McCartney (45) points out that this is often because a sufficiently thorough search can not be made. Belt (11) also points out that often enough one is able to demonstrate pulmonary emboli, but is unable to find their point of origin, and that on the other hand one may find an undiagnosed venous thrombosis, especially in the leg and pelvic veins, from which no emboli have arisen. Since complete dissection can rarely be made at autopsy, Belt suggests that a thrombus will often be dislodged from a femoral vein if the legs be elevated and massaged, but that failure does not prove a thrombus is not present. It is also not infrequently the case that a thrombus forming, for example, in one of the external iliac veins, may, when the embolus forms, be completely dislodged, leaving at the former site of the thrombus a smooth vessel wall showing no evident pathological alteration.
The Thrombus

"Coagulation of blood in the vessels after death or in the tissues or in the test tube presents a fundamental structural difference from thrombosis intra vitem", according to Belt (11) who points out that the chief constituent of the former is fibrin, while that of the latter is platelets. He continues: "This structural difference is reflected in the naked eye appearances. Ante-mortem clot tends to be firmer, less elastic, dry, brittle, and rough. If the clot be adherent to the lining of the vessel or if it be of a friable consistency, there can be no doubt as to its ante-mortem origin. Not infrequently one must rely on still other criteria. There is a characteristic laminated structure, made up of grayish layers interlarded with red; this feature is lacking in the post-mortem clot though it may be simulated by the haphazard admixture of white and red elements. Lastly, the ante-mortem clot is often characterized by a rippling of its surface with fine greyish "drifts", like the wavy ribbing of a sandy beach, the so-called lines of Zahn, made up of platelets. This rippling always means that the clot was laid down in a moving blood stream; sometimes, however, the phenomenon may be observed on the surface of agonal clots which have formed during the last period of life and which must be distinguished from true ante-mortem clots.

"It is rarely necessary to employ the microscope to distinguish thrombus from post-mortem clot. Microscopically, the post-mortem clot is made up largely of blood cells (red and white) matted together with frail strands of fibrin. There may be small clusters of platelets. The ante-mortem clot on the other hand has a large platelet count; platelets form the basis of the coagulum, enmeshing variable quantities of cellular elements. If one
can detect with the microscope any sign of organization of the clot, the ingrowth of fibroblasts, this is, of course, definite evidence of ante-mortem formation."

Homans (35) has described in considerable detail some of the more common and important forms of venous thrombosis of the lower extremities and pelvis, which are the two usual sources of pulmonary emboli, excepting the septic forms which arise from a site of suppuration. Thrombotic processes of the lower extremities he has classified into four chief types: superficial thrombosis, associated with varicosities of the legs; deep thrombosis of the lower legs; phlegmasia alba dolens; and phlebitis migrans. He says of the first form: "Thrombophlebitis in varicose veins is, obviously, related to the unhealthy state of the vein's wall. Whether a 'latent' infection is present is immaterial. The fibrosis and distortion, not to speak of the effect of sudden overstretching on particular occasions, are quite enough to account for thrombus formation. The leg as a whole is not swollen, the reaction being confined to the neighborhood of the varicose vein. The clot is usually quite well fixed, as one might expect, and is rarely detached, though I have, on one occasion, divided a thrombosed varicose vein at the groin because of repeated pulmonary infarction."

Patey (53) believes that varicose veins are a very rare source of emboli. Rabinowitz and Holzman (57) are of the opinion that many pulmonary emboli have their source from the deep veins of the legs and that at necropsy the lesions are overlooked because the bulk of the mass has broken loose and lodged in the pulmonary artery, while only in the small veins of the calf and leg will the remnants of the original thrombus be found. Homans considers this type of thrombosis to be of great etiological significance,
and describes the pathological findings and associated clinical syndrome: "A local, deep thrombosis in the lower leg begins with a variable but, on the whole, a moderate amount of discomfort in the calf, swelling of the ankle, and blueness of the foot; signs which are rather promptly made to disappear upon rest in bed, but which recur over and over again upon attempting the use of the leg. It is hard to believe that, as a result of elevation for only a day or two, the leg, actually the seat of the extensive deep thrombosis, can take on so nearly, or completely, normal an appearance. Yet autopsy in the fatal cases has shown a remarkable widespread, persistent thrombosis in the great vessels among the muscles of the calf. In each case, the femoral vein was actually unobstructed and the cause of the fatality was the detachment of a considerable fragment of an enormously long, insecure thrombus which had been waving, as it were in the current."

Phlegmasia alba dolens is primarily a pelvic process, though the thrombosis may extend for a long way peripherally. Homans says of this form: "Explorations by the writer have shown that in many instances there is an active exudative reaction about the external iliac artery and vein (the common iliac or even the vena cava in some cases). The great vein is solidly obstructed by a firm thrombus. The whole leg, not just the lower portion is swollen. In some instances, there is evidence of arterial spasm resulting in some degree of ischemia. In all cases, going to bed has little effect upon the disease, the swelling persisting in even the mildest cases for a week or ten days and occasionally for many months. There is often tenderness over the deep vessels at the groin and over the femoral canal. Sometimes the saphenous vein is noticeably involved. In other instances, it is seen to be dilated, particularly in the groin, as if it were acting as a
collateral. Embolism, considering the frequency of the disease, is uncommon, a matter which may be related to what seems to me to be the usual source of the process, that is, an inflammatory reaction within the arteriovenous sheath. This may give an adhesiveness to the thrombus which is absent in the type of disease which forms the subject of this paper (deep thrombosis of the lower legs). In this connection, Cruveilhier, who described deep, iliac phlebitis so many years ago, said that he had never seen inflammation within the vein, but always in its wall."

Thrombophlebitis of the migrating type, that is, the phlebitis migrans so commonly associated with thromboangiitis obliterans and occasionally seen as an independent disease, is a local superficial process, an inflammatory lesion which never leads to extensive thrombosis or swelling of the affected limb, according to Homans.

The Embolus

It may be at times a puzzling problem to determine whether an attached ante-mortem blood clot found in a pulmonary artery is a primary thrombus or an embolus which has become secondarily attached. In the study of the group of cases under consideration, a large number were found to show attached ante-mortem clots, some of which it would probably be impossible to designate with absolute certainty as embolic. Belt (11) has noted this difficulty, and has set down some of the essential findings which may aid in making the differentiation. "A thrombus of the pulmonary artery", he finds, "starts usually as a mural plaque-like clot with sessile base and shelving margins, firmly adherent to the intima. It may grow and completely occlude the vessel, but it always conforms to the size and shape of the pulmonary artery, whereas an embolus, on the other hand, having been
cast in the shape of some other vessels may betray its foreign origin in
a number of ways. It may be riding upon a bifurcation or coiled upon
itself, and this is particularly true of the long cylindrical emboli which
are usually caught in the main trunk of the pulmonary artery. An embolus
is likely to have a number of small twigs attached to it which represent
the moulds of small tributaries of the vein in which the thrombus was
formed. An embolus may have a ragged or 'fractured' end which will in-
dicate that the clot has been broken off from a larger mass in some other
part of the body."

A further difficulty, however, in making the differentiation between
pulmonary emboli and autochthonous thrombi lies in the fact that small
emboli may by accretion increase in size and the primary character of the
process be masked. Kampmeier (38) finds that there are two main causes
of pulmonary thrombosis—atheroma of the pulmonary artery and embolism.
Atheromata, he suggests, may be primary or of syphilitic origin, but are
probably more frequently secondary to fibrosis or emphysema of the lung,
or to mitral stenosis. Concerning embolism as a cause of pulmonary throm-
bosis he says: "It is believed by several authors that embolism occurs in
a branch too small to give the characteristic symptoms of pulmonary em-
bolism with infarction. The small embolus then by accretion develops into
a progressing thrombosis extending and involving the main branches of the
pulmonary artery."

Belt (11) agrees that some cases regarded as thrombosis may have had
embolic origin. It has seemed to the writer that pulmonary arterial throm-
bosis would be an unusual occurrence because of the character of the cir-
culatory mechanism concerned, which is arterial, and because the arteries
infrequently show the above-mentioned changes in the walls which Kampmeier
considers prerequisite to thrombosis. In none of the University Hospital cases reported was there evidence of pathological change in the walls of the pulmonary arteries sufficient to account for the formation of autochthonous thrombi. The questionable cases, wherein the blood clots found in the pulmonary arteries are described as thrombi, may, therefore, be considered to be primarily embolic processes, with secondary adherence to the vessel wall and with the addition at times of a certain amount of local clotting by accretion.

The Pathological Background

A consideration of the factors underlying the occurrence of pulmonary embolism is chiefly a consideration of the broader subject of the causes of the formation of thrombi from which pulmonary emboli may originate. Thrombosis is primarily a physiological process constituting an essential defense mechanism to the credit of which, says Homans (35), we must concede the preservation of the race as it came up through savagery to civilization. This defense mechanism comes into action in response to injury to the blood vessels and tissues by physical agents or by chemical, biochemical, or bacterial action. Its initiation appears to be through the action of some vital substance or substances called forth by the injury and variously known as fibrin ferment, early toxins, thromboplastin, and thrombokinase. The known factors in clotting Bancroft, Kugelmass, and Stanley-Brown (4) have concisely yet clearly outlined: "When blood is shed the plasma dissociates into substances which yield a clot. During the patent period of dissociation, antithrombin is precipitated and prothrombin is activated by calcium ions. The resulting thrombin gels soluble fibrinogen into insoluble fibrin."
Normally, Homans continues, clot formation sufficient for the purpose of plugging the severed vessels takes place and then ceases. Why it ceases is as great a mystery as why it starts. Such a normal reaction or defense mechanism becomes pathological by its excess, its location, and the surrounding conditions, of which the most important is its intrusion into the centripetal blood stream where it tends to self-propagation until overtaken by natural limiting forces.

**Physical and mechanical factors concerned in thrombosis and embolism:**

Thrombosis has been defined as an intravascular clotting during lifetime. The formation of an intravascular clot during lifetime is a condition which by its very nature presupposes a slowing of the circulation, and in this respect is not different from post-mortem clotting. Venous stasis is, then, a fundamental pathological alteration which must take place before a venous thrombus will form.

Bunn (16) emphasizes the importance of venous stasis in stating that: "Infection, trauma, and alteration of the physiology of blood clotting may be contributory causes, but slowing of the circulation appears to be the one constant factor necessary to permit a vein to be thrombosed."

Hawlett(33) also speaks of the importance in thrombosis and pulmonary embolism of a slowing of the blood stream, saying: "Among the conditions which favor the development of thrombi is a marked slowing of the blood current. This may be due to a general slowing of the blood stream throughout the body (cardiac insufficiency), or it may be due to some local obstruction to the blood flow. Marked slowing also occurs in certain portions of the eddies which always arise when any flowing stream passes an obstruction, a bend, or a sudden widening. It is evident, therefore,
that thrombus formation is favored particularly in the irregular dilata-
tions of varicose veins, such as occur in the lower limbs and in the pros-
tatic plexus of elderly men. The bend in the femoral veins near Poupart’s
ligament, and dilatation in the blood channel which occurs when the blood
enters an aneurism or an auricle, play a role in explaining the frequency of
thrombi in these locations. Compression of the left iliac vein by the ar-
terial trunks may account for the well-known frequency of thrombosis in the
left as compared with the right lower limb."

Clinical observation also yields confirmation of the theory of the
significance of stasis in the formation of venous thrombi. Pigford (55)
says that the role of stasis is suggested in those who develop thrombosis
during prescribed bed rest. When one recalls the marked shift in the
intravascular bed, and the attendent retardation of the blood flow incident-
al to the enforced bed rest, in cardiac, surgical, and obstetrical cases,
the possibility of a relationship between stasis and thrombosis is to be
considered. Belt (11) has found that: "In our cases there is a high
correlation between circulatory failure and pulmonary embolism. With many
other authors we believe that slowing of the blood flow is probably the
most important factor in predisposing to the development of the dangerous
type of thrombi within the veins."

The most common condition in which there is slowing of the blood flow
in the veins is cardiac disease, yet Steuer (66) points out that although
the literature abounds with general studies on thrombosis and embolism,
the relationship between pulmonary obstruction and heart disease has been
somewhat neglected.

Pigford (55) agrees that thrombosis is more frequently associated with
heart disease than any other one group, and this observation is in keeping with the findings in the series of thirty-nine University Hospital cases under consideration. Pigford continues: "As an accompaniment of acute and subacute endocarditis, and as a consequence of chronic cardiac valvular disease, coronary arterial disease, and as intramural thrombi associated with chronic myocardial insufficiency, it assumes a position of major importance. The stasis produced in the auricular appendages as a result of a systole in these chambers, probably accounts for the high incidence of thrombi in auricular fibrillation. The most common site for thrombi in the series of Harvey and Levine, were the auricles and the tip of the left ventricle, the points of least circulatory activity. in the heart chambers."

Virchow (Rosenthal, 61) was the first to designate in 1884 non-infectious processes in the causation of thrombi. His conception was that a sluggish circulation (marantic, compressional, dilatational, and traumatic), in addition to various changes in the blood proper, were predisposing factors. This viewpoint is essentially that of many contemporary students of the subject. The writer has in the preceding pages cited a similar view of Rosenthal's. Rosenthal (61) in a study of one thousand cases of thrombosis and embolism found the incidence highest in individuals over forty-one years of age in whom heart disease was present. According to Steuer (66), the inference would be that stasis of the blood resulting from a failing myocardium is responsible for thrombus formation, but he adds: "Experimental work, however, has shown that stasis alone, or in association with endothelial injury will not result in thrombus formation. It appears, therefore, that the changes in the blood itself, physical, chemical, and
colloidal changes are necessary in order that thrombus formation take place."
The latter factors, as well as the possibly essential role of inflammatory processes, often perhaps non-suppurative, will be considered in succeeding pages.

Mechanical and physical factors, other than impaired cardiac function, may be contributory to the formation of thrombi. It seems apparent, however, that all these factors are related again to an underlying stagnation or relative stasis in the systemic venous system. Such a factor is apparent in the constitutional types, which Rabinowitz and Holtzman (57) describe as being prone to the development of venous thrombosis. They state that a study of the individuals in whom venous thrombosis occurred revealed three very important facts: First, most occurred in the fifth and sixth decades. Second, these persons usually possessed a pyknic habitus, had a pasty pallor to the facies, were inclined towards marked obesity, and showed evidence of increased vagus tone—respiratory irregularity, bradycardia, and dermographism. Others have noted that they were also thyroid resistant in their failure to react with tachycardia to the use of thyroid extract. Third, they were markedly hyposensitive to pain.

Miller and Rogers (48) consider obesity to be an important factor relating to thrombosis, and say that it is effective because the patient moves about less in bed and has a more sluggish circulation. Rabinowitz and Holtzman also, in their discussion of factors which predispose to venous thrombosis, re-emphasize the significance of confinement to bed for over a week, and Schmidt (Vieor, 68) speaks of poor general condition and reduced resistance as deciding factors in embolic fatalities. In these instances the factor of relative venous stasis again appears to be of significance.
Local venous stasis—retarded return circulation, phlebosclerosis, varicosities—Rabinowitz and Holtzman consider to be yet another important factor predisposing to venous thrombosis.

Trauma and operations for trauma seem to have a high incidence of embolism (Miller and Rogers, 48). Pigford (56) says that since trauma has been considered a requisite to the clotting of blood, it has also been considered a necessary precursor of thrombosis. This conclusion is not acceptable to many. Pigford adds that, although in a large number of cases of thrombosis, trauma, with incidental injury to the endothelium of a number of vessels, probably plays an important part, it is not present in all cases. Pickering (54) finds that in many cases of thrombosis there is no recognizable change in the vascular endothelium.

An interesting and frequent observation is that thrombosis and thrombophlebitis is more prevalent after operations below the diaphragm than following operations on the brain and skull. This observation gives rise to some interesting speculation upon the etiology of thrombosis, and is discussed by Bancroft and Stanley-Brown (5), who observe that: (1) In cases in which the surgical approach has been through the abdominal wall, there is a constant motion in the field of repair during the first forty-eight hours; in operations on the skull, with a rigid skull cap, the field is at rest. With every breath taken and with the usual postoperative nausea and vomiting there is a constant thrust and pull upon the operative field, which might easily dislodge a thrombus or cause its extension into a larger vein. (2) The approach for an abdominal operation is through an area of subcutaneous fat, while in skull operations there is a relatively small amount of fat.
With the insertion of sutures, often under too great tension, and with the application of a tight abdominal dressing, necrosis of the traumatized fat may result. Experimental work tends to show this factor to cause a marked rise in the blood clotting index. (3) There tends to be a slowing of the return flow of blood through the vena cava after abdominal operations, one factor in the causation probably being the usual postoperative distension and consequent increase in intra-abdominal pressure. (4) After an abdominal operation there may be an increased influx of bacteria into the blood due to altered absorptive capacity of the intestinal walls. (5) Dehydration, with resultant increased viscosity of the blood, may occur after any operative procedure. It is hard to estimate in the first forty-eight hours after operation, the increase of fluid output over the fluid intake. With postoperative purgation, increased sweating due to postoperative elevation of the temperature, vomiting, and urination, the fluid output is tremendously increased. At the same time the intake of fluids is usually markedly diminished.

The same exception may be taken to these conjectures of Bancroft and Stanley-Brown that has been emphasized elsewhere in this discussion: that thrombosis is as frequent in medical as in surgical cases, and that as a consequence thrombosis, except when related to frank suppuration in an operative wound, may have little direct relationship to surgical procedures.

Biochemical factors concerned in thrombosis and pulmonary embolism:
Steuer (66) has been quoted above as saying that stasis alone, or in association with endothelial injury, is insufficient, at least experimentally, to produce thrombosis. He adds that changes in the blood itself are doubtlessly necessary in order that thrombus formation take place. With this view
Rosenthal (62) agrees, saying, indeed, that all modern writers concur in the conception of the essential role of blood changes in thrombosis. As to the nature of the admittedly essential blood changes, there is, however, much disagreement.

It has long been recognized, according to Bancroft, Kugelmass, and Stanley-Brown (4), that a clot can be started by throwing out to the periphery the blood platelets when the blood stream is slowed down. As these blood platelets clump along the portion of the vessel wall, there takes place a coagulation of the blood, forming a red clot around this nucleus of platelets. Again, the great question which comes up is whether this formation of clot can take place with only a slowing of the circulation or with trauma, or whether there must be first a change in the blood-clotting elements of the blood. That such blood-changes take place has been repeatedly demonstrated, and Bancroft, Kugelmass, and Stanley-Brown, for example, found that, in eleven cases of proven thrombosis, phlebitis, or embolism which they studied, all had a high clotting index and a low antithrombin; in addition a small percentage of postoperative cases, not proven to have thrombosis, showed high clotting factors. They also determined experimentally that there is an increase in the clotting factors of animals following postoperative infection and gangrene, and a less increase following ether anesthesia.

A most interesting piece of work has been done by Mills (49, 50, 51) in connection with the effect of diet on clotting and basal metabolism. In this work he shows that a carbohydrate and fat diet will raise the basal metabolism, but will not increase clotting, while a protein diet not only raises the basal metabolism, but definitely increases the blood clotting elements. He attributes this phenomenon to some unknown factor connected
possibly with the amino acids derived from protein metabolism, but says that "a closer analysis of this protein effect in 1928 led us to the conclusion that it was intimately related to a more rapid platelet clumping and lysis which takes place". Bancroft, Kugelmass, and Stanley-Brown (4, 5) have gone further in demonstrating the relationship of diet and coagulability, showing that one can change the coagulation properties of the blood almost at will, a diet rich in nucleoproteins causing a marked increase in clotting factors, and a diet low in fat and protein causing a decrease in clotting factors.

The relation of the platelet count to thrombosis has been repeatedly studied. In postoperative, post partum, and post-febrile cases, it has been found by a number of investigators (24, 25, 42, 50, 58) that the platelet count, which suffers a rather severe depression during fevers and parturi-
tion, begins to rise soon afterwards, reaching a peak on the eighth to the eleventh day after the fever subsides, or after childbirth or operation. This peak usually shows a platelet count of almost twice normal. A sub-
sidence back to normal takes place in the next four or five days. Mills (50), who discusses this problem, points out that the platelet rise takes place just at the time most patients of the above classes are being allowed up for mild exercise and at the time when full diet is permitted. He says:

"Thus we have a period when all factors favoring thrombosis are at a maximum; the platelets are greatly increased; increased protein intake increases their tendency to clump and disintegrate; and this is further aided by the exertion of moving around; and finally the action of the sluggish circulation is intensified during the first few days of sitting up or getting out of bed."

Pickering and Mathur (55) found, however, that the whole of the
platelets in the circulation can be disintegrated without provoking thrombosis, and Pickering (55) and Mackay (44) showed that a superabundance of platelets does not alone suffice for the inception of thrombosis. Nevertheless, Pickering (55) also agrees that "the presence of a great excess of circulating platelets probably contributes to the rapid growth of a thrombus, particularly when the histological structure of the thrombus shows laminae of platelets alternating with clotted blood, and this suggestion may account for the correspondence in time—of the clinical incidences of postoperative thrombosis with a rise in the number of circulating platelets".

Again, Brock (14) says: "Almost all observers, although not in full agreement as to the exact degree of importance of the platelets in coagulation, seem agreed that the presence of an excess of platelets can certainly result in a great acceleration of the rate of formation of the clot once the actual factors necessary for clotting have commenced the process. On the other hand, I have seen thrombosis in cases where the platelet count showed no evidence of any thrombosis. Mackay has also shown this. It is clear that an increase in the number of circulating platelets cannot be the sole factor causing the formation of the thrombus; there is, however, strong evidence that the rise in numbers is a factor of great importance in the actual final stages."

Pickering (55) has studied the effect of tissue juices in thrombus formation. He states that after trauma tissue juices may gain access to the blood stream, resulting in coagulation of blood. On the other hand, he says "many aspects of natural thrombosis remain obscure, such as the common absence of the rapid occurrence of intravascular clotting after extensive trauma when fresh tissue juices may enter the blood stream and the
relatively high frequency of thrombosis during the puerperium, particularly after childbirth."

Pickering therefore concludes that the ingress of the juices of broken tissues into the circulation, although it may primarily induce hypercoagulability of the blood and later provoke an increase of the platelets in the circulation, does not in itself suffice for the inception of thrombosis; but both these factors are probably important participants in the inception or growth of thrombi when the condition of the blood plasma favors the deposition and clumping of platelets or when the stability of the plasma colloids is reduced.

In recent years considerable attention has been given to the rate of settling of red cells as seen in various disease conditions. This phenomenon, as applied to the problem of thrombosis, has been recorded. Van Allen's observations, says Pickering (54), suggest that the speed of sedimentation of blood corpuscles is correlated with the changes in plasma which inaugurate clotting. He found that sedimentation of cells preceded clotting, and continued until clotting occurred. Since the sedimentation rate is accelerated in many infections, and since the tendency to thrombosis is common in infections, it would appear that this phenomenon is associated with thrombosis. Pigford (56) says, however, that, according to Hegler, in the polycythemias the sedimentation rate is slow and the incidence of thrombosis is high; and Miller and Rogers (48) declare that although Fähraeus has noted that increased sedimentation time of the red cells may have some influence in starting the thrombus, there is as yet no definite evidence for this statement.

Many other blood changes have been studied, and a number have been said
to be important in the etiology of thrombosis. Dehydration, which causes an increased viscosity of the blood, is mentioned by Miller and Rogers (48). Allen (1) believes definite and constant changes in the consistency of the blood—erythrocytes, leucocytes, prothrombin time, and fibrinogen—occurring after operation, to be contributory to thrombosis. Pickering (54) stresses the significance of the various factors which may increase the agglutinability of red cells, white cells, or blood platelets; thus platelet thrombi, for example, are seen in pneumonia and in anaphylactic shock. Thrombi are frequent in both puerperal and inflammatory states, and both conditions, according to Pickering, are distinguished by a marked excess of fibrinogen in the plasma and by increased sedimentation time.

A problem which frequently arises in consideration of the question of thrombosis and pulmonary embolism is that of the etiological relationship of intravenous medication. The series of University Hospital cases were examined, therefore, to determine whether intravenous therapy or other medication might have been related to the occurrence of thrombosis and pulmonary embolism. Nothing of significance whatsoever in this relationship could be discerned in the hospital records.

Speaking of the relationship of drugs to thrombosis, Pigford (56) says that some of the European authors believe that present day methods of treatment tend to increase the incidence of thrombosis. "They call attention," he continues, "to the increased use of intravenous medications and antitoxic sera. It is interesting to note that the fibrinogen content of the blood is increased following intravenous administration of glucose. Autopsies of patients dying following the intravenous use of drugs frequently show widespread thrombotic processes. Hewlett calls attention to the
production of minute thrombi in experimental animals following the injection of certain tissue extracts and sera. The change in the mode of administration of digitalis from small to large doses is mentioned by the Continental authors. It has been suggested that the increased use of anesthetics, possibly through a change in colloidal activity of the cells, may influence postoperative thrombotic phenomena."

Nevertheless, it is becoming generally accepted that intravenous injections are probably insignificant or at least uncommon causative factors in thrombosis. According to Bartels (9), intravenous therapy has no apparent relationship to pulmonary embolism in the opinion of Killian, Giessendorfer, and Adolph and Hopmann. Miller and Rogers (48) emphatically state that various predisposing factors have been discussed as causing thrombosis, such as preoperative intravenous medication, but there is no adequate reason for this assumption. "Injections of arsenic preparations for syphilis," they say, "have not been followed by massive thrombosis and embolism." The injection treatment of varicose veins was responsible for but five cases of embolism in 53,000 injections, or 0.01 per cent, they finally point out. This incidence is considerably below the postoperative incidence of thrombosis and pulmonary embolism.

May it be emphasized in conclusion of the consideration of the biochemical factors in thrombosis and pulmonary embolism, which largely concern the blood, that Bancroft (3) says: "Physiochemical studies reveal that blood plasma, so long as its constituents are not dissociated by external forces, is a single complex in equilibrium, rather than a mixture of substances. The initial views of Harvey (1633) and of Woodbridge (1886) have come again into their own—'blood plasma is protoplasm, and clotting is the
last act of living blood". Therefore, may not the factors, discussed as important in thrombosis, be considered, not as entitative pathological changes, but as inter-associated and inter-dependent relationships concerned in an intricate disease process—thrombosis. Miller and Rogers (48) agree that no one factor is of outstanding importance in thrombosis, and Bankoff (7) declares: "I now wish to emphasize my opinion that thrombosis can never be regarded as due to only one class of causes: it is a pathological state which can arise from different causes at any time the equilibrium of the patient is destroyed".

The role of infection: Injury to the vessels and endothelium seems to be an important factor contributory to thrombosis, and has previously been discussed. With development of an inflammatory process in the wall of a vein, a factor—phlebitis, considered by Joel (Bartles, 9) to be of dangerous significance—is set up. However, Brown (15) studied eighty-seven cases of postoperative phlebitis without encountering one complicating pulmonary embolism. Thomas and Alyea (67) reported thrombophlebitis as rarely yielding fatal embolism, as the embolus is usually dislodged before phlebitis is recognized clinically. Bernheim (13) reported a low incidence of grave pulmonary embolism after phlebitis, but a high incidence of pulmonary infarction. Varicose veins he found to be of little, if any, significance, in producing pulmonary embolism. The role of infection in the frankly suppurative types of thrombosis is unquestioned; it is considered, however, to be a separate problem beyond the scope of this paper, and will not be discussed in detail.

Hunt (37) suggests in discussion of postoperative pulmonary embolism that the most prominent factors related to pathological thrombosis are:
(1) changes in the blood itself of such a nature as to increase its tendency to form clots; (2) blood stasis due to slowing of the blood stream from mechanical causes, depressed circulation, and lowered metabolism; (3) influence of disease processes, notably cardiovascular conditions; and, (4) infection.

He says of the latter: "That none of the foregoing causes of thrombosis (1, 2, and 3) are sufficient of themselves implies the existence of some factor common to all. An infection, of more or less specific character, already resident in the host or introduced in some manner by the operation, hypothetically would fill the need. Practically all writers entertain much respect for the role of infection, but find objections to it as a cause of those cases of fatal embolism wherein no suppurations are macroscopically evident."

In the University Hospital series of cases but seven revealed definite macroscopic evidence of a suppurative origin of the thrombotic processes. Thirty-five of ninety-three cases of postoperative pulmonary embolism reported by Hunt showed primary or secondary wound infection associated with the thrombosis; the remainder were so-called "clean" cases. Hunt points out, however, that wound infections usually considered clean have almost always received a considerable bacterial contamination, whether or not locally manifest. He suggests that "occult" infections arising at operation may account for certain complications remote from the wound, of which the various types of thrombotic processes are examples. He theorizes that "a latent or occult infection activated by a variety of conditions which profoundly alter the metabolism, the circulatory mechanism, and the composition of the blood, best answers the requirements of the situation."

Rosenow (60) takes perhaps a broader view of the situation, suggesting
a microbic etiology of thrombosis and pulmonary embolism, but not attributing the process specifically to invasion through operative wounds. By means of special methods he isolated a diplostreptococcus, identical to one he had obtained a number of years before in similar cases, in each of five cases of postoperative pulmonary embolism and in one case of portal thrombosis, and also demonstrated a morphologically identical organism within the thrombus or embolus or infarcted areas in all but two of twenty-five additional cases. The organism he found to be of low virulence, and to rarely cause lesions in the various tissues, except those secondary to thrombosis or embolism. He says of his study of the behavior of the diplostreptococcus: "It often shortens the coagulation time of the blood of animals after repeated intravenous injection, and with pure cultures thrombosis sometimes associated with pulmonary embolism has been produced experimentally in three species of animals. Experiments have been successful with each of the four strains injected and isolated from thrombi and with one strain isolated from foci of infection at the apaxes of teeth. Such results have not been obtained in numerous experiments following injection of morphologically similar organisms from cases other than pulmonary embolism."

Rosenow furthermore states that the factors, such as anesthesia, operative procedures, slowed circulation, and trauma of vessels, which are considered as etiologic in human cases, appeared to favor clot formation in experimental cases, but in some instances the mere injection of the organism sufficed. He continues: "The experimentally produced thrombi resembled those in man in their frequent formation in large veins and their large size; in being loosely attached, leading to embolism; in gross and microscopic appearance, including the deposition of fibrin; in not leading to suppuration, in the presence of relatively small numbers of the diplococcus in pure
form within the thrombus, and in the relatively slight circumscribed areas of endophlebitis. The number of bacteria was relatively small and in some instances the production of a local focus, as in the eye, or even subcutaneous injections, sufficed to incite the formation of thrombi. He concludes that the diplostreptococcus, isolated from postoperative emboli and thrombi and used by him experimentally in different animals, is the common cause of postoperative and nonoperative massive thrombosis, leading to fatal pulmonary embolism, and perhaps of closely allied conditions such as infarction of the heart or brain.

Indirect verification of the significance of Rosenow's work is evidenced in the failure to produce typical thrombosis by other experimental means. According to Rosenthal (62) stasis alone, from an experimental standpoint, does not terminate in thrombus formation. He says that "this was first shown by Baumgarten in 1877, and has been verified by Miller and Rogers, and by Armentrout. On adding endothelial injury to stasis, Baumgarten and more recently Armentrout (1931) reported thrombus formation. It is questionable whether true thrombi were produced. More likely, mere coagulation took place, for Miller and Rogers, using sixty-three cats, were unable to produce true thrombi by double ligation of veins with scarring of the endothelium, interposition of muscle, etc." It is seemingly apparent, therefore, that these workers have set up a number of the predisposing factors conducive to thrombosis, but that some further essential factor is lacking; and Miller and Rogers did produce one typical thrombus in their series of experimental cases where infection had set in.
General Considerations

In comparing statistical compilations of various clinics in attempt to determine the incidence of thrombosis and pulmonary embolism, a wide variation is noted, which, says Rosenthal (61) may be explained by the fact that different types of clinical material are reported and that different pathologists evince varying interest in these conditions. However, Rosenthal says, when an average is taken from all these reports, the similarity to the results he obtained in one thousand consecutive post-mortem examinations is striking. The average for thrombosis taken from all reports (1930), Rosenthal found to be 17.7 per cent, for embolism 12.5 per cent, and for fatal lung embolism 0.9 per cent. He obtained in his own work an incidence for thrombosis of 13.4 per cent, for embolism 7.6 per cent, and for fatal lung embolism 0.2 per cent.

Belt (11, 12) has employed extreme care in searching for pulmonary emboli at the time of post-mortem examination. He believes that probably there is no other autopsy finding more readily missed than pulmonary embolism, and reports that routine autopsies in the Department of Pathology at the University of Toronto and the Toronto General Hospital disclose pulmonary emboli in approximately ten per cent of adult cases in a series of 567 complete autopsies.

Thirty-nine cases of pulmonary embolism were discovered at the University Hospital in a three year series of 309 post-mortem examinations—an incidence of 12.6 per cent. Included in this group of cases were seven
cases of pulmonary embolism from sources of frank infection. This type of case Belt excludes from his series. With the exclusion of these cases from the University Hospital series, for purposes of more accurate comparison, the incidence of "bland" pulmonary embolism is found to be 10.4 per cent, a figure almost identical to Belt's determination.

Relation of Age to Pulmonary Embolism

Rosenthal (62) says the average age incidence for thrombosis and pulmonary embolism, as found in the Toronto General Hospital, Canada, in the Northwestern University affiliated hospitals, Chicago, and in the Stanford University Medical School, San Francisco, was about fifty years. At the Cook County Hospital, Chicago, the greatest number of cases occurred in persons between forty-one and fifty years of age, while the highest percentage of thrombosis and pulmonary embolism was that of cases in persons between sixty-one and seventy years of age.

European authors, according to Rosenthal, have reported an age incidence for thrombosis and pulmonary embolism which is similar to that in this country. Without exception, the European authors have found the greatest number and percentage of cases of thrombosis and fatal pulmonary embolism in persons between the ages of forty and seventy years. (Ruhn, Klinke, Singer and Morawitz, Oberndorfer, Höring, Adolph and Hopman, Sellheim, Geissendorfer, Killian, Grüber, Hutter and Urban, Schulz, Bauer, Qure).

Twenty-five of the thirty-nine University Hospital cases of pulmonary embolism were over forty-five years of age. The average age for the group was 45.7 years.
Relation of Sex to Pulmonary Embolism

According to Rosenthal (61) the male represented by far the largest number of thromboses, as compared to the female, in his series of one thousand post-mortem examinations. Non-fatal embolism showed the same relationship. His two cases of fatal lung embolism were in females. In Belt's (12) fifty-six cases of pulmonary embolism there were thirty-five males and twenty-one females.

On the other hand, but sixteen of the University Hospital cases of pulmonary embolism were males, and twenty-three were females. Kuhn (Rosenthal, 61) has shown a definite increase of thrombi in the female over the male. Fahr and Rueck (Rosenthal, 61) believe that sex does not play a noteworthy role in thrombosis. For fatal pulmonary embolism, Rosenthal says, all authors agree that the female sex has the predominance. (Höring, Oberndorfer, Singer, Kuhn).

Relation of Race to Pulmonary Embolism

Rosenthal (61) says that the incidence of thrombosis and embolism are about equal in the white and colored races. None of the University Hospital cases were colored.

The Sources of Pulmonary Emboli

Often at necropsy evidence of pulmonary embolism will be found, and yet no thrombosis can be demonstrated. There are two reasons for this occurrence, which have already been pointed out: A thrombus may completely detach itself at its site of formation, leaving behind it no demonstrable alteration in the wall of the vein; or, more frequently, a sufficiently thorough search for the thrombus is impracticable. In thirty-two of the
thirty-nine University Hospital cases the probable primary site of thrombosis was found or was suggested by clinical or autopsy findings. In all cases, excepting those of suppurative thrombosis, the emboli had their apparent source in the veins of the legs or pelvis, or from the right heart.

Relation of Pulmonary Embolism to the Primary Disease

The principle or primary diagnoses in the series of University Hospital cases are listed. (Table 1). A large proportion of the cases are cardiac, a number are infectious, and many are chronic debilitating processes.

Such a compilation yields little information relative to the etiology of pulmonary embolism. It does, however, illustrate one significant, and not too generally recognized fact—that pulmonary embolism may complicate practically any disease process persisting long enough to allow time for thrombosis to occur; it is frequently encountered in medical, or non-operated cases.
TABLE 1.
Classification of Cases of Pulmonary Embolism
According to the Primary Diagnosis

1. Cardiac--eleven cases.
   a. Decompensation due to various causes--seven cases (9, 13, 14, 17, 20, 21, 25).
   b. Toxic goiter with myocardial failure--three cases (10, 11, 12).
   c. Subacute bacterial endocarditis--one case (23).

2. Conditions involving the abdominal viscera--ten cases.
   a. Cholecystitis--two postoperative cases (5, 8).
   b. Kidney diseases--one postoperative case (16), and three unoperated cases (15, 24, 26).
   c. Umbilical hernia with partial strangulation--one case (3).
   d. Tuberculous enteritis--one case (6).
   e. Acute pancreatitis with retroperitoneal hemorrhage--one postoperative case (37).
   f. Amebic colitis with perforation--one case (38).

3. Suppurative processes with secondary infected thromboses--one post partum case (30), and six unoperated cases (27, 28, 29, 31, 32, 33).

4. Carcinoma--four cases.
   a. Carcinoma of the uterus--two cases (22, 39).
   b. Carcinoma of the breast--one postoperative case (7).
   c. Carcinoma of the colon--one case (34).

5. Two post partum cases (2, 4).

6. Miscellaneous conditions--five cases.
   a. Benign hypertrophy of the prostate--two postoperative cases (18, 19).
   b. Diffuse cortical atrophy--one case (35).
   c. Senile cataract--one postoperative case (36).
   d. Cystocele and rectocele--one postoperative case (1).
Fatal Pulmonary Embolism

University Hospital records for a three-year period ending December 31, 1934 reveal a smaller percentage of pulmonary emboli found at post-mortem examination during 1934 than during either of the two preceding years, although pulmonary embolism as the primary cause of death was more frequent in 1934. In the three-year period 309 autopsies were performed. In thirty-nine cases the post-mortem diagnosis of pulmonary embolism or infarction was made, and in nine cases pulmonary embolism was found to be the primary cause of death. The percentage incidence was 12.6 per cent for total cases showing pulmonary embolism and infarction, and 2.9 per cent for cases of fatal pulmonary embolism.

Six of the fatal embolic cases occurred in a period of less than four months during the latter part of 1934. There had been no cases of fatal pulmonary embolism during the first eight months of 1934, but one case in 1933, and two in 1932. The situation was dramatic, but no adequate explanation of the outbreak could be determined. The present study was therefore undertaken, in an attempt to discover any unrecognized etiological factors in the cases.

It was found that the cases presented a diversity of diagnoses and had been managed in a diversity of ways. Of the three cases seen in 1932 and 1933, case 1 was a postoperative gynecological patient, case 2 was an obstetrical patient eight days post partum, and case 3 was one of ventral hernia with partial obstruction which received only medical management.

Of the cases seen in 1934, one (case 4) was a post partum obstetrical patient, two (cases 5 and 8) followed cholecystectomy, one (case 7) followed a radical mastectomy, and two (cases 6 and 9) were medically managed.

The nine cases were rather readily fitted into two groups: three
medically managed cases, all showing cardiac damage; and six post partum and postoperative cases, only one of which showed evidence of cardiac damage.

In the entire group of thirty-nine cases showing evidence of pulmonary embolism at autopsy, there were only twelve which were either postoperative or post partum, or 30.8 per cent. Of this number, a rather high proportion, six of twelve, were in the fatal group.

On the other hand, a high proportion of the thirty-nine cases—53.8 per cent—showed cardiac damage at necropsy, but only four of this group died of fatal pulmonary embolism.

In a series of 567 autopsies Belt (12) encountered fifty-six cases of pulmonary embolism. Fifteen cases were of the type showing massive emboli which had been the cause of sudden death. The percentage incidence, curiously, was almost exactly the same as that for the University Hospital series—2.9 per cent as compared to 2.6 per cent. Furthermore, in Belt's cases of massive pulmonary embolism, the larger proportion, eleven of fifteen, were also surgical cases, and only four were medical cases; yet forty of his total group of fifty-six cases were medical.

The relationship of fatal pulmonary embolism to operative procedures can, therefore, not be neglected. Many attempts are made to dismiss these cases largely on the basis of circulatory stasis resulting from the operation and the enforced bed rest after operation. This explanation does not suffice, when it comes to the consideration of fatal embolic cases, for too great a proportion of the total cases are cardiac and yet non-fatal. In the writer's opinion, more attention should be given to the work of Rosenow (60) and Hunt (37), which has already been considered in detail. These workers emphasize the importance of infection of a "bland" or "occult" type in the
causation of pulmonary embolism, especially that form which occurs after operation. (Hunt).

Another important fact is revealed in a review of Belt's cases, as well as the University Hospital cases: Only occasionally is venous thrombosis recognized clinically prior to the embolic accident. But one of the nine University Hospital cases of fatal pulmonary embolism (case 8, page 56) complained of symptoms of thrombophlebitis. Belt says that probably sixty percent of the emboli in his fifty-six cases arose from clotted leg veins, vessels relatively easy to examine and easy enough of detection when they are painful, yet the majority came to autopsy without recognition of the primary thrombosis during life. It has already been pointed out that the greater the local reaction accompanying a venous thrombosis the less the likelihood of large emboli breaking off. If, in and around a vein, there is an inflammatory reaction of sufficient intensity, says Belt, to create local manifestations, the thrombus is likely to be securely attached to the vessel wall, and only small masses are capable of dislodgement.

The theory was postulated in the introductory section of this paper that, since pulmonary embolism depends upon the presence of a primary thrombotic process, the amount of thrombus which might break loose and reach the pulmonary arterial system through the blood stream would determine the gravity of the process; and thus the involvement of the lung is only an incidental or secondary occurrence. Since it has been repeatedly shown that no constant relationship exists between the incidence of embolism and the proportion of fatal cases, the occurrence of massive pulmonary embolism is well-nigh unpredictable. Consequently, it seems that a sudden rise in incidence of fatal cases is no cause for wonder, providing the total
incidence of thrombosis and embolism has not increased, although it is cause for institution of more thorough prophylactic and therapeutic measures.

Postoperative and Post Partum Pulmonary Embolism

Nine of the thirty-nine cases of pulmonary embolism seen at the University Hospital died shortly after operation (cases 1, 5, 7, 8, 16, 18, 19, 36, and 37). Three died shortly after delivery (cases 2, 4, and 30). In six of the cases death was attributed to massive pulmonary embolism. It was of considerable interest to the writer that but four of this group, or 33.3 per cent, showed cardiac pathology, although twenty-one cases, or 53.8 per cent of the entire group of thirty-nine cases showed cardiac pathology. Cardiac disease has been shown in the preceding sections to be one of the foremost predisposing factors in pulmonary embolism. Yet, if so small a group of cases as that at present under consideration, can be construed as characteristic, the implication would be that some factor besides cardiac disease is of more importance in the postoperative cases of pulmonary embolism than in the medical cases. The infectious conception of pulmonary embolism and thrombosis propounded by Rosenow (60) and by Hunt (37), and already discussed, suggests a possible explanation.

Relation of Heart Disease to Pulmonary Embolism

Hegler in 1926 was the first to call attention to the marked rise in incidence of thrombosis in St. Georg Hospital, Hamburg, according to Rosenthal (62) who, in a rather complete survey of the literature, found that there has been an increase in the incidence of thrombosis and pulmonary embolism in the clinics of Central Europe. As a rule, he found, the actual ascent began in 1919, became universal in 1922 and reached its height in
1928. Later than 1928 a decline became manifest. The rise was prevalent in the general, as well as the surgical, clinics, although more marked in the latter. There was furthermore a rather closely parallel rise in the incidence of cardiac and vascular disease in the clinics of Central Europe, and a less marked increase in infections and suppurative diseases. Rosenthal believes that the hunger, nervous irritability, and lack of vitamins that were especially manifest during the period of inflation (1919 to 1924) in Central Europe account for the accentuation of cardiac and vascular diseases, and concludes that the rise of circulatory disturbances may be largely responsible for the increase in thrombosis and embolism. No corresponding increase in thrombosis and embolism, or in vascular and cardiac disorders, was shown in reports from clinics in the United States and Canada.

Such statistical reviews as that cited in the preceding paragraph suggest the importance of venous stasis and cardiac disease in predisposition, at least, to thrombosis and embolism, and Hunt (37) adds: "As affecting surgical thromboses the degenerative diseases play an important part. Indeed Kuhn attributes the increase of fatal embolism observed at the Pathological Institute at Freiburg to the prolongation of life by the present day treatment of chronic heart disease." Twenty-five of ninety-three cases of postoperative thrombosis reported by Hunt showed cardiac impairment.

Rosenthal (61) studied the incidence of thrombosis and embolism in one thousand consecutive autopsies, and came to the conclusion that cardiac decompensation and arterial changes apparently play the more important role in the formation of thrombi and emboli. In one thousand consecutive autopsies there were 134 cases of thrombosis, seventy-six cases of embolism, and two cases of fatal lung embolism. Furthermore, of 149 cases of decompensation of the heart in the entire series of one thousand cases, there were ninety-
four with thrombosis, or sixty-three per cent; of the 172 cases with arterial changes, seventy-six, or forty-four per cent had thrombi; and of the 511 infectious cases, but fifty-seven, or 17.4 per cent had thrombi.

Twenty-one of the thirty-nine University Hospital autopsy cases of pulmonary embolism showed evidence of cardiac pathology (cases 3, 4, 6, 9, and 10 to 26 inclusive). In four cases (cases 3, 4, 6, and 9) the emboli process was so massive as to be the immediate cause of death. In the remainder (cases 10 to 26 inclusive) the embolic process sometimes complicated the clinical picture, but was often merely an incidental autopsy finding.

In a number of the University Hospital cases studied, notably cases 34 to 39 inclusive, there was present no apparent predisposing factor to suggest an explanation of the occurrence of thrombosis or pulmonary embolism, except perhaps the factor of circulatory stagnation or stasis due to rest in bed. All of these questionable cases showed pulmonary infarction; and all of the cases showing definite cardiac pathology also showed pulmonary infarction, excepting those cases in which embolism occurred too shortly prior to death for infarction to take place.

Belt (12) interprets the occurrence of bland hemorrhagic pulmonary infarcts in his cases as evidence of impairment of the return circulation to the heart. This interpretation is based on the work of Karsner and Ash (39) who showed in 1912 that simple embolism does not produce pulmonary infarction. Karsner and Ash found that, in experimental animals, it was only by slowing the circulation considerably, as by ligation of the pulmonary vein or by compressing the lungs, that infarction puts in its appearance after pulmonary embolism. They found that not only is stasis a necessary corollary of infarction, but also that, the greater the degree of stasis, the sooner true
infarction will be likely to appear.

In clinical cases such an impediment to the return circulation from the lungs may be brought about, according to Belt (12), by compression or thrombosis of the pulmonary veins or by stenosis or insufficiency of the mitral valve. In his cases of pulmonary infarction Belt found he was able to exclude obstruction of the pulmonary veins, and was therefore obliged to account for infarction on the grounds of inadequacy of the mitral valve, when no more specific heart lesion was demonstrable. Indeed, in re-checking the clinical records of these cases, he found that a mitral systolic murmur had been heard in many.

The above interpretation of pulmonary infarction may be open to criticism. However, it suggests an explanation for the occurrence of pulmonary embolism in otherwise unexplainable instances. It suggests the presence of cardiac incompetancy, which may be a predisposing factor in the formation of the primary thrombosis, as well as in the occurrence of infarction.

Twenty-five of Belt's fifty-six cases were invalided with myocardial insufficiency, and twenty-four more presented evidence of a disordered heart with either infarcts of the lungs, or pathological changes in the heart, or both. Thus, he says, forty-seven cases, or eighty-four per cent, were regarded as having impairment of cardiac function. He concludes: "From the present study it seems warrantable to emphasize another general principle concerning the occurrence of thrombosis, a principle that has received only casual attention in the literature, namely, that so-called spontaneous venous thrombosis has a high incidence in cases of actual or impending congestive heart failure."
Pulmonary Embolism Complicating Septic Thrombosis

A small proportion of infectious diseases, and, more frequently, supplicative processes, notably mastoiditis, will give rise to septic thrombosis and pulmonary embolism. Thrombosis and pulmonary embolism complicating such conditions are considerably less frequent than are thrombosis and pulmonary embolism complicating cardiac disease. (Rosenthal, 61). Seven of the University Hospital cases, or 17.9 per cent, showed infected pulmonary emboli secondary to primary septic thrombosis (cases 27 to 33 inclusive). This type of case forms a group more or less by itself, among thrombotic and embolic cases, in that the etiology is definite, while the etiology in the remainder of the cases is indeterminate.

Infection may play a role in all cases of pulmonary embolism, as it has been previously pointed out, but this possibility is open to question. Relatively few of the postoperative and post partum cases in the series were associated with cardiac disease; a possible explanation may be that they were associated with "occult" or non-suppurative low grade inflammatory thromboses related to primary or secondary wound infections. (Hunt, 37).

Relation of Therapy to Pulmonary Embolism

The problem of therapy, and its relationship to pulmonary embolism has been previously considered (page 27). Rosenthal (61) states that patients seldom die of pulmonary embolism due to intravenous and injection therapy. No relationship of therapy to the occurrence of thrombosis and pulmonary embolism could be ascertained in the University Hospital cases.
The thirty-nine autopsy cases of pulmonary embolism seen in the University Hospital during 1932, 1933, and 1934 are presented in the following pages. In the preceding pages of this section on the incidence of pulmonary embolism attempt has been made to bring out some of the impressions gained by a review of the cases. The review was not undertaken, however, with the purpose in mind of making a critical study of these case records, for the series of cases is too small. The study has been of interest because it demonstrates the total incidence of pulmonary embolism at the University Hospital to be comparable to that of other hospitals and clinics, and, most important of all, because it demonstrates no increase in total pulmonary embolism cases in 1934 corresponding to the increase in fatal pulmonary embolism cases during that year.

It has previously been pointed out that it may at times be a puzzling problem to determine whether an attached antemortem blood clot found in a pulmonary artery is a primary thrombus or an embolus which has become attached secondarily. In the group of cases under consideration, a large number were found to show ante-mortem clots in the pulmonary arteries which were attached and which, consequently, in the case records were termed thrombi. That these so-called "thrombi" are most probably all embolic in origin, it has previously been established. (Pages 15 to 17).

The thirty-nine case records are divided for convenience into four groups which necessarily overlap, for a number of the cases might be included in more than one group. Further discussion accompanies each case record.
Group 1 (cases 1 to 9 inclusive) consists of nine cases of fatal pulmonary embolism.

Group 2 (cases 10 to 26 inclusive) consists of seventeen cases showing the common finding of various forms of cardiac impairment.

Group 3 (cases 27 to 33 inclusive) consists of seven cases of suppurative thrombosis with metastatic involvement of the lungs.

Group 4 (cases 34 to 39 inclusive) consists of six miscellaneous cases, all but one of which showed pulmonary infarction, but no other definite evidence of cardiac impairment.
CASE 1.


Clinical diagnosis:
- Cystocele.
- Rectocele.
- Hernia of cul-de-sac.
- Pulmonary embolism.

Post-mortem diagnosis:
- Fatal pulmonary embolism.
- Anterior and posterior colporrhaphy, post-operative.

Clinical evidence of thrombosis and embolism:
"Patient had a sudden sharp pain in the epigastrium and complained of her heart. She became markedly dyspneic, her extremities became cold, and her heart irregular. Cyanosis was quite marked about the lips. Carbon dioxide and oxygen were given." Death occurred forty-five minutes after onset of symptoms. Diagnosis: Pulmonary embolism.

Post-mortem evidence of thrombosis:
About the operative sites a few small vessels were found to contain ante-mortem thrombi.

Post-mortem evidence of pulmonary embolism:
Large long ante-mortem thrombi were found in the pulmonary artery, measuring 5 to 10 mm. in diameter and up to 10 cm. in length. Similar material was found in the right auricle and in the large branches of the right pulmonary artery.

Evidence of circulatory failure:
None.

Comment:
Death occurred nine days post-operative and was due to massive pulmonary embolism. The apparent site of origin was the pelvic vessels, the thrombotic process extending from the operative sites.
CASE 2.


Clinical diagnosis:

Post-mortem diagnosis:
Thrombi in internal iliac vein. Fatal pulmonary embolism.

Clinical evidence of thrombosis and embolism:
Patient on the eighth post-partum day was taking the knee-chest position when she felt a sudden pain below the sternum. She became faint, dyspneic, and cyanotic. The pulse was rapid, fluttering. Oxygen and stimulants gave only temporary relief. The patient died one hour and twenty-seven minutes after onset of symptoms.

Post-mortem evidence of thrombosis:
A large mass of ante-mortem thrombus was found in the left internal iliac vein, not attached to the wall. There was no evidence of infection in the uterus or evidence of thrombi in its wall.

Post-mortem evidence of pulmonary embolism:
Several small masses of ante-mortem thrombi were found in the common pulmonary artery. Both lungs showed large masses of grayish-red and comparatively firm thrombus, at the points of bifurcation of the main branches of the pulmonary arteries, not adherent.

Evidence of circulatory failure:
None.

Comment:
In this case the probable source of the emboli was found--thrombosis of the left internal iliac vein. This is a typical case of post-partum fatal pulmonary embolism.
CASE 3.

M. L. -- White, married, female, aged 57. Hospital number 44668.
Entered 8/9/33. Died 8/11/33.

Clinical diagnosis:
Ventral hernia.
Intestinal obstruction.

Post-mortem diagnosis:
Umbilical hernia with partial strangulation.
Cholelithiasis.
Fatal pulmonary embolism.

Clinical evidence of thrombosis and embolism:
Varicose ulcer on the left leg with several varicose veins.
On 8/11/33 the patient suddenly became restless and died within ten minutes.

Post-mortem evidence of thrombosis:
None. The veins of the legs, however, were not dissected.

Post-mortem evidence of pulmonary embolism:
Several large ante-mortem emboli were found lying loosely in the lumen of the pulmonary artery. The emboli were one to four inches in length and up to one centimeter in diameter. There were also large thrombi in the main branches of the pulmonary artery. There was no infarction.

Evidence of circulatory failure:
Post-mortem -- The heart muscle was extremely soft, and there was a great deal of fat over the surface and mingled with the fibres.

Comment:
The venous pathology in the left leg suggests a possible source of the emboli. Pathological findings also suggest impaired cardiac function.
CASE 4.

G. S. — White, married, female, aged 35. Hospital number 47824. Entered 8/6/34. Delivery on 8/7/34 of three live baby girls, all breeches. Died 8/26/34.

Clinical diagnosis:
Triple pregnancy. Full term.
Pre-eclampsia.

Post-mortem diagnosis:
Thrombo-phlebitis of ovarian vein.
Fatal pulmonary embolism.
Infarction of lung.
Subinvolution of uterus.
Atresia of right Fallopian tube.
Subacute nephritis.

Clinical evidence of thrombosis and embolism:
On 8/10/34 and 8/11/34 the patient complained of rather sharp pains over the precordium with only slight difficulty in breathing. On 8/17/34 the patient had a severe pain in the right lower chest with radiation to the shoulder. Coarse rales were found in the lower right chest with diminished breath sounds. Following this the patient coughed considerably, with production of some blood-streaked sputum. On 8/26/34 the patient had been sitting up in bed, suddenly screamed, collapsed, and died about seven minutes later.

Post-mortem evidence of thrombosis:
The uterus measured 14 cm. in length. On the posterior wall there was a mass of organizing blood clot, measuring 7 x 5 x 2½ cm. There were thrombi in the small veins of the uterine wall and about the posterior surface of the bladder. The right ovarian vein was dilated to 1.5 to 2 cm. in diameter and filled with rather firm laminated thrombus. It extended throughout the length of the vein. In the vena cava there was a mass of ante-mortem thrombus, measuring about 6 cm. in length, attached to the lateral wall. The left ovarian vein contained a few small masses of thrombus near the ovary, but the remainder of the vein was free of thrombus, although the wall was slightly granular.

Post-mortem evidence of pulmonary embolism:
The pulmonary artery was opened and probed; about fifteen grams of soft ante-mortem blood clot was removed from the main branches of the pulmonary artery. On opening the main branches of the pulmonary arteries of the right lung, large masses of ante-mortem blood clots were encountered extending down into the smallest ramifications. In the main pulmonary arterial branch to the right lower lobe a rather firm well organized thrombus was encountered attached to the wall. This thrombus was associated with a large infarct. The left lung was well-aerated throughout.
Evidence of circulatory failure:
Clinical -- None. Blood pressure of 160/90 was considered to be associated with a pre-eclamptic state.
Post-mortem -- The heart weighed 400 grams, and the left ventricle measured 18 to 20 mm. in thickness. Valves and musculature were normal.

Comment:
The thrombotic process was apparently associated with a sub-involution of the uterus, extending from the small veins of the uterus to the ovarian veins to the vena cava. At autopsy a large infarct was found in the right lung with a large associated thrombus, present for several days and corresponding in probable duration to the attack of chest pain and dyspnea on 8/17/34. Death was due to fatal pulmonary embolism on 8/26/34.
CASE 5.

E. W. -- White, married, female, aged 39. Hospital number 48038.
Entered 8/31/34. Cholecystectomy and appendectomy under 250 mg.
novacine spinal anesthesia, 9/10/34. Died 9/15/34.

Clinical diagnosis:
Chronic cholecystitis.
Chronic appendicitis.
On pathological examination of the tissues a diagnosis of
cholesterosis of the gall bladder and negative appendix was
made.

Post-mortem diagnosis:
Cholecystitis, post-operative.
Appendectomy, post-operative.
Fatal pulmonary embolism.
Fibroids of uterus.
Slight atelectasis of lungs.
Ascaris infestation.

Clinical evidence of thrombosis and embolism:
The patient progressed well until the fifth post-operative day
when she suddenly sat up in bed, breathing rapidly and showing
considerable cyanosis. She complained of no pain. She was
given morphine, caffeine sodio-benzoate, and digalen intra-
venously, but she died two hours and twenty-five minutes after
the onset of the symptoms. Diagnosed as probable pulmonary
embolism.

Post-mortem evidence of thrombosis:
The operative sites were clean and healing normally. No thrombi
were found in any of the large veins, although the veins of the
legs were not explored.

Post-mortem evidence of pulmonary embolism:
There was an ante-mortem thrombus in the pulmonary artery 60 cm.
in length. The thrombus was firm and granular, and of practically
uniform diameter, about 1 cm. There were no thrombi in the branches
of the pulmonary arteries and there were no infarcts in the lungs.

Evidence of circulatory failure:
None.

Comment:
On post-mortem examination no change was noted in the vessels of
the pelvis. Because of the enormous length of the embolus—sixty
centimeters—one can conclude that the only possible source could
be a large vein in one of the legs with the thrombus perhaps ex-
tending into the pelvis. There was no history of varicosities
of the legs or of thrombo-phlebitis.
CASE 6.

Entered 10/7/34. Died 10/13/34.

Clinical diagnosis:
Subacute nephritis.
Parasinusitis, acute, right.
Lateral pharyngitis.

Post-mortem diagnosis:
Tuberculous enteritis.
Rheumatic heart disease.
Mitral insufficiency.
Fatal pulmonary embolism.

Clinical evidence of thrombosis and embolism:
On the morning of 10/13/34 the patient became cyanotic and the respirations labored and gasping. The pulse was weak and thready, but the tones at the apex were relatively strong. The patient expelled frothy material from her nose and expired about twelve minutes after the onset of symptoms.

Post-mortem evidence of thrombosis:
None.

Post-mortem evidence of pulmonary embolism:
On probing the common pulmonary artery several masses of antemortem thrombi were found; the largest of these measured 7 x 1 cm.

Evidence of circulatory failure:
History of rheumatic fever in 1931. On entrance the patient complained of dyspnea on exertion. On examination, there was a soft systolic murmur at the apex, and the rhythm was regular but fast.
Post-mortem -- The heart weighed 200 grams. The mitral orifice admitted three fingers; the edges of the mitral cusps were somewhat thickened and rolled; and there was some thickening of the chorda tendinae. The aortic cusps were slightly thickened and there were a few adhesions in the anterior commissure. The other valves, musculature, and coronary arteries showed no change.

Comment:
This was an unusual case in that fatal pulmonary embolism is rarely seen in a patient as young as this one. It may therefore be concluded that the heart pathology was an important factor for mere bed rest is rarely complicated by pulmonary embolism in children and adolescents.
CASE 7.

M. P. -- White, married, female, aged 63. Hospital number 48368. Entered 10/9/34. Radical mastectomy under gas-ether anesthesia on 10/20/34. Died 10/22/34.

Clinical diagnosis:
- Carcinoma of the left breast of a duration of about one year.
- Varicosities of both legs.
- Varicose ulcers of both legs.
- Marked rectocele.

Post-mortem diagnosis:
- Fatal pulmonary embolism.
- Carcinoma of breast, post-operative.
- Carcinoma of fundus of uterus.
- Pyelonephrosis of right kidney.
- Compensatory hypertrophy of left kidney.
- Healed duodenal ulcers.
- Diverticuli of colon.
- Polypi of colon.
- Bilirubin calculi in gall bladder.
- Cystitis cystica.

Clinical evidence of thrombosis and embolism:
- History of "milk leg" fifteen years ago, and of ulcers on the right leg more or less continually for the past fifteen years. On examination varicosities were noticed on both thighs, and there were ulcers on both lower legs. Dry heat with local application of olive oil was employed in management of the ulcers during the patient's hospitalization. The patient died suddenly two days after a left radical mastectomy, apparently a respiratory death. She lived only fifteen minutes after the onset of symptoms.

Post-mortem evidence of thrombosis:
- None.

Post-mortem evidence of pulmonary embolism:
- The pulmonary artery was filled with a large mass of ante-mortem thrombus. There were similar masses in the main and smaller branches of the pulmonary artery. There were no areas of infarction.

Evidence of circulatory failure:
- None.

Comment:
- The patient, who showed no clinical or pathological evidence of cardiac disease, died suddenly two days post-operative with a massive pulmonary embolism. The primary site of the thrombotic process was not determined at necropsy. However, the presence of variceal veins and ulcers, and history of phlegmasia alba dolens suggest the source to have been some of the large veins in the legs. Venous stasis due to enforced bed-rest over a period of nearly two weeks was probably an important etiological factor.
CASE 8.


Clinical diagnosis:
Chronic cholecystitis.
Acute cholecystitis on examination of pathological specimen. Cholelithiasis.

Post-mortem diagnosis:
Cholecystitis, post-operative.
Fatal pulmonary embolism.
Mild atelectasis of right lung.

Clinical evidence of thrombosis and embolism:
The patient had made an apparently uneventful post-operative recovery until the ninth day after operation when during the night she complained of cold feet and pain in the legs below the knees. In the morning she had a sudden pain in her chest and became markedly dyspneic. The expression was one of extreme anxiety. She died twenty-five minutes after the onset of symptoms.

Post-mortem evidence of thrombosis:
The superficial veins on both legs were visible; those on the right were distended. The veins of the legs were not opened. There were no thrombi in the iliac veins. There was no roughening of the intima of the vena cava. The operative site was clean. There was a stone high in the common duct, but it did not appear to be causing obstruction.

Post-mortem evidence of pulmonary embolism:
There were two large masses of ante-mortem thrombus in the main branches of the pulmonary artery. The larger branches of the arteries to each lung contained small masses of ante-mortem thrombus. There were no areas of infarction.

Evidence of circulatory failure:
None.

Comment:
This case of fatal pulmonary embolism presented an unusual symptom-complex—pain in the legs and cold feet shortly before the occurrence of the pulmonary embolism—suggestive of acute thrombo-phlebitis. It may be concluded that the source of the pulmonary emboli were the veins of the legs.
CASE 9.

C. S. — White, male, aged 72. Hospital number 48897. Entered 12/21/34. Died 12/12/34.

Clinical diagnosis:
Arteriosclerosis.
Pulmonary embolism.

Post-mortem diagnosis:
Fatal pulmonary embolism.
Coronary sclerosis.
Myocardial fibrosis.
Pelvic thrombosis.
Arteriosclerosis, generalized.

Clinical evidence of thrombosis and embolism:
On 12/12/34 the patient, who was sent to the hospital as a case of probable chronic gall bladder irritation, was apparently feeling well when he walked into the admitting room. After taking a bath he was seized with a sudden attack of dyspnea and cyanosis, accompanied by a "cold sweat". He complained of distress over the precordium. However, the apex beat was regular and slow. In the ward the patient was observed to be extremely dyspneic. The skin was pale, and a grayish cyanosis was noted. The patient was frightened and convinced he was about to die. He did not respond well, but said he had had a similar attack about one month ago. Morphine did not greatly relieve the restlessness. The patient died about twenty-five minutes after the onset of the symptoms.

Post-mortem evidence of thrombosis:
There were a few small thrombi in the plexus around the prostate and bladder.

Post-mortem evidence of pulmonary embolism:
There was a mass of ante-mortem thrombus about 23 cm. long lodged in the pulmonary artery. In the various branches of the pulmonary arteries were a number of various sized thrombi, some of which were firmly attached to the arterial walls. There were several infarcts in the lungs.

Evidence of circulatory failure:
Clinical — The referring physician stated the patient had had heart trouble and arteriosclerosis for some time. The patient died before his history could be taken or adequate study of the cardio-vascular and other systems could be made.
Post-mortem — The heart weighed 480 grams. The coronary arteries showed extensive sclerosis. The lumen was definitely diminished in the left coronary artery, but a complete occlusion was not demonstrated. Small areas of softening and scarring were seen in the ventricles.
Comment:
This case of fatal pulmonary embolism was of especial interest because there was a history of previous less severe attacks of symptoms suggesting the occurrence of pulmonary embolism, and because the autopsy findings of emboli of various ages in the lungs confirmed the clinical interpretation. The case was of further interest because stagnation of circulation due to confinement to bed was not a factor, while cardiac pathological changes were marked.
CASE 10.

R. H. — White, married, male, aged 60. Hospital number 37526. Entered 1/8/32. Died 1/12/32.

Clinical diagnosis:
Toxic goiter with myocardial failure and auricular fibrillation.

Post-mortem diagnosis:
Colloid adenoma of thyroid.
Cardiac hypertrophy and dilatation.
Infarction of lungs, kidneys, and right popliteal artery.
Mural thrombi of auricles.

Clinical evidence of thrombosis and embolism:
Swollen, painful right leg on which the skin blistered and peeled away.

Post-mortem evidence of thrombosis:
Mural thrombi in auricles.
Thrombus at bifurcation of popliteal artery.
Infarcts in kidneys.

Post-mortem evidence of pulmonary embolism:
Several small thrombi were found in the pulmonary arterial branches, with infarction.

Evidence of circulatory failure:
Clinical — Cardiac failure and auricular fibrillation.
Post-mortem — Cardiac hypertrophy and dilatation.

Comment:
There was evidence of thrombosis in both arterial systems, and there were mural thrombi in both auricles. The mural thrombi may be considered primary, their formation being associated with the cardiac hypertrophy and dilatation; and the other vascular occlusions may be considered as metastatic, or embolic, probably from the auricles.
Pulmonary embolism is considered an unusual occurrence in thyroid disease. This case and the two following cases of thyroid disease, however, showed post-mortem evidence of pulmonary embolism. The associated cardiac pathology present in each case probably best explains the occurrence of pulmonary embolism in the three cases.
CASE II.


Clinical diagnosis:
Syphilis.
Cardiac failure.
Toxic goiter.

Post-mortem diagnosis:
Confluent broncho-pneumonia, left.
Pulmonary infarcts, right.
Acute suppurative nephritis.
Thrombosis of hypogastric vein, right.
Myocardial degeneration.
Hyperplasia of thyroid.

Clinical evidence of thrombosis and embolism:
None.

Post-mortem evidence of thrombosis:
There were no thrombi in the heart.
Thrombosis of the right hypogastric vein.

Post-mortem evidence of pulmonary embolism:
A 4 x 6 cm. infarct was found in the lower lobe of the right lung.

Evidence of circulatory failure:
Clinical -- Dyspnea. Swelling of feet and ankles.
Post-mortem -- Myocardial degeneration.

Comment:
The presence of a thrombus in the right hypogastric vein suggests the pelvic vessels as a source of the pulmonary embolus which caused the infarction.
CASE 12.


Clinical diagnosis:
Hyperthyroidism.
Cardiac failure.

Post-mortem diagnosis:
Adenomata and hyperplasia of thyroid.
Myocardial degeneration.
Edema of lungs.
Chronic passive congestion of liver and spleen.
Thrombosis of pelvic veins.
Pulmonary infarction.

Clinical evidence of thrombosis and embolism:
None.

Post-mortem evidence of thrombosis:
There were no thrombi in the heart.
There were small thrombi in a number of the vessels of the pelvic walls.

Post-mortem evidence of pulmonary embolism:
Infarcts in both lungs.
Thrombi causing the larger infarct were found.

Evidence of circulatory failure:
Clinical -- Dyspnea. Swelling of lower extremities.
Post-mortem -- Chronic myocardial degeneration. Edema of lungs.
Chronic passive congestion of the liver and spleen.

Comment:
Dr. J. P. Tollman: "There are small thrombi in a number of the vessels of the pelvic wall, and we interpret the pulmonary infarcts as coming from this source".
CASE 13.


Clinical diagnosis:
Coronary occlusion.
X-ray -- Moderate cardiac enlargement suggestive of general loss of cardiac tone and myocardial insufficiency.

Post-mortem diagnosis:
Cardiac infarction with mural thrombi in the left ventricle.
Thrombosis of internal iliac veins.
Pulmonary infarction.
Right hydrothorax.
Generalized arteriosclerosis.

Clinical evidence of thrombosis and embolism:
None.

Post-mortem evidence of thrombosis:
Small ante-mortem thrombi in the tip of the right auricle.
Large thrombus in the left ventricle.
Several thrombi in the internal iliac veins.
Smaller vessels of the pelvis were uniformly filled with thrombi.
Coronary thrombosis.

Post-mortem evidence of pulmonary embolism:
Right lung -- The pulmonary artery to the lower lobe was filled with large non-attached emboli. Another thrombus was found in the center of the lobe, with infarction. Large, recent thrombi were found near the hilum.
Left lung -- Infarcts up to 7 cm. in diameter were found.

Evidence of circulatory failure:
Clinical -- Precordial pain. Shortness of breath. Moderate cardiac enlargement.

Comment:
This case is another showing circulatory failure due to cardiac pathology. There are two possible sources of the pulmonary emboli: mural thrombi in the right auricle, and thrombosis in the internal iliac veins.
CASE 14.


Clinical diagnosis:
Decompensated heart.
Myocardial degeneration.
X-ray -- Marked cardiac enlargement suggestive of myocardial insufficiency.

Post-mortem diagnosis:
Cardiac infarction with mural thrombi in the left ventricle.
Thrombosis of iliac veins.
Pulmonary infarction.
Infarct in spleen.
Dependent edema, generalized.

Clinical evidence of thrombosis and embolism:
An entry in the patient's record on 5/3/32 stated that there had been hemoptysis for three days. The patient complained of pain over the liver. On percussion there was dullness over the lower lobe of the right lung.

Post-mortem evidence of thrombosis:
Thrombi were adherent to the anterior wall of the left ventricle and interventricular septum, associated with cardiac infarctions and marked coronary sclerosis and tortuosity.
There was extensive thrombosis of the internal iliac vein on both sides and in the lateral veins about the uterus. (Uterus was negative).

Post-mortem evidence of pulmonary embolism:
Right lung -- A large hemorrhagic infarct was found in the lower lobe. A large mass of ante-mortem thrombus, adherent to the walls, was found occluding the vessels to the region. Several more recent infarcts were present.
Left lung -- Several 1 to 4 cm. infarcts with small thrombi were present.

Evidence of circulatory failure:
Clinical -- Attacks of precordial pain. Dependent edema. Anasarca.
Post-mortem -- Coronary sclerosis with left ventricular infarction.

Comment:
Circulatory failure and consequent venous stasis suggests an explanation for the occurrence of thrombosis of the internal iliac veins. Emboli from this source lodged in the lungs with resultant pulmonary infarction.
CASE 15.

F. P. -- White, married, male, aged 70. Hospital number 39319.
Entered 6/10/32. Died 6/18/32.

Clinical diagnosis:
Old prostatectomy (1930).
Not otherwise diagnosed. Symptoms suggested a terminal uremic state, but N. P. N. was 36.5 mg. %. Blood sugar on admission was 268 mg. %.

Post-mortem diagnosis:
Pyelonephritis, marked.
Arteriosclerosis, generalized.
Cardiac hypertrophy and dilatation.
Chronic myocarditis.
Pulmonary embolism.

Clinical evidence of thrombosis and embolism:
None.

Post-mortem evidence of thrombosis:
None.

Post-mortem evidence of pulmonary embolism:
A rather large ante-mortem thrombus was found in the pulmonary branch to the left lung. The thrombus was not attached, and there was no corresponding area of infarction.

Evidence of circulatory failure:
Post-mortem -- Cardiac hypertrophy and dilatation. Chronic myocarditis.

Comment:
This was a case of pulmonary embolism associated with cardiac failure, without presence of post-mortem evidence of thrombosis elsewhere.
CASE 16.


Clinical diagnosis:
Myocarditis with beginning cardiac decompensation.
Hydronephrosis.

Post-mortem diagnosis:
Nephrectomy, post-operative.
Thrombosis of pulmonary arteries.
Carcinoma of right breast, recurrent, metastatic to lymph node.
Atelectasis of lungs.
Congenital cysts of the liver.

Clinical evidence of thrombosis and embolism:
None.

Post-mortem evidence of thrombosis:
None.

Post-mortem evidence of pulmonary embolism:
Considerable amounts of recent and friable ante-mortem thrombi were found firmly attached to the walls of the pulmonary arterial branches in the lungs. Grayish-red vegetative masses, appearing to be infected, were present in the pulmonary arteries. There was marked atelectasis of both lower lobes.

Evidence of circulatory failure:
Clinical -- Early myocardial failure.
Post-mortem -- Scarring of myocardium.

Comment:
Death occurred two days post-operative. A probable source of the emboli was the infected area. A contributory factor was a failing circulation.
CASE 17.

M. C. -- White, married, male, aged 64. Hospital number 41745. Entered 12/19/32. Died 12/29/32.

Clinical diagnosis:
Cardiac decompensation on a vascular basis.

Post-mortem diagnosis:
Cardiac hypertrophy.
Recent cardiac infarction in the left ventricle.
Broncho-pneumonia.
Cerebral infarction.
Infarcts of kidneys and spleen.
Embolism, left pulmonary artery.

Clinical evidence of thrombosis and embolism:
None.

Post-mortem evidence of thrombosis:
Thrombi in both auricles and left ventricle.

Post-mortem evidence of pulmonary embolism:
Recent embolus in left pulmonary artery.

Evidence of circulatory failure:
Clinical -- Evidence of cardiac decompensation.
Post-mortem -- Cardiac hypertrophy. Recent infarction in the left ventricle associated with coronary sclerosis and thrombosis. Thrombi in both auricles and the left ventricle.

Comment:
There were mural thrombi in both auricles and the left ventricle; these were probably the source of pulmonary emboli and of the emboli causing infarcts of the kidneys and spleen.
CASE 18.

S. S. -- White, single, male, aged 75. Hospital number 41915. Entered 1/2/33. Perineal prostatectomy, 1/19/33 (sacral anesthesia with gas). Drainage of blood-filled cystic cavity beneath posterior sheath of recti muscles, 2/6/33. Died 2/21/33.

Clinical diagnosis:
Prostatic hypertrophy, benign. N.P.N. on admission was 38.7 mg. %.
Hematocoele, postoperative.

Post-mortem diagnosis:
Prostatectomy, postoperative.
Hemorrhage into anterior abdominal wall.
Thrombosis of left femoral vein and veins of the left arm.
Pulmonary infarction.
Infarction of heart muscle, old and recent.

Clinical evidence of thrombosis and embolism:
On 2/12/33 it was noticed that the patient's left leg was swollen to twice normal size.
On 2/15/33 the left arm and leg became swollen and painful.

Post-mortem evidence of thrombosis:
The left femoral vein was occluded by a rather firm blood clot which was beginning to soften in only a few places. Several veins of the left arm were found to be occluded by rather firm thrombi, and some purulent material was found in these vessels.

Post-mortem evidence of pulmonary embolism:
Right lung -- The lower lobe presented a partially broken down infarct along the lower border of the lower lobe, the apparent cause of the pleurisy with effusion found on this side.

Evidence of circulatory failure:
Post-mortem -- Large areas of scarring were found in the left ventricle, the largest measuring 3 x 4 cm., and several more recent infarcts. Marked sclerosis of the coronary arteries.

Comment:
The probable source of the embolus causing the pulmonary infarction was the venous thrombosis of the left femoral vein or the veins of the left arm. Etiological factors were impaired cardiac action and prolonged enforced bed rest. The case may be considered one of postoperative pulmonary embolism.
CASE 19.

J. G. -- White, married, male, aged 51. Hospital number 42294. Entered 1/30/33. Transurethral resection, 2/13/33. Died 2/22/33.

Clinical diagnosis:
Carcinoma of prostate. N.P.N. on admission was 31.5 mg. %.
Metastasis to lungs.
Left sided hemiplegia, old.
Coronary thrombosis.
X-ray -- Aortic valvular lesion with left ventricular and right auricular hypertrophy. Passive congestion of the lung field. Gastro-enterostomy in 1924 for peptic ulcer.

Post-mortem diagnosis:
Benign hypertrophy of prostate.
Necrosis of bladder epithelium.
Pyelonephritis.
Thrombosis of pelvic veins.
Pulmonary infarction.
Cardiac infarction, old and recent.
False porencephaly, right cerebral hemisphere.
Healed duodenal ulcer.
Anterior gastro-enterostomy.

Clinical evidence of thrombosis and embolism:
Attacks of chest pain on 2/16/33 and 2/17/33 were interpreted as coronary thrombosis and not pulmonary embolism.

Post-mortem evidence of thrombosis:
The femoral veins were occluded by a thrombus which extended into the inferior vena cava to the level of the lower border of the kidney. The thrombus was softening and contained puriform material in some places.

Post-mortem evidence of pulmonary embolism:
Left lung -- On opening the main vessels in the left lung a large thrombus was found lodged at the first bifurcation. It was firmly attached and did not completely occlude the lumen.
Right lung -- A 4 X 5 cm. infarct was found near the base of the lower lobe. There were several other scattered areas of infarction, some quite recent. There were several large firmly attached thrombi in the vessels.

Evidence of circulatory failure:
Clinical -- Severe chill on 2/16/33 followed by knife-like pains in region of heart, with irregular pulse, marked dyspnea, and fibrillation at times. Interpreted as coronary thrombosis. There was a similar attack on 2/17/33.
Post-mortem -- Moderate enlargement of heart. The left ventricle showed an area of scarring extending from the apex of the left ventricle to within 1 cm. of the atrioventricular ring. Several small quite recent areas of infarction. Marked sclerosis and calcification of coronary vessels.
Comment:
A probable source of the emboli was found in the thrombus in the inferior vena cava. Cardiac failure and postoperative enforced bed rest were doubtlessly important causative factors.
CASE 20.

P. P. -- White, married, female, aged 47. Hospital number 42725.
Entered 3/5/33. Died 3/19/33.

Clinical diagnosis:
Congestive heart failure.
Auricular fibrillation.

Post-mortem diagnosis:
Mitral stenosis and insufficiency.
Chronic passive congestion of lungs, liver, kidneys, and spleen.
Pulmonary infarction.

Clinical evidence of thrombosis and embolism:
None.

Post-mortem evidence of thrombosis:
A large ante-mortem thrombus was found in the left auricle.

Post-mortem evidence of pulmonary embolism:
In both lungs thrombi were found deep in the pulmonary arteries.
There were infarcts in both upper lobes.

Evidence of circulatory failure:
Clinical -- Complaints of shortness of breath, cough, weakness, and swelling of the feet. The patient had some shortness of breath since the age of 13. On examination a total irregularity of the heart was noted. There was a systolic murmur best heard at the apex and a soft diastolic murmur best heard at Erb's point.
Post-mortem -- The mitral orifice measured about 1 cm. in diameter with fusion of the cusps. The right ventricle measured 8 to 9 mm. in thickness. The heart weighed 360 grams.

Comment:
A possible source of the pulmonary emboli was not found. This is another case of pulmonary embolism associated with heart failure.
CASE 21.


Clinical diagnosis:
Hypertension.
Auricular fibrillation and decompensation.

Post-mortem diagnosis:
Cardiac hypertrophy and dilatation.
Cardiac infarction.
Myocardial fibrosis.
Infarction of lung.
Chronic passive congestion of kidneys and liver.

Clinical evidence of thrombosis and embolism:
None.

Post-mortem evidence of thrombosis:
A mass of ante-mortem thrombus one centimeter in diameter was found in the tip of the left ventricle over an area of infarction.

Post-mortem evidence of pulmonary embolism:
A 7 X 10 cm. infarct was found in the left lower lobe. It was broken down and jelly-like in consistency. On opening the pulmonary artery the thrombus causing the infarct was found. There were several small infarcts in the right lung.

Evidence of circulatory failure:
Clinical -- Two months prior to entrance the patient began to have attacks of tachycardia with dyspnea and orthopnea and swelling of her feet and ankles. Exacerbation two weeks before entrance with severe pain across the upper abdomen which "seemed as if it prevented her from breathing". On physical examination the heart was found to be considerably enlarged, breathing was difficult, and there were rales in both bases. The heart was fibrillating, and the blood pressure was 198/122.
Post-mortem -- The heart was considerably enlarged and weighed 500 grams. The tricuspid ring easily admitted five fingers, indicating considerable dilatation. There were several small infarcts in the walls of the right and left ventricles and in the septum. The coronary vessels on gross examination showed little change, but microscopically the blood vessels were found to be of small caliber and to show considerable intimal proliferation. Corresponding intimal proliferation was found in the blood vessels of the kidney.

Comment:
A possible source of the embolus was not found. This is another case of pulmonary embolism associated with cardiac failure.
CASE 22.

N. C. -- White, married, female, aged 59. Hospital number 44820. Entered 8/23/33. Pan-hysterectomy (spinal, novocaine anesthesia) on 9/6/33. On 9/15/33 the upper one-third of the wound, which had broken down, was sutured after an extruded loop of bowel was replaced. Died 9/17/33.

Clinical diagnosis:
Adeno-carcinoma of uterus.

Post-mortem diagnosis:
Adeno-carcinoma of the uterus.
Paralytic ileus.
Pelvic thrombosis.
Infarction of lung.
Duodenal ulcer, healed.

Clinical evidence of thrombosis and embolism:
None.

Post-mortem evidence of thrombosis:
There were many thrombi in the veins of the pelvis. A thrombus in the left internal iliac vein extended into the inferior vena cava almost to the renal vein.

Post-mortem evidence of pulmonary embolism:
The main branches of the pulmonary artery contained a number of small masses of ante-mortem thrombi. Small masses were lodged deeper in the lung tissue causing infarction which had gone on to early gangrene.

Evidence of circulatory failure:
Clinical -- Swelling of ankles with some dyspnea on exertion. Blood pressure was 220/120.
Post-mortem -- The heart weighed 440 grams. The left ventricle measured 25 to 28 mm. in thickness.

Comment:
This case presents evidence of early circulatory failure. This factor with the additional factor of prolonged bed rest in an extremely ill patient probably accounts for the pelvic thrombosis with metastases to the lungs.
CASE 23.


Clinical diagnosis:
Bacterial endocarditis.

Post-mortem diagnosis:
Subacute bacterial endocarditis.
Infarct of lung.
Infarcts of spleen.
Embolic nephritis.
Broncho-pneumonia.

Clinical evidence of thrombosis and embolism:
There were several attacks of acute abdominal pain attributed to various causes until it was found that the patient had a splenomegaly and that her heart was bad.

Post-mortem evidence of thrombosis:
Numerous old and recent infarcts of the spleen. There were thrombi in several of the coronary arteries, although these did not completely occlude the vessels. The left auricle showed a mass of warty vegetations on the wall immediately above the mitral ring. Warty masses of soft reddish material were found attached to both mitral cusps. There was a 1 cm. infarct in the wall of the left ventricle. The right side of the heart was entirely normal in appearance.

Post-mortem evidence of pulmonary embolism:
A huge long infarct was present in the periphery of the right lung. No large masses of thrombus were found in the pulmonary artery.

Evidence of circulatory failure:
Clinical — On admission to the hospital there was a palpable thrill over the cardiac area. The heart sounds were regular with only an occasional extrasystole. There was a very rough murmur replacing the first sound at the apex. A gallop rhythm was noted at the base. Blood pressure was 90/54. The fingers were cyanotic.
X-ray — Cardiac enlargement apparently involving the right heart, and slight passive congestion of the lungs.
Post-mortem — There was some degree of passive congestion of the lungs. There was partial occlusion of several of the coronary branches due to thrombi. There was a 1 cm. infarct in the left ventricular wall. Vegetations of subacute bacterial endocarditis were found on the mitral cusps, and on the endocardium of the left auricle and ventricle. There was extensive fibrosis through the cardiac musculature.

Comment:
A case of subacute bacterial endocarditis showed at autopsy evidence of infarction in systemic and pulmonary arterial systems. The former can readily be regarded as embolic from the lesions in
the left heart. The latter are more difficult to interpret, but were probably metastatic from venous thrombi which developed after the onset of cardiac failure.
CASE 24.

J. K. -- White, married, male, aged 52. Hospital number 48252. Entered 9/25/34. Died 10/17/34.

Clinical diagnosis:
  Diabetes mellitus. Blood sugar on entrance was 216 mg. %. N.P.N. on entrance was 58 mg. %.

Post-mortem diagnosis:
  Cardiac hypertrophy.
  Infarct of heart muscle.
  Coronary thrombosis.
  Uremic pericarditis.
  Subacute glomerular nephritis.
  Hydrothorax.
  Pulmonary edema.

Clinical evidence of thrombosis and embolism:
  None.

Post-mortem evidence of thrombosis:
  Several masses of ante-mortem thrombus were attached to the wall of the left auricular appendage. There was a 9 x 6½ cm. infarct at the left apex with an attached liquified mural thrombus.

Post-mortem evidence of pulmonary embolism:
  There was a small infarct in the right lower lobe.

Evidence of circulatory failure:
  Clinical -- There was a marked diastolic murmur best heard at the apex. Swelling of ankles and scrotum which, however, was not attributed to cardiac pathology. No pain in the chest.
  Post-mortem -- The heart weighed 430 grams. There was a large left ventricular infarct, with a corresponding coronary thrombosis. There was marked sclerosis of the coronary arteries. Uremic pericarditis. Ascites. Anasarca.

Comment:
  Only a small infarct in the right lower lobe was found as evidence of pulmonary embolism. The mural thrombi, which were all found in the left heart, would not account for the infarction. Formation of a thrombus in the venous circulation, with embolism to the lung, may be postulated on the basis of cardiac failure.
CASE 25.


Clinical diagnosis:
Myocardial decompensation secondary to coronary endarteritis with thrombosis.

Post-mortem diagnosis:
Cardiac infarct, left ventricle.
Cardiac hypertrophy and dilatation.
Broncho-pneumonia, right lower lobe.
Chronic passive congestion of lungs and liver.
Small infarcts of lungs.
Small infarcts of left kidney.

Clinical evidence of thrombosis and embolism:
None, excepting coronary thrombosis.

Post-mortem evidence of thrombosis:
Cardiac infarct in left ventricle associated with a large mural thrombus.

Post-mortem evidence of pulmonary embolism:
A small mass of ante-mortem thrombus was found in a small branch of the pulmonary artery in the middle lobe of the right lung. Small masses of ante-mortem thrombus were found in association with infarction in the lower lobe of the left lung.

Evidence of circulatory failure:
Clinical -- Patient was well until 18 months before entrance to the hospital. He had had several attacks characteristic of coronary artery occlusion. Complained of shortness of breath and weakness on exertion. There was coughing and spitting of bloody sputum with the first attack. On entrance there was a marked orthopnea. The heart showed extra systoles; rate was 120; blood pressure was 102/70. The heart was moderately enlarged.
X-ray -- Passive congestion of lung fields. Cardiac enlargement with preponderance of the right heart.
Post-mortem -- The heart weighed 520 grams. The coronary arteries showed severe atheromatous change, with complete occlusion by atheromatous plaques of the right and left coronary arteries. There was a 9 X 9 cm. infarct in the posterior wall of the left ventricle, with marked thinning of the wall. There was a large recent infarct on the anterior wall, with an attached large mural thrombus.

Comment:
This case showed a congestive heart failure due to coronary artery occlusion. A probable source of the pulmonary emboli was not found at autopsy.
CASE 26.


Clinical diagnosis:
Renal insufficiency with right hydronephrosis.
Cardiac insufficiency with hypertension.
Multiple thromboses with infarctions of lung, spleen, and left lower leg.

Post-mortem diagnosis:
Old pyonephrosis, right kidney.
Arteriolar sclerosis, left kidney.
Cardiac hypertrophy and dilatation.
Mural thrombi in right auricle, right ventricle, and left ventricle.
Pulmonary embolism with infarction.
Embolus in aorta.
Infarcts of spleen and kidney.
Healed duodenal ulcer.
Cholesterol of gall bladder.

Clinical evidence of thrombosis and embolism:
Four days after entrance the patient complained of moderate pain and distress in the chest. She began the next day to cough up some blood-streaked sputum, particularly in the evenings. Rales were heard in both bases. Thirteen days after entrance the patient began to complain of swelling and pain in her legs. On examination the legs were found to be cold and numb, cyanotic, and swollen. The symptoms gradually progressed to the time of her death.

Post-mortem evidence of thrombosis:
There were mural thrombi in the right auricle and in both ventricles. There were numerous small thrombi in the small veins of the pelvis. The aorta was obstructed by an ante-mortem thrombus beginning about 2 cm. below the renal artery.

Post-mortem evidence of pulmonary embolism:
There was almost complete consolidation of the lower lobe of the right lung, and the corresponding artery to the right lower lobe contained a large mass of ante-mortem thrombus. Small ante-mortem thrombi were present in the small branches in the left lung.

Evidence of circulatory failure:
Clinical -- Six months ago, after the birth of her last child, the patient had "high blood pressure, fast pulse, and was blown up like a barrel". Orthopnea for past six months. On physical examination there was quite marked cardiac enlargement to the left demonstrable. There was a gallop rhythm. Heart rate was 96; blood pressure was 200/150. There was only slight edema of the ankles.
X-ray -- Gross cardiac enlargement involving primarily the left ventricle. Evidence of ascites.
Post-mortem -- The heart weighed 500 grams and measured 15 x 11 cm. There were mural thrombi in the right auricle and right and left ventricles. The mitral ring admitted three fingers easily. The muscle of the left ventricle was soft and measured up to 25 mm. in thickness.

Comment:
Thrombi were found in the pelvic veins and in the right auricle. Either may have been the source of the pulmonary emboli. A recent thrombus was also found in the aorta, and smaller thrombi had probably previously lodged in the arteries supplying the legs, to account for the clinical symptoms of arterial occlusion; there were also infarcts of the spleen and kidney. Thrombi were found in the left auricle and ventricle, and it was probably from one or both of these sites that the systemic emboli originated.
CASE 27.

L. K. -- White, male, aged 2½. Hospital number 37979. Entered 2/20/32. Died 2/21/32.

Clinical diagnosis:
Osteomyelitis of right femur.

Post-mortem diagnosis:
Osteomyelitis of right femur.
Infarcts of lung.
Abscesses of lung, heart, and kidney.
Broncho-pneumonia.

Clinical evidence of thrombosis and embolism:
None, excepting the osteomyelitis, which might give rise to a localized thrombo-phlebitis.

Post-mortem evidence of thrombosis:
None.

Post-mortem evidence of pulmonary embolism:
Infarcts in lungs, some of which were purulent, and measured ½ to 3 cm. in diameter.

Evidence of circulatory failure:
None.

Comment:
Following the onset of osteomyelitis, infected emboli probably from the site of infection, reached the lungs to set up metastatic infarcts and abscesses.
CASE 28.


Clinical diagnosis:
Carbuncle of the neck.
Septicemia. Blood culture positive after twenty-four hours for Staphylococcus aureus.
Broncho-pneumonia.

Post-mortem diagnosis:
Carbuncle of the neck.
Multiple lung abscesses.
Infarcts of lung.
Broncho-pneumonia.
Infected thrombi of jugular vein.

Clinical evidence of thrombosis and embolism:
Marked edema was noted over left side of neck and scalp with numerous small areas where the scalp had broken down.

Post-mortem evidence of thrombosis:
The left jugular vein shows a few bits of very soft gray thrombi.

Post-mortem evidence of pulmonary embolism:
Small thrombi in the pulmonary arterial branches.
Small infarcts and abscesses of the lungs.

Evidence of circulatory failure:
None.

Comment:
Infected thrombi in the left jugular vein gave rise to emboli which lodged in the pulmonary arterial branches causing infarction and abscess formation.
CASE 29.


Clinical diagnosis:
Infected upper lip with cellulitis of face and neck.
Septicemia. Blood culture was positive for Staphylococcus aureus.

Post-mortem diagnosis:
Abscess of upper lip with extension to face.
Infected thrombosis of right jugular vein.
Pulmonary infarction.

Clinical evidence of thrombosis and embolism:
None described in record.

Post-mortem evidence of thrombosis:
Infected ante-mortem thrombi were found in the veins of the face and in the right jugular vein.

Post-mortem evidence of pulmonary embolism:
Both lungs showed infarcts ranging from $\frac{1}{2}$ to 5 cm. in diameter. At least some of the infarcts had undergone abscess formation. Small ante-mortem thrombi were found in the corresponding arterial branches.

Evidence of circulatory failure:
None.

Comment:
Dr. J. P. Tollman: "The immediate cause of this woman's death is the abscess of the upper lip extending through the veins of the face. One of these veins stood out prominently and ante-mortem thrombi were removed from the right jugular vein." The infected thrombi in the facial and right jugular veins were the probable sources of the metastatic pulmonary thrombosis which gave rise to pulmonary infarction and abscess formation.
CASE 30.


Clinical diagnosis:
Diabetes mellitus. Diabetic coma. Blood sugar was 186 mg. %.
NPN was 60 mg. %.
Pregnancy, six months.
Pyelonephritis.
Inevitable abortion, 9/29/32, with delivery of a dead macerated fetus.
Broncho-pneumonia.
Parametritis.

Post-mortem diagnosis:
Atrophy of pancreas.
Broncho-pneumonia.
Acute vegetative endocarditis.
Abscesses of lung, kidney, and broad ligament.
Infarct of lung, left.
Hemorrhage and thrombosis of uterine wall.
Pelvic thrombosis.

Clinical evidence of thrombosis and embolism:
None.

Post-mortem evidence of thrombosis:
There was a small vegetation about 3 mm. in diameter on the anterior cusp of the mitral valve, with no associated destruction of the valve cusp.
The uterus was enlarged, discolored, and filled with clotted blood. There was thrombosis extending into the vessels of the wall. Several thrombosed veins were encountered in the broad ligament, and in one of these purulent material was found.

Post-mortem evidence of pulmonary embolism:
There was a 3 x 4 cm. infarct in the left lower lobe; it was semi-fluid in consistency due to infection.

Evidence of circulatory failure:
Post-mortem -- There was a mitral vegetative lesion, but no myocardial change was found. The heart was normal in size.

Comment:
The mitral vegetative lesion was a possible source of the abscesses in the kidney. The infected pelvic thromboses were the probable source of the infected infarct in the left lung and also of the lung abscesses.
CASE 31.


Clinical diagnosis:
- Pansinusitis.
- Otitis media.
- Chronic glomerulo-nephritis.
- Terminal uremia.

Post-mortem diagnosis:
- Left mastoiditis.
- Abscesses of lung, liver, kidney, and heart.
- Broncho-pneumonia.
- Acute glomerulo-nephritis.

Clinical evidence of thrombosis and embolism:
- None.

Post-mortem evidence of thrombosis:
In the left lateral sinus no large thrombus was present, but immediately adjacent to the mastoid a small mass of granular material was found firmly attached to the lateral wall of the sinus. Some of this material was rather friable and broke off easily.

Post-mortem evidence of pulmonary embolism:
Left lung -- A mass of ante-mortem thrombus about 3.5 cm. in length and 6 mm. in diameter was found in the main branches of the pulmonary artery. Similar very small masses were found deep within the lung tissue and in association with these were sharply delimited wedge-shaped areas in which the lung was solid and very dark in color. There were several associated abscesses.
Right lung -- A few ante-mortem thrombi were found in the smaller pulmonary branches with corresponding areas of infarction and abscess formation.

Evidence of circulatory failure:
- None.

Comment:
In this case a left lateral sinus thrombus had undoubtedly been present, and was the probable source of the pulmonary emboli, which, because they arose from a septic source, gave rise to infarctions which showed abscess formation. The small abscesses in the other organs in the systemic circulation were probably on the basis of a bacteremia from the same source.
CASE 32.


Clinical diagnosis:
Furuncle, forehead.
Erysipelas.

Post-mortem diagnosis:
Furuncle, forehead.
Cavernous sinus thrombosis. Blood plates from cultures taken at autopsy were positive for Staphylococcus aureus.
Meningitis.
Abscesses and infarcts of lungs.
Broncho-pneumonia.

Clinical evidence of thrombosis and embolism:
None.

Post-mortem evidence of thrombosis:
Purulent material and ante-mortem thrombi were found in the left cavernous sinus with extension to the circular sinuses and slight involvement of the cavernous sinus on the right.

Post-mortem evidence of pulmonary embolism:
There were several small recent infarcts in both lungs, some of which had broken down to form abscesses.

Evidence of circulatory failure:
None.

Comment:
The infarcts of the lung were infected and showed abscess formation. The origin of the emboli causing the infarction may be postulated as the cavernous sinus where a purulent thrombotic process was found.
CASE 33.

D. C. — White, female, aged 8. Hospital number 48341.
Entered 10/5/34. Right radical mastoidectomy (gas-ether anesthesia) on 10/6/34. Died 10/6/34.

Clinical diagnosis:
Bilateral chronic otitis media.
Acute mastoiditis, right.
Lateral sinus abscess, right.

Post-mortem diagnosis:
Radical mastoidectomy cavity, right.
Lateral sinus thrombosis, right.
Inflammation of the dura mater.
Multiple small infarct of lungs.
Broncho-pneumonia.
Cloudy swelling of liver and kidneys.
Infectious hyperplasia of spleen.

Clinical evidence of thrombosis and embolism:
Symptoms suggested a right lateral sinus thrombosis complicating the right mastoiditis. Tobey-Ayer test was positive. At operation a small sinus was found in the right cavernous sinus through which foul smelling pus escaped.

Post-mortem evidence of thrombosis:
No definite thrombus was found in either lateral sinus at autopsy, but some granulations were noted in the angle of the right lateral sinus. The jugular bulb on the right was filled with fairly firm ante-mortem thrombus.

Post-mortem evidence of pulmonary embolism:
The pleural surfaces of the lungs were spotted with many brown areas, triangular in shape, extending into the lung substance, and measuring up to 1 mm. in diameter. On microscopic examination the small infarcts showed considerable inflammatory reaction.

Evidence of circulatory failure:
None.

Comment:
A chronic mastoiditis resulted in eventual perforation of the right lateral sinus with extension of the suppurative process into the sinus. Small infected emboli, breaking loose, gave rise to multiple pulmonary infarctions which would have formed frank abscesses if the patient had lived longer.
CASE 34.

C. A. -- White, married, male, aged 52. Hospital number 40662. Entered 10/8/32. Died 11/1/32.

Clinical diagnosis:
Duodenal-colic fistula (X-ray).
Secondary anemia.

Post-mortem diagnosis:
Carcinoma of colon involving liver and duodenum.
Thrombosis of left external iliac vein.
Pulmonary embolism.
Pulmonary infarction.
Pulmonary edema.
Broncho-pneumonia.

Clinical evidence of thrombosis and embolism:
Twelve days after admission the patient developed a sudden severe pain over the liver area, and found it hard to get his breath.

Post-mortem evidence of thrombosis:
Several ante-mortem thrombi were found in the left external iliac vein.

Post-mortem evidence of pulmonary embolism:
Right lung -- A number of thrombi were firmly attached to the walls of the pulmonary arteries, most noticeable in the lower lobe. The deeper thrombi appeared older, so that the picture was that of a retrograde thrombosis.
Left lung -- A few small thrombi were found.

Evidence of circulatory failure:
None.

Comment:
There was no very definite clinical evidence of circulatory failure in this case to suggest an explanation of the thrombosis of the left external iliac vein. The heart was negative on pathological examination. Prolonged bed rest in a debilitated individual suggests an explanation of the formation of the thrombi, with embolism and infarction of the lungs.
CASE 35.

H. S. -- White, married, male, aged 65. Hospital number 41114.
Entered 10/29/32. Died 11/22/32.

Clinical diagnosis:
Cortical atrophy, etiology not determined (encephalogram).

Post-mortem diagnosis:
Diffuse cortical atrophy.
Thrombosis of pelvic veins.
Pulmonary infarction.
Broncho-pneumonia.
Passive congestion of spleen.

Clinical evidence of thrombosis and embolism:
None.

Post-mortem evidence of thrombosis:
A number of ante-mortem thrombi were found in the veins of the pelvic wall.

Post-mortem evidence of pulmonary embolism:
Small thrombi were found in the left lung with infarcts 1 to 4 cm. in diameter.
Large emboli, occluding practically all the principle vessels, with infarction were found in the right lung.

Evidence of circulatory failure:
Post-mortem -- Passive congestion of spleen.

Comment:
Nothing very definite was found to account for the occurrence of the pelvic thrombi which were the probable source of the pulmonary emboli.
CASE 36.


Clinical diagnosis:
Bilateral senile cataracts.
Right indirect inguinal hernia.

Post-mortem diagnosis:
Thrombosis of pelvic veins.
Pulmonary embolism with infarction.
Gangrene of lung, left lower lobe.
Arteriosclerosis, generalized.

Clinical evidence of thrombosis and embolism:
Four days after operation the patient developed a sudden severe pain in the left upper abdomen and chest with dyspnea and pain on respiration. The abdomen was distended and rigid on the left side. There was some limitation of motion on the left side, especially at the base. An enema gave considerable relief. Adhesive strapping of left chest also afforded some relief.

Post-mortem evidence of thrombosis:
Several ante-mortem thrombi in several of the deeper branches of the pelvic veins, particularly those to the muscles of the gluteal region.

Post-mortem evidence of pulmonary embolism:
Left lung -- Numerous small infarcts in upper lobe. Gangrene of whole lower lobe with liquefaction and formation of a large ragged cavity. A large gray ante-mortem thrombus occluded all of the vessels to the lower lobe.
Right lung -- No thrombi were found in any of the pulmonary arteries.

Evidence of circulatory failure:
None.

Comment:
Dr. J. P. Tollman: "This is interpreted as being a pelvic thrombosis. Some of these thrombi became loosened and caused infarction of the left lower lobe of the lung. It subsequently became gangrenous. The sudden death is interpreted as a massive hemorrhage into this gangrenous lung and pleura on the left side. The recent eye operation shows evidence of normal healing and is only indirectly the cause of death in that it was necessary to keep him in bed for several days allowing the pelvic thrombosis to occur."
The time of occurrence of the embolism was very definitely set by the clinical record as four days postoperative.
CASE 37.


Clinical diagnosis:
- Acute cholecystitis.
- Possible empyema of the gall bladder.

Post-mortem diagnosis:
- Acute pancreatitis with retroperitoneal hemorrhage.
- Fat necrosis of mesentery.
- Broncho-pneumonia.
- Infarction of lung.

Clinical evidence of thrombosis and embolism:
None.

Post-mortem evidence of thrombosis:
None.

Post-mortem evidence of pulmonary embolism:
Several ante-mortem thrombi were found lodged in the various branches of the pulmonary artery, and in several places large dark, rather soft, infarcts were found to correspond with these emboli.

Evidence of circulatory failure:
None.

Comment:
This case presents the finding of pulmonary embolism and infarction with no demonstrable primary thrombus. The marked prostration and consequent certain amount of venous stasis which was probably present may have resulted in the formation of thrombi which either were overlooked at autopsy due to inaccessibility or were completely dislodged before death. The importance of the acute pancreatitis as a direct factor in formation of thrombi it would be difficult to estimate.
CASE 38.


Clinical diagnosis:
No definite clinical diagnosis was made. Stools were negative for protozoa and parasites on numerous occasions.
X-ray — Sinus tracts were found in the hepatic flexure region and descending colon, extending off from the colon.

Post-mortem diagnosis:
Amebic colitis with perforation.
Peritonitis.
Pulmonary thrombosis.
Lobar pneumonia.
Broncho-pneumonia.
Thrombosis of the left iliac vein.

Clinical evidence of thrombosis and embolism:
None.

Post-mortem evidence of thrombosis:
Thrombosis of left iliac vein.

Post-mortem evidence of pulmonary embolism:
Left lung — The pulmonary artery showed a thrombus rather firmly attached to the wall and extending into numerous branches, but apparently without complete occlusion of any except the smaller divisions.
Right lung — A similar thrombus was found in the pulmonary vessels.

Evidence of circulatory failure:
None.

Comment:
This patient was in the hospital for one month. During this time he was very weak and unresponsive, lying very quietly in bed. It would appear, therefore, that stasis was a most important factor which might account for formation of a venous thrombosis with embolic passage to the lungs.
CASE 39.

A. M. -- White, married, female, aged 73. Hospital number 48477. Entered 10/23/34. Died 10/29/34.

Clinical diagnosis:
   Malignancy of cecum with degeneration and abscess formation.

Post-mortem diagnosis:
   Adenocarcinoma of body of uterus.
   Metastases to wall of abdomen and to periaortic lymph nodes.
   Abscess of wall of pelvis, right.
   Small emboli in pulmonary arteries (no infarcts).

Clinical evidence of thrombosis and embolism:
   None.

Post-mortem evidence of thrombosis:
   Many small veins around the bladder and the uterus contained ante-mortem thrombi.

Post-mortem evidence of pulmonary embolism:
   At the second bifurcation of the pulmonary artery to the right lung there was an ante-mortem thrombus attached to the wall with no accompanying infarction. There were smaller thrombi in the pulmonary branches to both lungs.

Evidence of circulatory failure:
   None.

Comment:
   Thrombi were found in the veins of the pelvis, and were the probable source of the ante-mortem blood clots found in the pulmonary artery. Venous stasis in a prostrate patient is suggested as an important etiological factor.
NOTES ON THERAPEUTICS

It is not the object of the writer to include in the present discussion of the problem of pulmonary embolism a detailed consideration of treatment of the condition, yet a few remarks upon therapeutics are perhaps timely in relation to what has gone before. A defective circulatory mechanism has been emphasized as the one well recognized factor in the formation of venous thromboses. It has been pointed out that the present day conception of the matter has advanced little since the time of Virchow who first proposed the theory of circulatory stasis in addition to blood changes as the predisposing factors essential to formation of intra-vitam blood clots. Therapeutics has therefore found its most practical application in the attempt to maintain adequate circulatory tone in those cases wherein it is thought possible or probable that venous thrombosis and pulmonary embolism may occur.

David (Walters, 70) has emphasized these considerations, and says:

"Until more definite facts are known concerning the mechanics and chemistry of blood coagulation, our efforts must be aimed at removal of factors which predispose to thrombosis." A perusal of the literature reveals in general two methods of approach in prophylaxis of thrombosis and pulmonary embolism:

The first, and older method deals chiefly with the individual patient. The clinician attempts to recognize early signs of thrombosis, and watches for evidence of small pulmonary embolic accidents which may be premonitory of larger emboli to follow. Having previously carried out the well known general methods for prevention of thrombosis and embolism (frequent change in position of the bed-ridden patient, preservation of free mobility of the
chest, encouragement of early systematic exercise after operation, avoidance of tight bandages, daily elevation of the foot of the bed as a mechanical method of increasing the venous flow from the dependent pelvic region, and so forth), an exactly reverse procedure is now instituted, and the guiding principle of management is rest not only to the part where the trouble is manifest but to the entire body. (Homans, 35; Hunt, 37; Rabinowitz and Holtzman, 57; Vistor, 68; Walters, 70).

The second method of prophylaxis of thrombosis and pulmonary embolism is more or less experimental, and deals with groups of patients. It is an attempt in application of some of the experimental knowledge of blood changes in thrombosis unearthed in recent years; and is furthermore an attempt to apply this knowledge to groups of patients, since pulmonary embolism is so very often unpredictable in individual patients. Perhaps the most notable attempt is that of Walters (70), who, by the routine administration of thyroid extract to postoperative patients, has apparently been able to reduce to a minimum the postoperative incidence of fatal pulmonary embolism at the Mayo Clinic. Mills (49, 50, 51), and Bancroft, Kugelmass, and Stanley-Brown (3, 4, 5) have found that by varying the protein content of the diet the coagulability of the blood can be controlled at will, and the latter have employed this knowledge in management of clinical cases.

A paper on the subject of pulmonary embolism would hardly be complete without mention of the Trendelenberg operation. A few brilliant successes have been achieved by this method of management of cases of massive pulmonary embolism (Kirschner, Meyer, Gintz, Crafoord, and Nystrom). The operation is possible because in many cases occlusion of the arterial lumen by an embolus may be so far from complete that the circulation is
carried on for some time, although under a mechanical disadvantage that ultimately leads to death.

Hunt (37) says that since it has been shown to be possible to rescue a patient from the extremity of an otherwise fatal pulmonary embolism, an obligation is laid upon every hospital to have suitable instruments available and a member of the staff specially qualified. When a case is in imminent danger of a massive embolism a suitable operating room, instruments, patient, surgeon should be in such close relationship that the operation can be begun almost instantly. Of the University Hospital cases of massive pulmonary embolism, at least two (cases 1 and 5) would have been excellent candidates for the Trendelenberg operation, had the necessary facilities been available.

Hunt concludes: "The difficulties in the way of such a coordination and the possibilities of an error in diagnosis are obvious. A successful operation is likely to remain the rare achievement of a watchful, fearless, and capable surgeon. As Nystrom well says, 'It is upon prevention that we have to place our hope of being able to defeat at some future time one of the most distressing complications with which, after the victories won by the introduction of antiseptics, surgery has still to wrestle.'"
SUMMARY

1. Thirty-nine necropsy cases of pulmonary embolism were seen in the University Hospital in a three year period (1932 to 1935) in which 309 autopsies were performed.

2. The percentage incidence was 12.6 for total cases of pulmonary embolism, 10.4 for cases of "bland" pulmonary embolism, and 2.6 for cases of massive (fatal) pulmonary embolism.

3. Twenty-one of the thirty-nine cases showed definite cardiac pathology. Relatively few of the cases of massive pulmonary embolism and of post partum and postoperative pulmonary embolism showed cardiac pathology; and a relatively large proportion of the medical cases showed cardiac pathology.

4. Although the series of University Hospital cases studied was small, the findings were comparable to those of other hospitals and clinics.

5. The general problem of pulmonary embolism is discussed with special reference to the cases seen at the University Hospital.

6. Attempt was not made to discuss treatment of pulmonary embolism in detail. However, it is emphasized that prophylactic measures will be the chief means of approaching the problem. Several of the University Hospital cases of massive pulmonary embolism would have been excellent candidates for the Trendelenberg operation.

7. Attempt will be made in the Department of Pathology at the University Hospital to carry out a study of the relation of infection to the occurrence of thrombosis and pulmonary embolism of the so-called "bland" type.
BIBLIOGRAPHY

1. Allen, E. V.  
   1927 -- Changes in the Blood Following Operation.  

   1932 -- The Inception of Blood Clotting.  

3. Bancroft, F. W.  
   1931 -- Thrombosis and Embolism.  

4. Bancroft, F. W., Kugelmass, I. N., and Stanley-Brown, M.  

5. Bancroft, F. W. and Stanley-Brown, M.  
   1932 -- Postoperative Thrombosis, Thrombophlebitis, and Embolism.  
   Surg., Gyn., and Obst. 54: 898-906.

6. Banet, W. D.  
   1924 -- Thrombosis and Embolism.  

7. Bankoff, G.  
   1934 -- Thrombosis, Embolism, and Their Treatment.  

8. Barker, H. W.  
   1935 -- Axillary Thrombophlebitis Caused by Strain or Effort.  

   1933 -- Fatal Postoperative Pulmonary Embolism.  
   Minn. Med. 16: 409-416.

10. Beattie, J.  
    1932 -- Pulmonary Embolism in Relation to Pregnancy.  

11. Belt, T. H.  
    1934 -- Pulmonary Embolism.  

12. Belt, T. H.  
    1934 -- Thrombosis and Pulmonary Embolism.  
    Am. J. Path. 10: 129-144.
13. Bernheim, B. W.

14. Brock, R. C.
1933 -- Postoperative Venous Thrombosis and the Platelet Count.
Lancet 1: 688-690.

15. Brown, G. E.
1927 -- Postoperative Phlebitis.

16. Bunn, W. H.
1934 -- Vagaries of Venous Thrombosis.
Ohio State Med. J. 30: 159-162.

17. Cabot, R. C.
1933 -- Three Cases of Postoperative Fatality.

18. Churchill, E. D.
1934 -- The Mechanism of Death in Massive Pulmonary Embolism.

19. Conner, L. A.
1914 -- A Pulmonary Attack Simulating Primary Lobar Pneumonia, Caused by Pulmonary Embolism and Infarction from a Latent Venous Thrombosis.

20. Drinker, K. R. and Drinker, C. K.
1915 -- Factors Affecting the Coagulation Time of Blood. VI. The Effect of Rapid Progressive Hemorrhage upon the Factors of Coagulation.
Am. J. Physiol. 36: 305-324.

21. Earlam, F. and Evans, W. H.
1928 -- The Relation of the Blood Platelets to Thrombosis after Operation and Parturition.
J. Path. and Bact. 31: 833-873.

22. Evans, J. A. and Paxon, J.
1932 -- Embolism During Convalescence from Thyroidectomy for Toxic Goiter Complicated by Auricular Fibrillation.

23. Farr, C. E. and Spiegel, R.
1929 -- Pulmonary Infarction and Embolism.

1934 -- The Blood Platelet Count in Postoperative Thrombosis.

25. Gram, H. C.
1920 -- On the Platelet Count and Bleeding Time in Diseases of the Blood.


39. Karsner, H. T. and Ash, J. E.

40. Kilbourne, N. J.
1929 -- Treatment of Varicose Veins of the Legs.

41. Kuhn, J. K.
1929 -- Causes of Increased Incidence of Thrombosis and Embolism from 1924 to 1927.

42. Lee, R. I., Minot, G. R., and Vincent, B.
1916 -- Splenectomy in Pernicious Anemia.

43. Lowenstein, P. S.
1924 -- Thrombosis of the Axillary Vein.

44. Mackay, W.
1931 -- The Blood Platelet: Its Clinical Significance.

45. McCartney, J. S., Jr.
1927 -- Pulmonary Embolism.
Arch. Path. 3: 921-937.

46. Means, J. H. and Mallory, T. B.
1931 -- Total Occlusion of the Right Branch of the Pulmonary Artery by an Organized Thrombus.

47. Meyer, A. W.
1930 -- The Operative Treatment of Embolism of the Lungs.
Surg., Gyn., and Obst. 50: 891-898.

48. Miller, R. H. and Rogers, H.
1929 -- Postoperative Embolism and Phlebitis.

49. Mills, C. A.
1923 -- Effect of Food Ingestion on the Clotting Time of the Blood.

50. Mills, C. A.
1930 -- Relation of Protein Diet to Thrombosis.

51. Mills, C. A. and Necheles, H.
1927 -- Specific Dynamic Action of Food and Blood Coagulability.
PROBLEM OF PULMONARY EMBOLISM

52. Nystrom, G.
1930 — Experiences with the Trendelenberg Operation for Pulmonary Embolism.

53. Patey, D. H.
1931 — Injection Treatment of Varicose Veins and Its Bearing on the Problem of Thrombosis.

54. Pickering, J. W.
1928 — The Blood Plasma in Health and Disease.
Pages 162-177.

55. Pickering, J. W. and Mathur, S. N.
1932 — The Role of Tissue Juices in Thrombosis.

56. Pigford, R. C.
1933 — The Problem of Thrombosis.

57. Rabinowitz, M. A. and Holtzman, I. H.
1934 — The Early Recognition of Peripheral Venous Thrombosis.
N. Y. State J. M. 34: 973-977.

58. Reimann, H. A.
1924 — The Blood Platelets in Pneumococcus Infections.

59. Rieckhoff, G. G. and Turcotte, V. J.
1933 — Embolism of the Pulmonary Artery.

60. Rosenow, E. C.
1927 — A Bacteriologic Study of Pulmonary Embolism.

61. Rosenthal, S. R.
1930 — Thrombosis and Embolism. An Analysis of 1000 Autopsies.

62. Rosenthal, S. R.
1932 — Thrombosis and Fatal Pulmonary Embolism.

63. Rumold, M. J.
1935 — Experimental Pulmonary Embolism Associated with Venoclysis.
Arch. Surg. 30: 685-701.

64. Shivers, G. C.
1933 — Pulmonary Embolism from Arsenicals Injected Intravenously.
Arch. Dermat. and Syph. 27: 901-922.
65. Snell, A. M.
1927 -- The Relation of Obesity to Fatal Postoperative Pulmonary Embolism.
Arch. Surg. 15: 237-244.

66. Steuer, L. G.
1933 -- Embolism and Thrombosis of the Large Branches of the Pulmonary Artery in Heart Disease.

67. Thomas, H. M. and Alyea, E.
1929 -- Pulmonary Embolism Following Urological Surgery.

68. Victor, J. A.
1925 -- Clinical Considerations of Thrombosis and Embolism.

69. Walters, W.
1927 -- The Suggested Use of Thyroid Extract to Reduce the Incidence of Postoperative Embolism.

70. Walters, W.
Surg., Gyn., and Obst. 50: 154-159.

71. Wilson, L. B.
1912 -- Fatal Postoperative Embolism.