An Autopsy Study of Leg Vein Thrombosis

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SUMMARY
An autopsy study of leg veins in unselected patients was performed in which postmortem venography, complete gross dissection, and microscopic examination were utilized in order to assess the incidence, location, origin, and mode of propagation of venous thrombi in the leg. The incidence of leg vein thrombosis is high; 13 of 27 patients studied (48%) had antemortem thrombi. Thrombosis in the veins of the thigh occurred often (eight patients), but thrombosis in the veins of the calf was even more frequent (12 patients). Thrombi large enough to cause significant pulmonary embolism were found in seven patients. Leg vein thrombi were found in five of the six patients in this study who had pulmonary embolism at autopsy. Initiation of thrombosis was noted in the veins of both the thighs and the calves. The valve pockets were a frequent site of origin of thrombi. Inflammation of the wall of the vein (phlebitis) secondary to thrombosis was found in one patient.

Postmortem venography is a useful and simple adjunct for the autopsy study of leg vein thrombosis. It is particularly reliable for the detection of thrombi in the thigh.

Additional Indexing Words:
Phlebitis Anatomy of leg veins Venous valves Pulmonary embolism

Since Virchow1 outlined the three basic factors in thrombosis as (1) change in the state of the vessel wall, (2) change in the rate of flow, and (3) change in the composition of the blood, many postulates have been made concerning the relative importance of each of these factors.

Inflammation of the wall of the vein was thought to be of primary importance because of Hunter's2 observation that thrombosis occurred in the presence of septic phlebitis. On the basis of this and the observation of Welch3 and of others,4 the clinical concepts of thrombophlebitis and phlebothrombosis emerged as well as an apparent importance of differentiating between these entities.

Change in the rate of flow has been shown to be responsible for the origin of thrombosis in many instances. Early observations of Virchow5 and Aschoff6 of thrombosis occurring in the valve pockets of the femoral veins led to the concept of retrograde propagation of these thrombi. Later, Denecke7 and Olow8 observed that the earliest clinical symptoms of thrombosis appeared in the calves and soles, suggesting that thrombosis starts in the lower portion of the leg. This concept was supported by the extensive leg dissections of Rössle,9 Neumann,10 and Putzer11 which showed a high incidence of thrombosis in the calves and soles. From these observations developed the concept of ascending propagation of venous thrombi.

Despite the extensive studies cited above, some questions concerning the incidence and distribution of thrombi in the leg veins remain unanswered. The relationship of phlebitis to thrombosis, the manner of propagation of thrombi, and the site of origin of thrombi are not entirely clear. Since leg vein thrombosis constitutes a serious disorder because of its
frequent termination in fatal pulmonary embolism, these questions have broad implications with respect to diagnosis, prophylaxis, and management. This autopsy study was undertaken to answer these questions through utilization of all available radiological and pathological techniques. Postmortem venography was combined with complete gross dissection and microscopic examination to determine the incidence, location, origin, and mode of propagation of leg vein thrombi in unselected autopsy patients.

Methods

Patients Studied

Twenty-seven unselected autopsies constituted the material for this study. The age range was 22 to 86 years, mean 57. Eleven were female; 16 were male. Ten were surgical and 17 were medical patients. The duration of hospitalization varied from 1 to 90 days, mean 22 days. The diagnoses were as follows: malignancy (eight), chronic rheumatic heart disease (five), chronic renal disease (four), peritonitis (three), acute myocardial infarction (three), pneumonia (two), cerebral hemorrhage (one), and malignant hypertension (one).

Postmortem Venography

Postmortem venograms were performed in the following manner. The greater saphenous vein just anterior to the medial malleolus was exposed through a small transverse incision and cannulated with an 18-gauge polyethylene catheter. The heel was elevated to eliminate pressure on the calf thereby allowing free flow in the superficial veins. Forty milliliters of 75% Hypaque* was injected by hand to fill the superficial veins. Then a tourniquet was applied just beyond the tip of the catheter and an additional 120 ml of contrast material was injected to fill the deep veins. Roentgenograms of the calves were taken in the lateral projection to avoid superposition of bone over the deep veins. A 14 by 17-inch metal cassette without grid was placed under the thighs for the anteroposterior views, and a 10 by 12-inch cassette was placed next to the calf for lateral views. Angiograms were taken with a Phillips portable x-ray machine at a distance of 40 inches. Settings were 72 to 85 kv, 0.10 to 0.15 sec, and 20 ma depending on the thickness of the leg. Dupont Cronex II film was used. The films were developed in a Kodak X-Omat Processor and were available for comparison with gross dissections.

Method of Dissection

After opening the inferior vena cava, common, and external iliac veins, incisions were made in the thighs from the saphenous ring to the medial femoral condyle and the sartorius muscle was divided. The superficial and deep femoral veins, the greater saphenous, and many unnamed branches of these veins were opened and examined for thrombi. The body was then turned to the prone position and posterior incisions were made from the midthigh to the ankle. The distal portion of the femoral, the popliteal, anterior and posterior tibial, peroneal, and lesser saphenous veins were exposed and dissected. The only major veins not accessible to this technique were the greater saphenous vein distal to the knee and the distal portion of the anterior tibial veins. After the veins were dissected, serial transverse incisions were made in the soleus muscle in order to examine the soleal plexus of veins.

A comment on this technique of dissection seems appropriate. Many pathologists raise the objections that: (1) it is offensive to funeral directors, and (2) it prolongs the autopsy excessively. In this study, large arteries were not cut, and the incisions were well sutured. Therefore, the dissection neither interfered with embalming nor disfigured the body. There were no complaints from funeral directors. The time involved was 2 to 3 hours per autopsy, including the time needed to inject the veins and develop the roentgenograms. Since the method of total evisceration is used at this hospital, the leg vein dissection could be carried out simultaneously with the examination of organs without interfering with the work of the prosector.

Method of Microscopic Examination

Thrombi were examined microscopically to differentiate them from postmortem clots, and to determine their age and the duration of thrombogenesis. Thrombi were dated according to the criteria established by Irniger. One transverse section of soleus muscle from each patient was examined for the presence of thrombi of microscopic size. Sections of all thrombi and soleus muscle were fixed in 10% Formalin and, after customary histological processing with paraffin embedding, were stained with hematoxylin and eosin.

Anatomy of the Leg Veins

The veins of the calf and foot are unique in that two veins accompany each artery. The major deep veins of the calf are the anterior and posterior tibial and the peroneal (fig. 1). The peroneal veins drain into

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*Sodium and meglumine diatrizoates.
LEG VEIN THROMBOSIS

Figure 1
Normal postmortem venogram of calf (lateral projection). The anterior tibial (AT), posterior tibial (PT) and peroneal veins (Pe) are well filled with contrast material. The deep veins are paired.

Figure 2
Normal postmortem venogram of thighs (anteroposterior projection). The femoral (F), deep femoral (DF), greater saphenous (GS), and popliteal (P) veins are clearly visible. The vessels are smooth and of normal caliber. Valve pockets (VP) are shown.

the deep femoral vein within the femoral triangle. From this point to the inguinal ligament it is known as the common femoral vein. However, in this study no distinction was made between the superficial and common femoral veins, and the term "femoral vein" will be used for both. The greater saphenous vein enters the femoral vein at the fossa ovalis.

In addition to these major veins and their numerous unnamed branches, there is a rich venous plexus within the soleus muscle, which is not described in the standard anatomy textbooks. However, it has been studied in great detail and, as will be discussed, is important in thrombophlebitis.

Results
Dissection
Macroscopic thrombi were found by dissection of the leg veins in 13 of the 27 patients (48%). One additional patient had a thrombus in the inferior vena cava, but the leg veins were clear. In seven patients the thrombi were 3 cm long or longer. In six patients, the thrombi were small (less than 0.5 cm in greatest dimension) and were usually within valve pockets. One patient, not included in the above statistics, had a thrombus in a
small vein within the soleus muscle seen only on microscopic examination. No gross thrombi were found in that patient.

The incidence of thrombi by vein is shown in table 1. Thigh and calf vein thromboses are compared in table 2. The vein most often involved by thrombosis was the posterior tibial. The other veins, in order of frequency

### Table 1

**Incidence of Thrombi by Vein**

<table>
<thead>
<tr>
<th>Vein</th>
<th>No. of thrombi</th>
<th>No. of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inferior vena cava</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Common iliac</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>External iliac</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Femoral</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td>Deep femoral</td>
<td>6</td>
<td>4</td>
</tr>
<tr>
<td>Greater saphenous</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Popliteal</td>
<td>8</td>
<td>5</td>
</tr>
<tr>
<td>Lesser saphenous</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Anterior tibial</td>
<td>9</td>
<td>5</td>
</tr>
<tr>
<td>Posterior tibial</td>
<td>16</td>
<td>11</td>
</tr>
<tr>
<td>Peroneal</td>
<td>9</td>
<td>5</td>
</tr>
<tr>
<td>Soleal plexus (microscopic examination)</td>
<td>11</td>
<td>5</td>
</tr>
</tbody>
</table>

### Table 2

**Thrombosis in Thigh and Calf Veins**

<table>
<thead>
<tr>
<th>Case</th>
<th>Thigh</th>
<th>Thigh and calf</th>
<th>Calf</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.2 cm.*, valve pocket, femoral vein</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Extensive, all large veins of thigh and calf, right</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Extensive, all large veins of left thigh and calf, and right calf</td>
<td></td>
<td>0.2 cm., valve pocket, posterior tibial vein, left</td>
</tr>
<tr>
<td>4</td>
<td>Extensive bilaterally, all large veins of thighs and calves</td>
<td></td>
<td>0.5 cm., valve pocket, posterior tibial vein, right</td>
</tr>
<tr>
<td>5</td>
<td>0.2 cm., valve pocket, left femoral vein; 0.2 cm., valve pocket, right posterior tibial vein</td>
<td></td>
<td>3 cm., posterior tibial vein, left</td>
</tr>
<tr>
<td>6</td>
<td>3 cm., branch of left femoral vein; 3 cm., left and right posterior tibial veins</td>
<td></td>
<td>0.2 cm., valve pocket, posterior tibial vein, right</td>
</tr>
<tr>
<td>7</td>
<td>Extensive, deep femoral, popliteal, and all large calf veins, left, and popliteal and all large calf veins, right</td>
<td></td>
<td>Extensive, popliteal and all calf veins, bilaterally, and deep femoral vein, right</td>
</tr>
<tr>
<td>8</td>
<td>Extensive, all large calf veins, bilaterally, and deep femoral vein, right</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Size, when listed, refers to greatest dimension of thrombus.
of involvement, were as follows: soleal plexus, anterior tibial, peroneal, popliteal, femoral, deep femoral, and greater saphenous. In seven of 13 patients (54%), both thigh and calf veins were thrombosed. Calf veins alone contained thrombi in five patients (38%); only one patient had a thrombus in a thigh vein without thrombi in the calves.

Pulmonary embolism was found at autopsy in six patients (22%). It was the immediate cause of death in three. Five of the six patients who had pulmonary emboli had leg vein thrombi. The patient in whom thrombi were not found had only two small pulmonary emboli.

**Postmortem Venograms**

The following abnormalities were observed in venograms: intraluminal filling defects, absence of vessels, dilatation of veins, enlarged

![Postmortem venograms](http://circ.ahajournals.org/)

**Figure 3**

*Postmortem venograms. (Left) Both thighs. Extensive thrombosis of the femoral, deep femoral, and popliteal veins was found by dissection of the left thigh. The veins of the right thigh were normal. The venogram of the left thigh shows absence of filling of the popliteal and deep femoral veins and only a faint outline of the femoral vein (F). The right greater saphenous vein (GS) is dilated and joined by numerous collateral vessels. (Right) Right thigh. The femoral vein has not filled with contrast material because of the presence of thrombus. The greater saphenous vein (GS) is distended. An antemortem thrombus was located by dissection in the greater saphenous vein (arrow). Collateral vessels around the occluding thrombus are shown.*
valve pockets, and collateral circulation around occlusions.

Filling defects or apparent absence of veins were caused by thrombosis (fig. 3). All thrombi, 3 cm or larger, in major thigh veins were detected by these roentgenographic signs. One 3 cm thrombus in an unnamed branch of the femoral vein was not detected.

Filling defects due to postmortem clots occurred in only one patient, and that patient had had bilateral femoral vein ligations. False-positive filling defects due to poor flow of contrast material in the thighs occurred in five limbs. In approximately 90% of the examinations of the veins in the thigh, the phlebo- graphic impression corresponded to the anatomic findings. Correlations with dissection are summarized in table 3.

Filling of the calf veins in general was less adequate. Therefore, in the calves, apparent filling defects or absence of vessels was an unreliable guide to the presence of thrombosis.

Dilated veins and enlarged valve pockets (fig. 4) were frequently seen. There was no significant correlation of either of these abnormalities with the presence of thrombosis. Collateral circulation around a thrombotic occlusion was demonstrated in three patients (figs. 3 and 5).

Table 3
Correlation of Venographic Findings with Results of Dissections in Forty-seven Limbs

<table>
<thead>
<tr>
<th>Vein</th>
<th>Good correlation</th>
<th>Poor correlation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Femoral vein</td>
<td>89% (42)</td>
<td>10% (5)‡</td>
</tr>
<tr>
<td>Deep femoral vein</td>
<td>87% (41)</td>
<td>13% (6)</td>
</tr>
<tr>
<td>Popliteal vein</td>
<td>100% (47)</td>
<td>0% (0)</td>
</tr>
<tr>
<td>Greater saphenous vein</td>
<td>96% (45)</td>
<td>4% (2)</td>
</tr>
</tbody>
</table>

*Good correlation = adequate filling and no clot; or filling defect or absence of filling and antemortem thrombosis. Poor correlation = filling defect and postmortem clot; poor or absent filling and no thrombi on dissection; or normal filling and clots over 0.5 cm. in largest dimension on dissection.

†Numbers in parentheses refer to number of limbs in which the correlation listed was found.

‡Two of these poor correlations were due to postmortem clots in a patient who had had bilateral femoral vein ligations. This was the only patient with postmortem clots.

Microscopic Examination

Thrombi ranged in age from 1 day to 6 weeks, except for one which consisted of fibrous bands (over 6 months). All thrombi

Figure 4
Postmortem venogram of left thigh. The dilated valve pocket (arrow) on dissection appeared incompetent. The femoral (F) and deep femoral (DF) veins are labeled.
deep venous system of a leg was thrombosed, the thrombi in the calf veins were older than those in the femoral veins.

**Discussion**

**Utilization of Postmortem Venography**

Prior to this study, there has been no utilization of postmortem venography for the purpose of studying leg vein thrombosis, although postmortem venography has been utilized to demonstrate the anatomy of the veins of the legs. Correlations in this study (table 3) show that postmortem phlebograms are reliable for the detection of antemortem thrombi in the veins of the thighs. Postmortem phlebograms readily showed collateral channels and dilated valve pockets and aided in the location of thrombi by dissection.

**Incidence and Distribution of Thrombi in Leg Veins**

The incidence and distribution of leg vein thrombi found at autopsy, as reported in the literature, are given in table 4. The aggregate incidence obtained from several studies of lower limb thrombosis in unselected autopsies is 43% (460 of 1,072 patients). In our study, the incidence was 48%. This consistent incidence of thrombosis suggests some basic mechanism or series of events causing a thrombus to form in the leg veins of almost one of every two general hospital patients who die.

The distribution of thrombi within the leg suggests that local factors are important. In a series collected from the literature (table 4) the incidence of thrombi in the calves (44%) is higher than that in the thighs (17%) and thrombi in the thighs alone are the least common. Our findings are in accord with this distribution (table 2).

Numerous anatomic structures in the legs have been cited as sources of pressure causing decreased flow. Examples of such anatomic structures are the soleus muscle, which compresses the posterior tibial vein, the adductor ring, which compresses the popliteal vein, and the inguinal ligament, which compresses the femoral vein. Since stasis is the single

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**Figure 5**

Postmortem venogram of the thighs. There is definite radiographic evidence of occlusion of the right femoral vein between points 1 and 2. There is no filling of the femoral vein (F) between these points. Dilated and tortuous collaterals pass around the site of occlusion. No thrombus was found on dissection of the veins of the thigh of this patient, presumably because dissection was carried out along the collateral vessels in this area rather than along the femoral vein. (This apparent femoral vein occlusion was not included among the positive cases reported in the results of this study).

had fresh components, indicating that thrombosis was continuing. The age of all thrombi except the oldest fell within the period of rest in bed, and the patient with the oldest had a previous hospitalization. Only one patient had clinical thrombophlebitis. Microscopic examination of that patient's veins showed mild lymphocytic infiltration in the media.

Thrombi located in valve pockets consisted of well-organized, fibrous points of attachment capped by fresh fibrin and red cell clot. These represented two stages of thrombosis, the site of attachment being about 6 weeks old, the superficial part, 1 to several days old. Two of the larger thrombi were definitely attached to the endothelium in valve pockets. In all cases in which the entire
### Table 4
Incidence and Distribution of Thrombi Found in Leg Veins at Autopsy from the Literature

<table>
<thead>
<tr>
<th>Patient selection</th>
<th>No. of patients</th>
<th>Lower limb thrombosis</th>
<th>Distribution in limb Site</th>
<th>No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rössle(^9)</td>
<td>Unselected autopsies</td>
<td>324</td>
<td>88 (27%)</td>
<td>Femoral vein and calves</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Calves only</td>
<td>100 (30%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Femoral vein or hypogastric vein</td>
<td>7 (2%)</td>
</tr>
<tr>
<td>Putzer(^11)</td>
<td>Unselected autopsies</td>
<td>370</td>
<td>100 (27%)</td>
<td>Only calf veins dissected</td>
</tr>
<tr>
<td>Hunter et al.(^2)</td>
<td>Unselected autopsies</td>
<td>351</td>
<td>185 (53%)</td>
<td>Only calf muscles dissected</td>
</tr>
<tr>
<td>Hunter et al.(^2)</td>
<td>Unselected autopsies</td>
<td>200</td>
<td>88 (44%)</td>
<td>Thighs and calves</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Thighs only</td>
<td>3 (1.5%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Calves only</td>
<td>57 (28%)</td>
</tr>
<tr>
<td>Neumann(^10)</td>
<td>Unselected consecutive autopsies</td>
<td>165</td>
<td>100 (60%)</td>
<td>Thighs</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Calves</td>
<td>87 (53%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Internal malleolus region</td>
<td>20 (12%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Plantar region</td>
<td>71 (43%)</td>
</tr>
<tr>
<td>Greenstein(^24)</td>
<td>Unselected consecutive autopsies</td>
<td>100</td>
<td>51 (51%)</td>
<td>Calf veins only; no comment on thighs</td>
</tr>
<tr>
<td>Raeburn(^22)</td>
<td>Unselected consecutive autopsies</td>
<td>130</td>
<td>35 (27%)</td>
<td>No comment on calves vs. thighs</td>
</tr>
<tr>
<td>Gibbs(^20)</td>
<td>Unselected autopsies</td>
<td>253</td>
<td>149 (59%)</td>
<td>Thighs and calves</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Thighs only</td>
<td>24 (10%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Calves only</td>
<td>86 (34%)</td>
</tr>
<tr>
<td>McLachlin and Paterson(^25)</td>
<td>Male autopsies over age 40 yr</td>
<td>100</td>
<td>32 (32%)</td>
<td>Thighs and calves</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Thighs only</td>
<td>18 (18%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Calves only</td>
<td>4 (4%)</td>
</tr>
<tr>
<td>Short(^26)</td>
<td>Pulmonary embolism present at autopsy</td>
<td>29</td>
<td>24 (83%)</td>
<td>No comment on calves vs. thighs</td>
</tr>
<tr>
<td>Sevitt and Gallagher(^27)</td>
<td>Patients dying of burns or trauma</td>
<td>125</td>
<td>81 (65%)</td>
<td>Iliofemoral</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Calf vein</td>
<td>60 (48%)</td>
</tr>
</tbody>
</table>

Most important factor contributing to thrombosis,\(^28\) the high incidence of thrombi in these veins (table 1) may at least in part be accounted for by these pressure points.

Intramuscular veins, such as the veins of the soleal plexus, are particularly dependent on muscular contractions for emptying because they are thin-walled and tortuous and have no venous impulse.\(^20\) With inactivity they become distended by a stagnant column of blood.\(^20\) The high incidence of thrombosis found in the intramuscular veins in this study (table 1) and by others\(^11, 20, 29\) may be explained by these characteristics.

Valve pockets are frequent sites of thrombus origin. Five of the six patients in this study who had small (less than 0.5 cm) thrombi had them within valve pockets and
some of the larger thrombi could clearly be traced to origins in valve pockets. Clinical venography has demonstrated pooling of contrast medium at these sites. The eddying of blood with consequent silting of platelets and leukocytes within these structures creates a situation wherein thrombosis is readily precipitated.

Several investigators have found thrombi in the left leg more frequently than in the right. This is attributed to compression of the left common iliac vein by the right common iliac artery and to pressure of the rectosigmoid colon on this vein. In our study, thrombi on the left were not more common, but this may be due to the small size of the series.

Forward Versus Retrograde Thrombosis

Some early workers, not knowing that thrombus are more prevalent in calf veins than in thigh veins, presumed that all thrombosis propagated in a retrograde fashion. This opinion, however, was not uniformly accepted. Welch, in 1899, stated that, “an occluding thrombus may lead to such disturbances of the circulation as to cause the formation of discontinuous multiple thrombi, on both the central and peripheral sides, and these may become connected by red or mixed thrombi.” With the development of the clinical concept of ascending thrombosis, followed by thorough pathological studies of the leg veins showing a higher incidence of calf vein thrombosis than thigh vein thrombosis, the opinion developed that all thrombosis begins in the small intramuscular veins and progresses in the direction of blood flow. The more recent work of Sevitt and Gallagher indicates that thrombi arise independently in large and small veins, both in the thigh and calf, and that propagation is both forward and retrograde.

In our series, thrombi were found to originate both in the thigh and in the calf; however, origin in the calf was more common, and in every case in which the thigh and calf were thrombosed in continuity, the thrombi in the calf were older than those in the thigh. These findings support the conclusion that forward thrombosis is more common than retrograde thrombosis, although both occur.

Relationship of Thrombosis to Phlebitis

John Hunter, after studying infected venesection wounds both in human beings and in horses, became the first to attribute thrombosis to phlebitis. Virchow, on the other hand, observed that cellular reaction in the vein wall usually does not appear until after the thrombus has been laid down. Welch, in studying venous thrombosis in infectious diseases such as typhoid fever, found an inflammatory lesion beneath the endothelium in which he could not demonstrate organisms. He termed this “toxic endophlebitis” and attributed thrombosis to it. However, he cautioned that “while bacteria and primary phlebitis play an important role in thrombosis, attempts to refer all medical thromboses to them go beyond demonstrated facts.”

Subsequently, patients were described who had clinical evidence of thrombosed leg veins and also had clinical signs of inflammation (for example, warmth, swelling, and tenderness). A clinical diagnosis therefore was made of thrombophlebitis. In view of Welch’s observations, it was concluded that the primary event in thrombophlebitis is inflammation of the vein wall. In contrast, patients later were described with no clinical signs in the legs who had thrombosis of the lower extremities that resulted in pulmonary embolism. These patients because of the lack of leg signs were said to have phlebothrombosis. Thus, clinical concepts of thrombophlebitis and phlebothrombosis evolved.

Histological investigations have not supported the sharp distinction, made on a clinical basis, between thrombophlebitis and phlebothrombosis. While there are situations in which phlebitis is primary and thrombosis is secondary (such as mechanical and chemical injury), these are rare, as compared with the incidence of thrombosis without in-
flammation. The presence of a thrombus can induce inflammation in the underlying vein wall, and this inflammation in some patients is extensive enough to produce pain, tenderness, swelling, and fever compatible with the clinical diagnosis of "thrombophlebitis." However, the underlying pathogenetic mechanism is primary thrombosis and not primary phlebitis.

One patient in our series had clinical thrombophlebitis. At autopsy there was inflammation of the venous wall and extensive thrombosis. The inflammation occurred not only at the sites of attachment of the thrombus, but also in places where the thrombus was apposed to the endothelium without being attached, suggesting that the thrombus induced the inflammation, and not vice versa.

Hunter and associates showed that about 12.5% of patients who died with asymptomatic leg vein thrombosis (phlebothrombosis) died from pulmonary embolism. Three of 12 patients in this study who had leg vein thrombosis without leg signs or symptoms died of pulmonary embolism. On the other hand, fatal pulmonary embolism is not uncommon in patients with clinical evidence of thrombophlebitis. In a study reported by Byrne, 37% of 347 patients who were treated neither with anticoagulants nor by venous ligation died of pulmonary embolism. No clear evidence indicates that inflammation of the veins prevents thrombi from embolizing or that embolization is more frequent in those patients with leg vein thrombi not associated with venous inflammation.

It is concluded that thrombosis of the lower limbs as seen in this era of medicine usually occurs without inflammation. Inflammation when associated with thrombosis is usually secondary to the thrombosis. The likelihood of embolization is high both in patients with and without inflammation associated with leg vein thrombosis.

*Subtle changes in the endothelium, seen only with special histological techniques, are not considered to be inflammation in the usual sense and may be postulated to occur in any patient with thrombosis.

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