DEEP THROMBOPHLEBITIS

Pathophysiology and Treatment

by

J. Alex Haller, Jr., M.D

Volume VI in the Series

MAJOR PROBLEMS IN CLINICAL SURGERY

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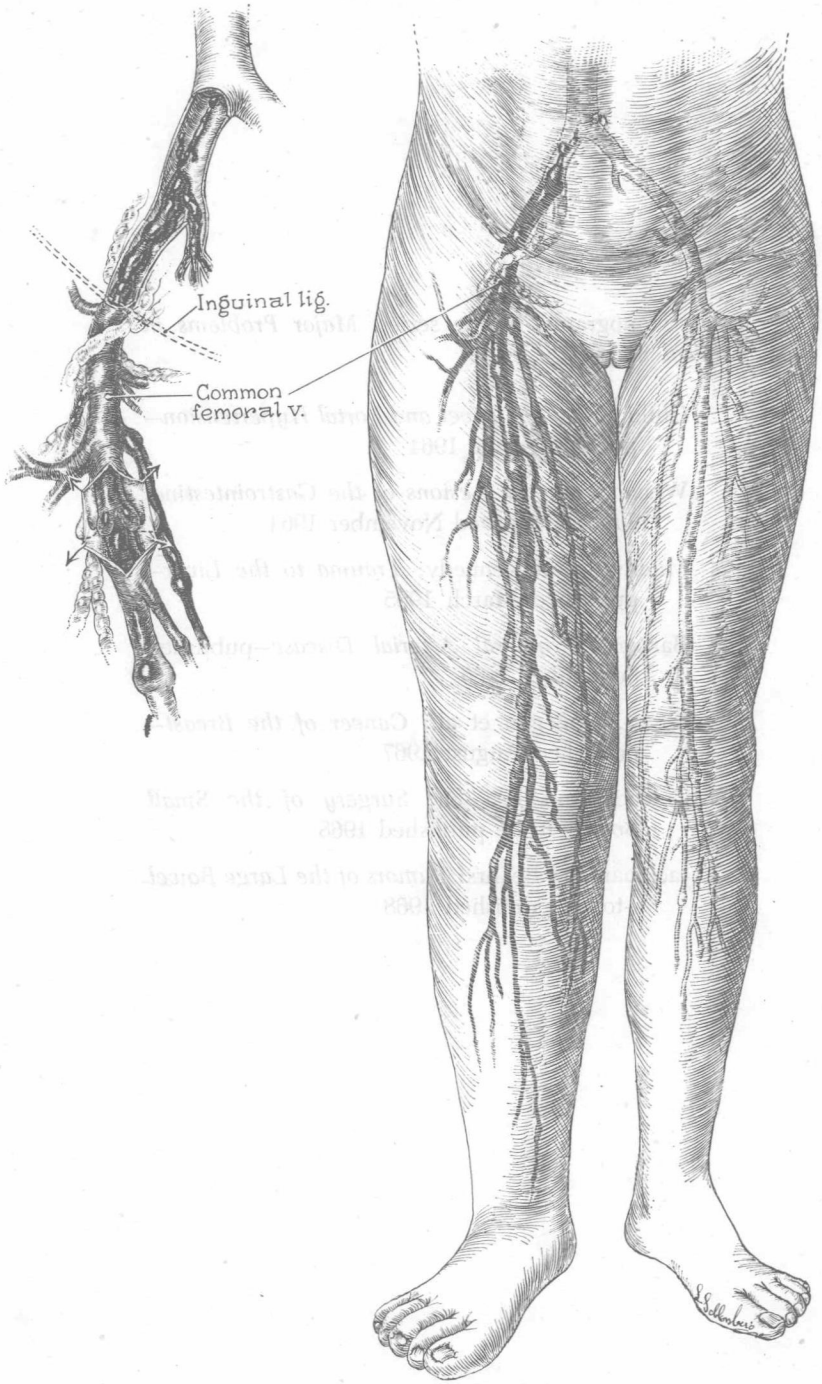

The pathologic anatomy of phlegmasia alba dolens.

Foreword

There is considerable controversy among both physicians and surgeons over the best means of prevention and the treatment of deep iliofemoral thrombophlebitis. In this authoritative volume Dr. Haller summarizes the historical development of the subject, and sets down criteria for diagnosis and treatment based upon the underlying pathophysiology of both acute and chronic thrombophlebitis. Anticoagulant therapy and the indications and technique for surgical intervention are described in detail. From his own extensive experience, as well as the work of others, he presents a strong case for prompt medical and aggressive surgical management.

J. Englebert Dunphy

Preface

Diseases of veins are less dramatic than arterial diseases, and their importance in the debility and discomfort of the patient has received meager emphasis. The general purpose of this monograph is to bring into more realistic focus the acute and chronic problems of inflammation and thrombosis in the veins; its specific objective is to correlate the pathophysiology with altered hemodynamics in acute thrombophlebitis and in the postphlebitic limb. Understanding of these functional changes leads to more effective prevention and management of deep thrombophlebitis. Improvement of patient care is the ultimate goal for teacher, researcher, and clinician.

The author's experience and impressions have been the main sources for the monograph, but these have been richly supplemented by a frequent interchange of ideas with many colleagues, both students and teachers.

Many of the experimental and clinical data were obtained while the author was a member of the Department of Surgery at the University of Louisville, Kentucky. The author is grateful to his former chief in Louisville, Rudolf J. Noer, for his support, and to the John W. and Barbara Price Trust Fund Fellowship, which provided financial assistance for much of this work.

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J. Alex Haller, Jr.

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Chapter One

INCIDENCE AND CLINICAL SIGNIFICANCE OF DEEP THROMBOPHLEBITIS

The clinical significance of deep thrombophlebitis is a summation of the effects of the acute and chronic phases of the disease. The initial discomfort and severe incapacitation, including hospitalization, in the acute phase must be first evaluated and then added to the chronic invalidism of the post-thrombophlebitic limb with the late sequelae of dependent edema, pain, and ulceration. The exact incidence of these two arbitrary phases of thrombophlebitis is not known, but they are common complications in every specialty area in the practice of medicine, except pediatrics.

It is the physician in a nonsurgical specialty who usually treats the acute phases of deep thrombophlebitis unless or until life-threatening complications occur—specifically, repeated pulmonary embolization. For this reason most internists and general practitioners are gravely concerned with acute thrombophlebitis and are well versed in its clinical picture and therapy, but they are often woefully unaware of the serious problems of postphlebitic venous incompetence. On the other hand, management of the complications of venous stasis has fallen largely in the surgeon's domain and yet few surgeons are fully aware of the manifold problems of the acute phase. This transection of the clinical course of deep thrombophle-

bitis has been largely responsible for confusion in therapy and lack of a comprehensive attack on this scourge of the lower extremities. As Lockhart-Mummery has acidly commented, "Perhaps because nobody dies of varicose ulcers, i.e., postphlebitic incompetence, the subject has been much neglected" (Lockhart-Mummery and Smitham, 1951).

Indeed, the one potential liaison between these two groups of physicians, namely the patient himself, is often negated by the remote onset of significant sequelae of stasis. They may not become overt for several years after the acute disease so that the patient may not recognize a cause and effect relationship.

As a result of this confusion internists have been pleased with their treatment of the acute phase because they are not aware of the high percentage of postphlebitic complications. Surgeons have often treated local symptoms and stasis ulcers with a resigned foreboding born of chronicity. There has often been no clear understanding of the pathologic process which leaves the patient saddled with the sequelae of stasis. One of the major purposes of this monograph is to trace the natural history of extensive deep thrombophlebitis from acute thrombosis to final stasis necrosis. Only in this way can the surgeon become aware of the internist's problems, and vice versa. Hopefully, a better understanding of the pathologic processes will result in better and more comprehensive care for the patient with deep thrombophlebitis.

The clinical significance of acute deep thrombophlebitis is largely determined by the individual circumstances under which it occurs. For example, venous thrombosis may develop spontaneously in an apparently healthy ambulatory adult. More commonly, it occurs in the postpartum woman, in the hospitalized patient with a chronic disease, in the postoperative patient, especially one who has undergone recent pelvic surgery, or in the patient with soft tissue and bone trauma, especially one with pelvic and hip fractures.

Thrombophlebitis may thus be a primary disease, as in the ambulatory patient, and cause severe discomfort, requiring hospitalization and forcing a six to 12 week loss of time from work. A postpartum patient who is just beginning to nurse her baby must give up the care of her infant and take to her bed. For several weeks she is completely incapacitated and must rely on family, friends, or hired help to care for her baby and the rest of the family. The patient who is already hospitalized is made worse by secondary thrombophlebitis and is much more likely to have the dreaded com-

plication of pulmonary embolization. Acutely injured tissues may become dangerously compromised by superimposed deep venous thrombosis, as in patients with a fractured hip or pelvis associated with retroperitoneal bleeding. Postoperative recovery may be changed into a long, arduous hospital stay by the development of acute thrombophlebitis. In all of these patients the threat of pulmonary embolization and massive deep extension of the thrombosis further underlines the significance of an acute episode of thrombophlebitis.

How many patients with extensive deep thrombophlebitis, phlegmasia alba dolens, will develop significant postphlebitic venous incompetence if healing is allowed to take place naturally without operative intervention? No single author has been able to accumulate this kind of experience, and the collected clinical data are almost wholly retrospective. The data included in this discussion are presented in an attempt to answer the question, "How many patients with serious postphlebitic limbs give a history of extensive deep thrombophlebitis?" Positive histories of deep phlebitis in patients with stasis sequelae range from 10 (Cokkinis, 1933) to 87 per cent (Bauer, 1965) in the reported series. The wide discrepancy is probably due largely to differences in criteria for previous thrombophlebitis. In our experience, it seems likely that if not all, at least the vast majority of cases of significant deep venous incompetence result from phlegmasia alba dolens or from smaller recurrent episodes of deep thrombophlebitis which eventually involve the same deep venous system.

The first question, i.e., the incidence of postphlebitic incompetence after thrombosis, is equally pertinent but much more difficult to answer. If the natural pathogenesis of iliofemoral thrombophlebitis runs toward resolution with a low incidence of venous incompetence, then questions of comparative therapy are almost academic. But the natural process of healing in thrombosis is well established (Hadfield, 1950). There can be little question that a clotted vein regularly becomes recanalized, and its valves are predictably and demonstrably incompetent (Edwards and Edwards, 1937). It is our impression that in few patients with phlegmasia alba dolens deep thrombosis will be naturally resolved without significant venous incompetence. Those lucky few in whom resolution does take place probably have a higher potential for clot lysis than for organization and recanalization, and also have a larger collateral venous bed with undamaged valves.

In any event, the personal significance of the late sequelae is

largely dependent upon the activity demands of each patient. If every patient with a postphlebitic limb could keep his feet elevated and clip coupons for a living, there would be no serious medical or economic problems. Most patients with stasis sequelae, however, are young or middle-aged adults who must work for a living, and their crippled limb is a heavy cross to bear. A young mother with an aching, edematous leg may find it intolerable to wash dishes, to cook, and to care for her young children (Haller, 1961b). The farmer cannot walk or plow his fields; the laborer cannot stand for the necessary long hours on his job. Very few occupations do not involve leg usage and foot dependency. Much can be done to control symptoms and prevent further organic damage in these patients, but they are all seriously handicapped by their postphlebitic venous incompetence. Treatment and prophylaxis are discussed in greater detail in later chapters.

Cost of medical care and financial loss due to time off from work are relatively small in the acute phase of thrombophlebitis when they are compared with potential economic loss from the crippling effects of severe venous stasis. The vastness of this problem has never been appreciated in the United States, and yet a visit to the vascular or dressing clinic of any large university or metropolitan hospital will reveal impressive numbers of open, draining stasis ulcers under various forms of palliative treatment. In other economic and educational strata, similar postphlebitic stasis problems are being more effectively treated because of better participation by the patient in his therapy. But at whatever socioeconomic level and in whatever stage of the disease process, this is a crippled population group.

Some assessment of the economic and sociologic consequences of postphlebitic stasis sequelae has been made in several European countries. In 1953 Merz estimated that the cost to the Swiss community as a whole of managing chronic postphlebitic ulcers was equal to the cost of treating pulmonary tuberculosis at that time. Chemotherapy and operative excision have strikingly decreased both the expense and incidence of tuberculosis treatment in the past 30 years, but in 1932 every Swiss canton had several large sanitoria filled with tuberculous patients. In 1951 Lockhart-Mummery and Smitham estimated that there were 200,000 postphlebitic patients in England alone, involving an annual expenditure of nine million dollars. In Sweden a survey in 1950 showed that of the then six million inhabitants, 400 new patients with post-thrombotic ulcers

applied for treatment annually (Stürup and Højensgard). A study in Vienna in 1953 showed that 0.91 per cent of the population who were under the national insurance plan were receiving treatment for tuberculosis, and 0.18 per cent of the population had various complications of varicose veins—thrombosis sequelae (cited by Fontaine, 1957).

The cost of treatment cannot be calculated as the only economic loss to the community. Absences from work, lowered efficiency, and often a necessary shift to lighter work contribute to the total bill. Stürup has estimated that patients with chronic leg ulcers spend approximately 25 days away from work because of them each year (Stürup and Højensgard, 1950). This does not take into account any of the discomfort and outright misery that stasis edema and ulceration cause. There must be added to these disabilities the frequently offensive discharge from the ulcers and the inconvenience of elastic bandages worn for many months and years. With this insight, it is not hard to believe that to the medical profession and to the unfortunate patients postphlebitic stasis edema and ulceration are very serious problems.

OCCURRENCE OF PHLEGMASIA ALBA DOLENS

Acute deep thrombophlebitis may occur spontaneously in an apparently healthy individual who is engaged in normal activities with no known predisposing factors, but the condition is seen much more predictably in certain high risk situations and medical conditions. These include postpartum women, postoperative patients, stroke and terminal carcinoma patients, patients with pelvic fractures, patients who have had a previous episode of deep thrombophlebitis, and an occasional patient who has had an indwelling venous catheter for a long period of time.

The classic example of phlegmasia alba dolens is its occurrence in the young postpartum woman near the onset of lactation. This is the well-known and time-honored "milk leg." Why deep thrombophlebitis should so characteristically occur during lactation remains a mystery. Most of the recognized factors which are responsible for intravascular clotting are more prominently present in the terminal stages of pregnancy than after delivery. These third trimester factors are *stasis,* due to the pressure of the heavy uterus and increased

abdominal distention, and *vascular trauma,* due to the baby's head pounding against the pelvic veins. After delivery increased coagulability of blood in the postpartum period has been implicated as a factor in thrombosis—as has the physiological hemoconcentration which replaces the hemodilution of the third trimester of pregnancy. There remains a possibility that iliofemoral thrombosis represents an abnormal progression or extension of the normal thrombosis which occurs in the uterine wall at the site of deplacentation (Haller, 1961b). If centrifugal clotting migrates down the uterine veins, the internal iliac vein is a natural route of propagation. It has not been possible to document this hypothetical mechanism (Fig. 1–1), but it seems as logical as any of the other possibilities which have been suggested. Deep thrombophlebitis at the onset of lactation is particularly distressing because it practically prohibits the new mother from caring for her baby and may seriously compromise her ability to stand or walk comfortably for several weeks.

Antepartum thrombophlebitis is rarely seen, but Villasanta reported 12 personal cases and referred to 250 other cases of deep thrombosis during gestation. The onset may be at any stage of pregnancy, but it most often occurs in the third trimester. Treatment of the acute episode with either heparin or clinical dextran is effective. The use of coumarin derivatives is reported to result in a high incidence of fetal and neonatal hemorrhagic complications (Villasanta, 1965). This is thought to result from selective passage of coumarin compounds across the placenta. In a few cases operative thrombectomy has been carried out with good results (Haller, 1966). (See Chapter Seven, p. 97.) Neither heparin anticoagulation nor operative removal of clot has interfered with eventual labor and delivery, but long-term follow-up data are quite meager.

Postoperative deep thrombophlebitis may follow any type of surgical procedure. It is most frequent after pelvic surgery, especially hysterectomy and prostatectomy. The natural inference is that pelvic veins are traumatized during the procedures and that local thrombosis extends to involve the deep venous system. Although logically appealing, this hypothesis does not explain iliofemoral thrombosis after stomach or gallbladder surgery. Earlier postoperative ambulation—i.e., up and walking, not up and sitting in a chair—has significantly lowered the incidence of postoperative thrombophlebitis, but it remains a frequent complication of convalescence. Earliest signs of the onset of postoperative deep thrombosis may be slight tenderness in the involved calf and a slowly rising pulse rate

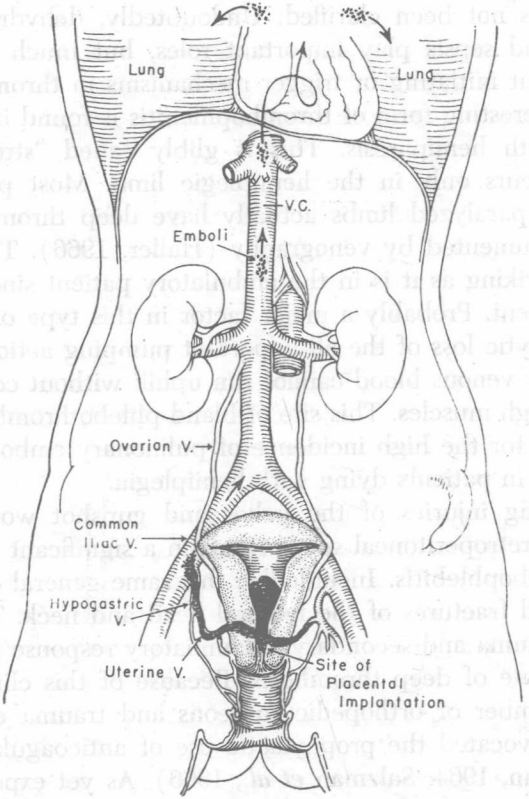

Figure 1–1. Possible route of propagation of thrombus from placental site in postpartum iliofemoral venous thrombosis. Note extension into hypogastric and into iliac veins. (Modified from Eastman, N. J.: *Williams Obstetrics,* Ed. 11. New York, Appleton-Century-Crofts, Inc., 1956, p. 982.)

without comparable fever. Edema may not appear for several days if there is little inflammatory response because the legs are not dependent in bed.

Phlegmasia alba dolens occurs commonly in debilitated patients during chronic hospitalization. A high incidence of thrombophlebitis in the terminal carcinoma patient is well documented, but its exact etiology has not been clarified. Undoubtedly, dehydration, hypovolemia, and sepsis play important roles, but much remains unknown about initiating or trigger mechanisms in thrombophlebitis.

An interesting form of thrombophlebitis is found in debilitated patients with hemiparesis. This is glibly called "stroke edema," since it occurs only in the hemiplegic limb. Most patients with edematous paralyzed limbs actually have deep thrombosis which can be documented by venography (Haller, 1966). The edema is never as striking as it is in the ambulatory patient since the leg is not dependent. Probably a major factor in this type of thrombosis is the paralytic loss of the all-important pumping action of the leg muscles, for venous blood cannot run uphill without contraction of calf and thigh muscles. This site of bland phlebothrombosis may be responsible for the high incidence of pulmonary emboli which has been noted in patients dying with hemiplegia.

Crushing injuries of the pelvis and gunshot wounds of the pelvic and retroperitoneal space result in a significant incidence of deep thrombophlebitis. Included in this same general category are comminuted fractures of the femoral head and neck. The primary vascular trauma and secondary inflammatory response predicate an increased rate of deep thrombosis. Because of this clinical experience, a number of orthopedic surgeons and trauma experts have recently advocated the prophylactic use of anticoagulants in such cases (Fagan, 1964; Salzman *et al.*, 1966). As yet experience with this realistic approach to prophylaxis is too limited to warrant evaluation.

Patients who have had one episode of deep thrombophlebitis may have repeated attacks. Recurrent thrombophlebitis is most likely to occur in an already damaged deep venous system or in established varicose veins. Recurrence of deep thrombophlebitis is itself a potent argument for long-term anticoagulant therapy because of this cycle of recurring attacks. Each episode further destroys valvular competence of the deep system and increases the likelihood of stasis sequelae.