

1939

Etiology and treatment of varicose veins of the lower extremities

Wilbur E. Johnson
University of Nebraska Medical Center

This manuscript is historical in nature and may not reflect current medical research and practice. Search [PubMed](#) for current research.

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



Part of the [Medical Education Commons](#)

Recommended Citation

Johnson, Wilbur E., "Etiology and treatment of varicose veins of the lower extremities" (1939). *MD Theses*. 755.

<https://digitalcommons.unmc.edu/mdtheses/755>

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.

ETIOLOGY AND TREATMENT OF VARICOSE VEINS OF
THE LOWER EXTREMITIES

Wilbur E. Johnson

Senior Thesis

1939.

The University of Nebraska

College of Medicine

Omaha

Nebraska.

INTRODUCTION

The erect position and the resulting specialized development of the upper extremities is undoubtedly one of the main factors in the evolution of man, but it seems as if perfect adjustment to this position has not taken place, and that the circulatory system at any rate is meeting but imperfectly the requirements which the erect posture has made upon it. In the lower extremities the maladjustment has given rise to varicose veins.

A service in the Surgery Clinic at the University Dispensary has convinced me that the problem of varicose veins is a common one and responsible for much disability. For this reason varicose veins was selected as the subject of my thesis.

Varicosities have been reported in the hemorrhoidal veins, the pampiniform plexus of the spermatic cord, in the subcutaneous veins of the abdominal wall, in the bladder, in the brain, but most frequently in the lower extremities. This thesis shall be limited to a discussion of varicosities of the lower extremities.

Varicose Veins may be defined as those having a permanent dilation due to changes in their walls.

HISTORY

Any thesis on management of varicose veins must of necessity discuss the development and evolution of the treatment as a proper background.

The recognition and treatment of varicose veins of the lower extremities is as old as medical literature. Hippocrates (1), described a method of obliteration of a varix by scarification with the sharpest and most slender instruments of iron. It is interesting to note that the first recorded attempt to treat varicose veins was an attempt to obliterate them in situ and is exactly the same theory as the modern so-called injection treatment of varicose veins.

Mayo (41), in his history of treatment of varicose veins, mentions puncture with the Paquelin cautery or with electro-cautery, cutaneous and subcutaneous suture and ligature as practiced by Valpean and Delpech. The first surgical interference referred to in the literature is ligation of a varicose vein above the ulcer, performed by Celsus (2), during the first century.

Aetius (20), in the 6th century, and Paulus Aegineta in the 7th century A.D., were probably the first to adopt actual section and ligation of the saphenous vein itself. Par'e in 1579 and Howe in 1797

carried out the same procedure. Brodie (6), in 1846 very clearly understood the reverse flow in varicose veins and urged ligation of these veins, especially the saphenous, but also recommended other methods of blocking the vein, such as compression or tamponage.

Schede (63), in 1877 described his operation which consisted of a more or less extensive division between ligatures of the superficial veins above an ulcer. In 1884 Madelung (40), published his method of treatment which consisted in complete extirpation of the entire greater saphenous vein and as many of its branches as seemed indicated. Trendelenburg (69), in 1890 and 1891, described the test bearing his name and basing his judgment thereon, advocated high ligation of the saphenous vein as a therapeutic measure. In 1899 Casati (52), described a method of tearing out the vein (saphenous) through multiple short incisions. Keller in 1905 (32), described a new method of extirpating the saphenous with a small wire, stripping the vein subcutaneously by completely everting it. One year later, 1906, Mayo introduced his vein stripping operation which has been most widely used. (41).

Coincident with the development of the surgical treatment of varicose veins there were attempts by others to cure the condition by the injection of sol-

utions directly into the vein lumen. The exact cause and method of obliteration was not known although the veins did thrombose and disappear in many cases.

The actual injection of varicose veins followed the invention of the Pravoz syringe in 1851 (17). De-Takats and Quint (17), state that Pravoz injected perchloride of iron into varicose veins as early as 1853. According to Johnson (30), Des granges' in 1855 used iodotannic solution without accident, but accompanied with a great deal of pain. Many different solutions were used such as phenol, alcohol, Lugol's solution, but these solutions fell into disrepute because of toxicity and irritating properties. In 1870 in Continental Clinics especially in those in Vienna developed the "Era of Perivenous Injections". The solutions used were, phenol, ergot, iron perchloride and alcohol. Obliteration of the vein was the result of excessive fibrosis of surrounding tissues. This type of treatment was found to be entirely dissatisfactory. (10).

Sicard, Model, and Linser are given credit for recent development of the treatment of varicose veins by injection. Sicard and co-workers discovered sclerosing properties of drugs used in the treatment of syphilis. Linser noted the excellent venous thrombosis and obliteration sometimes produced by the intravenous injection of bichloride of mercury in the treatment of syphilis

(1925). Also reporting the same results using 15 to 25 percent sodium chloride. Borchers (5), reports curing varicose veins and syphilis simultaneously by intravenous injection of salvarsan. During the first part of the 20th century treatment of varicose veins was based on the results of both operative and injection treatments. Schiassi (64), in 1908 was the first to use the combined treatment. He was the first to inject solution into the distal segment at the time of ligation.

ANATOMY

The veins of the lower extremity are subdivided into three great groups; 1) the superficial veins which are placed beneath the integument, between two layers of fascia, 2) the deep veins, accompanying the arteries and forming the venae comites of those vessels, 3) communicating system, which connects the two sets of veins.

The Deep Veins: All of the arteries of the lower extremity with the exception of the femoral and popliteal artery are accompanied by two venae comites. (11). These veins (venae comites) usually lie one on each side of the artery and are connected by transverse channels which may pass in front of or behind the artery, and are provided with numerous valves. The posterior tibial vein is formed by the uniting of the external and internal plantar veins. The anterior tibial veins are formed by the continuation upward of the venae comites of the dorsalis ped-

is artery. The valves in these veins are quiet numerous. The popliteal vein is formed by the junction of the venae comites of the posterior and anterior tibial veins. This vein contains usually four bicuspid valves. (23). The popliteal vein ascends through the popliteal space to the tendinous aperture in the adductor magnus where it becomes the femoral vein. This vein accompanies the femoral artery through the upper two-thirds of the thigh, and after receiving the profunda femoris and internal saphenous vein in the femoral sheath at the fossa ovale becomes the external iliac vein. (23). The valves are four to five in number.

The Superficial Veins: The superficial veins lie in the subcutaneous connective tissue between the skin and the strong fasciae. They are composed of the great saphenous and the small saphenous vein. *V. Saphena Magna* (interna) begins at the ankle and the anterior surface of the internal malleolus, rises almost vertically, crossing the medial margin of the tibia, enters the hollow between the calf of the leg and the knee, and passes immediately posterior to the medial condyle of the femur. In the thigh it ascends obliquely, in a somewhat anterior and lateral direction, parallel with the sartorius muscle, perforates the fascia cribrosa, passing over plica falciformis and terminates in the femoral vein 3-4 cm. below Poupart's ligament. *V. Saphena parva* (external), begins posterior to the

external malleolus, and ascends towards the poples, at first passing along lateral border of the tendo- Achilles and then running up in the interstice between the two bellies of the gastrocnemius. In the upper fourth of the calf it ceases to be subcutaneous and now continues in a fibrous channel in the aponeurosis. At the level of the knee-joint it bends forwards into the depth of the popliteal space and terminates in the popliteal vein. Anomalies in the formation of the superficial system may occur. Often, there maybe a bifurcation of the great saphenous, with the formation of a smaller branch, the minor saphenous which arises on the anterior surface of the ankle-joint, crossing the main trunk mid-way on the leg, ascending posterior to this and joining it just below the knee. Likewise there is often an additional small saphena which comes from the lateral side of the foot and ascends on the lateral surface of the leg.

The Communicating System: The saphenous veins of the leg tend to drain into the posterior tibial vein, while the great saphenous above the knee drains into the femoral. Loder, quoted by Meisen tabulated the number and distribution of the communications as follows:

6 in the foot
15 in the leg
7 in the thigh

R'emy (49) found a similar number.

The Venous Valves: In the lower extremity the vertical

veins-- deep as well as superficial are equipped with valves. The horizontal and oblique branches have no valves. The communications, however form an exception to this rule, with the exception of the foot, their valves indicate flow from the surface to the deep veins. In the direct communications Berntsen found valves to be absent in eight out of twenty-five cases. (49). Valves are more plentiful in the deep veins. R'emy found three pairs of valves in the great saphenous, nine in the anterior tibial, nine in the posterior tibial, and seven in the peroneal. Average of five valves in the thigh and four in the leg in the great saphenous. Berntsen, found an average of seven valves; the number varying between three and fifteen. In the thigh the great saphenous usually has three valves, and distal to the inlet to the femoral vein, one at the knee and one mid-way between the two. In the communicating veins the arrangement of valves is the same as in the great saphenous. At its inlet into the femoral vein; as a rule there are a pair of valves immediately before the inlet of the communication into a deep vein, and an additional pair of "reserve valves" a little farther back. In the femoral vein the last valve is located in the immediate neighborhood of poupart's ligament just before or after the passage of the vein under the ligament. According to Gray (23), the distribution of the valves is: great saphenous 10-20

small saphenous	9-12
popliteal	4 usually
femoral	3

PHYSIOLOGY OF THE BLOOD FLOW.

The passage of the blood from the arteries to the enormously developed capillary network is associated with a marked slowing down of the stream and a decrease of the blood pressure. (49). This is believed due to the friction in the capillaries, and by the time the venules are reached most of the force imparted to it by the heart has been lost. (39). Never-the-less, this remaining vis-a-tergo must be considered as the basic cause for the movement of the venous blood near the periphery. As the veins become larger two or three other factors come into play: 1) the massaging influence of the muscles, and the 2) valves of the veins. By movement of the muscles the veins which lie between will be rhythmically compressed, and this will tend to cause the blood to be moved forward and backward in them, the backward movement being prevented by the operation of the valves. Two such valves are, as a rule, situated opposite to each other and allow only the passage of blood towards the heart under normal conditions. (68).

Recklinghausen, quoted by Meisen states that individuals standing quit still there will nevertheless, always be some involuntary muscular contraction which will promote

the venous flow. The velocity of the venous flow is increased by respiration, although the effect is slight in comparison with the vis-a-tergo and action of the skeletal muscles. Meisen states, that inspiration impedes the influx from the lower extremities, while expiration furthers it. In the foot the capillary pressure is lower than the hydrostatic pressure. The predominant role of the hydrostatic pressure is evident from the ready and quick emptying and filling of the subcutaneous veins of the extremities when these are elevated. (49). The importance of gravity to the circulation of the blood is also plainly evident from the experiments carried out by Leonard Hill, quoted by Meisen and Starling. In a snake suspended in the vertical position, the blood accumulates in the lower two-thirds of its body; the circulation returning to normal when the reptile was immersed in water. According to Hills' experiments, various animal species differ in adaptability of the circulation to various positions, this being partly dependent upon the vasomotor system controlling the blood volume passing through the smaller arteries, partly upon the tightness of the skin, and the strength of the fasciae, especially those of the lower extremities, and partly upon the general tonus of the skeletal muscles. Hill, also showed that the pressure in the veins of the foot is but little higher than that in the veins of the hand. (68). Therefore according to Starling,

when a man assumes the upright position, the arteries of the leg and foot are contracted down until, under the combined effects of the heart and gravity the blood supply of the capillaries is just adequate. The return of blood from the dependent parts is due to not only the action of the heart, (vis-a-tergo), but also to the contraction of the muscles of the limb which force the blood towards the heart due to the presences of valves which hinder its back flow. This explains why it is so difficult to stand for any length of time without moving and emphasises the need of moderate exercise for the maintenance of a normal circulation. (28).

HISTOLOGY

Maximow and Bloom (44), state that individual veins show much greater variations than do the arteries. Individual veins may show great variations in different parts. Therefore, each vein has its own structure. Most authors agree there are three layers in the walls of the veins; intima, media and adventitia. In reference to the veins of the lower extremity, the intima, consists of a layer of flat endothelial cells, supported by a layer of connective tissue which may be thickened in patches and contains bundles of smooth muscle fibres running parallel with the direction of the blood stream, 2) the tunica med-

ia is considerably thicker than the intima and consists of muscle bundles running slightly oblique to the long axis of the vessel. Each muscle bundle is enveloped by a rather abundant amount of connective tissue.(18)(49). Maximow and Bloom, state that the media of the saphenous, especially adjacent to the intima, is devoid of muscle and consists of longitudinal collagenous and elastic fibers. The adventitia is usually much thicker than the media and consists of a rather loose connective tissue made up of collagenous and elastic fibers. Within the adventitia are found the lymphatics, sympathetic nerve branches and vasa vasorum.

ETIOLOGY

Numerous theories have been brought forward to try to account for the histological appearance and various observers have attributed them to toxic, mechanical, inflammatory or atrophic changes.

Incidence. According to Berntsen (49), 75% of varicose veins occur before the age of thirty; 1% occur between ten and twenty years of age; 18.1% between twenty and thirty years of age; 27.5% thirty to forty; 24.7% forty to fifty; 16.75% fifty to sixty; 10.8% sixty to seventy, and 1% seventy to eighty years of age. The youngest patient being nine years old and the oldest seventy-seven.

Nicholson (51), states the age of predilection is between eighteen and twenty-five.

Sex. The various authors' reporting on the distribution of cases between males and females seem to vary to quite an extent. Berntsen and McPheeters find that varicose veins occur more frequently in the female, with the ratio of four to one. Meisen, finds a ratio of three to one. Nicholson, finds the ratio to be 69% males and 43% females in 112 cases. Nobl (53), states the lesion is just as frequent or more so in the male.

Occupation. As shown in the anatomy and physiology muscular contractions are responsible in a large part for the venous circulation and return of blood towards the heart. Individuals whose occupation requires standing for long hours at a time lose the pumping effect of the muscular contractions, and instead have continuous back pressure of the venous columns. (13)(47).

Heredity. From the etiological standpoint the family history is of extreme interest. Nicholson (51), found out of a group of 112 cases, sixty-two, or 55% gave a positive family history and fifty or 45% could not give a definite history, or gave a negative one. These facts seem significant, when one considers that in many instances the patient could not be expected to know a great deal about the condition of the legs of other members of their family; especially, might this be true of cases in which the var-

ices may have been slight and were not causing symptoms. Klotz (37), explains the formation of varicose veins by his belief that there is progressive degeneration of the valves with age, and thus consequent loss of function, allowing the reverse flow to occur. He based his theory on the embryology and development of the valves in the veins, many more valves being laid down in fetal growth from the third to the fifth month, than survived to even the period of fetal maturity. Many of the valves continued to degenerate and were not present in the adult.

Delbet in 1913 (47), advocates the theory that the valves are placed at intervals in the veins with the idea of preventing a reverse flow of the blood distally in the extremities after it has been carried forward towards the heart. His conclusions are, there is a primary weakening of the valves in the external iliac veins, which allows a back pressure to develop against the valves in succession. Morro (47), believes the insufficiency of the valves first develops in the communicating veins between the superficial and the deep, thus allowing for a reverse flow from the deep system. Zancani, Fischer and Schmeiden, by experimental work showed that dilatation of the varices is not due entirely to back pressure as a result of defective valves. These men made anastomoses between segments of the saphenous vein and femoral artery, or femoral artery with the femoral vein. Rarely did dilatation of the veins occur.

Hesse and Schaak, found the valves of the saphena magna under normal conditions could withstand a pressure of 180 mm. of mercury. From these findings they explained the formation of varicose veins on the basis of accepting the normal back pressure in the venous system due to intra-abdominal pressure acting on weakened valves.

Harper (24), believes the etiology may be due to increased intra-abdominal pressure. The abdominal veins have no valves and blood may be forced either towards the heart or in the opposite direction. During violent abdominal straining the thigh muscles are contracted, which protects the deep veins, but the valves of the saphenous veins have been shown to give way at a pressure of about 180 mm. of mercury, which is not unusually high for abdominal pressure during violent muscular work. As the upper valves give way, more pressure is transmitted to those below and the whole superficial system of veins becomes a wide open channel. Schumacher and Lederhose (47), believe that weakening of the valves may occur secondarily to many factors such as congenital weakness, injury or inflammation. Kashimura, a prominent Japanese surgeon explains the formation of varicose veins on the basis of it being entirely a congenital proposition, but that during life there is a loss of nervous and muscular tone of the walls of the veins which allows dilatation to take place. He further states that varicose veins are rare among his

people in their own country. This he attributes to the fact the oriental people do there work in the sitting posture. It is also a fact that some of the most severe cases of varicose veins are found among the oriental people inhabiting this country. They no longer use the sitting position for doing work but stand for many hours of the day in their laundries, which would cause the same etiological factors to be present as are found in our people. Varicosities during pregnancy are not due to pressure of the gravid uterus on the veins of the pelvis, because this is impossible, nor to increased intra-abdominal tension, because this seldom exists to such a degree. DeLee (14), believes there is some obstruction to the return circulation from the legs, but there must be some change in the vessel wall or of the blood which predisposes to venostasis during pregnancy. He also states there is some relationship between varicosities and corpus luteum vasodilating ferment, for the pelvic vessels tend to dilate as pregnancy progresses. Also the veins tend to dilate as soon as conception has occurred and collapse if the fetus dies in utero. Löhr and Kownatske' explain the formation of varicosities during pregnancy as being due to the dilatation of the genital collection vein, with its great increase in the volume of blood in the uterus. They believe this would account for the increase of the compensatory back pressure in the external iliac and saphenous veins.

Infection Theory. Much can be said in favor of the infection theory as the causative factor in the development of varicose veins. The origin of infection may be embolic or hematogenous, or may occur by extension from the surrounding tissues, such as occurs following trauma and injuries. This could be followed by low grade phlebitis or periphlebitis which would not give rise to clinical symptoms and yet sufficient to initiate destructive processes in the vein wall, which later goes on to muscle degeneration in the media and formation of fibrous connective tissue. McPheeters quotes Thorel as believing the condition starts as endophlebitis, later extending to the media and vessel wall. The fact that varicosities are associated with infectious diseases i.e., typhoid, diphtheria, influenza and bronchial infections lends evidence to the theory that infections may be classed as a primary causative agent.

Zeas, also presents a theory, he believes bacterial toxins or hemotoxic substances liberated in the blood stream during infectious processes in the body are responsible for destruction of the vein wall. He also calls attention to the fact that varicosities are associated with scarlet fever, rheumatic fever, pneumonia and other infectious diseases. (54).

Endocrine Theory. Perhaps the most outstanding advocate of the endocrine theory associated with the development of varicose veins is Professor Sicard. In his theory, he

speaks of the three endocrine and ovarian periods of a woman's life. The first-- before puberty, the second--before menopause, and the third-- menopause and thereafter. He draws attention to the fact the blue cords develop at puberty, becoming larger with each menstrual period until pregnancy, at which time they may become quite larger, and finally menopause, at which time they may become extreme. If this physiological condition is due entirely to endocrine dysfunction, why can it not be remedied by administration of endocrine products? This has not been accomplished although effects have been made along these lines. Other evidence against this theory is that varicose veins rarely occur following hysterectomies and double ovariectomies.

SYMPTOMS

The most common symptoms resulting from varicosities are 1) sensations of heaviness or pain, 2) cramps of the legs, 3) fatigue, 4) and burning. (51) (49). These symptoms are not always proportional to the extension or the severity of the varices; often they are dependent upon the demands that are made on the lower extremities as the working in the erect posture. Now and then it may be some comparatively small varices that give the most trouble. As a rule women complain of pain in their varices during menstruation. (49).

GROSS PATHOLOGY

Berntsen, quoted by McPheeters, classifies the varicose veins according to the pathological formation present or the type of varices:

1. Isolated or saccular varix. It is usually present on the main trunk of the saphenous magna in the thigh.
2. Serpentine or sinuous varix. These two forms are encountered at the same time on the principal trunk of the saphenous and the collaterals.
3. Varix of uniform dilatation. One may call it the normal vein interposed between two varicosed parts of the vein, yet where the wall is hypertrophied on account of the abnormal pressure caused by the true varices on both sides. This is seen in all parts of the thigh and leg.
4. These are the fine cutaneous dilatations most frequently found on the inner thigh of fleshy individuals.

DIAGNOSIS AND DIFFERENTIAL DIAGNOSIS

In making a diagnosis of varicose veins, not only those veins which show apparent dilation, but also veins which cause pain must be considered. Many conditions occurring in the lower extremities assimilate varicosities, and for that reason a differential diagnosis must be arrived at.

McPheeters (47), believes that rheumatism is the most common cause of pain, with the rheumatic pains about the knee and ankle. Often the two conditions are associated, or there may be a primary varicose vein about the knee with a secondary rheumatic infection developing. The rheumatic pains often disappearing following the treatment of the varicosity. Sometimes patients are seen with arthritic pains of the hip which are secondary to varices. Abnormal tension on the skin may result in irritation of the nerve endings and result in pain assimilating any condition of the lower extremity. True sciatica must be differentiated from the sciatic type of pain associated with varices, periostitis secondary to congested varix, ostitis and polyneuritis. Buerger's disease is sometimes found associated with or assimilating varix of the lower extremity. Varicose veins may be secondary to the presence of pelvic tumors, in which case the pelvic pathology should be cared for first. Arteriovenous aneurism may be diagnosed as congenital varicose veins, as the mother may state the condition has been present since birth. The diagnosis in this condition is arrived at by determination of the estimation of the oxygen content of the varices as compared to that of normal veins and arteries. Probably the chief differential diagnosis to be made is between a simple varix and a compensatory varicosity which is the result of

blockage of the deep circulation. Harper (24), states that pigmentation is diagnostic of impaired nutrition from varicose veins.

Before any type of treatment is started a complete physical examination should be done, including a urinalysis and a careful abdominal and pelvic examination--the latter in search for possible obstructing tumors. Secondly, certain tests should be done to determine the patency of the deep femoral vein.(31). This test is called the Perthes test and is performed by having the patient stand, applying a tourniquet above the knee tightly enough to cut off the superficial venous return and then having the patient walk the length of the room several times. If the deep venous return is not open the patient will experience pain very soon throughout the leg. If the deep system is open, no pain will be felt and the dilated veins will tend to collapse. When the deep venous return has been found to be open, the next most important test is to see whether the arterial supply is sufficient. Pulsations are felt for in the dorsalis pedis and the tibialis posterior arteries. In doubtful cases Samuels test is made, wherein the leg is elevated to an angle of 45' and the ankle is alternately flexed and extended, white blanching of the plantar surface of the foot and pain in the calf are ascertained. (35). A more accurate test can be used if needed. This is the so-called histamine acid phosphate

test as described by Sir Thomas Lewis of England. A 1:1,000 solution of histamine acid phosphate in physiological solution of sodium chloride is applied with a medicine dropper to the skin and six or seven punctures with a fine hypodermic needle are made through it, within a few minutes a response is observed. This consists of a small purple-red area, followed by a wheal and surrounded by a red flare around the puncture. This is the normal response. The degree of the flare and the latent period of its appearance are the points to be observed and recorded. (15). If the arterial system is not impaired, the question now arises as to just what veins should have treatment. In deciding this, two other tests are done. These are the Trendelenburg tests. With the patient lying on a table or bed the leg is elevated so that the vein drains out and a tourniquet is then applied above the knee. The patient is then asked to stand. If the veins fill quickly from below upward, it means that the valves of the communicating veins are incompetent and the deep system is overflowing into the superficial. This is called the Trendelenburg Negative test. If one should release the tourniquet as soon as the patient stands up and the saphenous fills rapidly from above, it is a sign that the valves at the sapheno-femoral opening are incompetent. This is the Trendelenburg positive test. A combination of the two tests is called a Trendelenburg Double test. (31).

Mahorner and Ochsner (43), presented to the profession a new test for determining incompetency of varicose veins. The test is carried out as follows: The patient is disrobed sufficiently to show the thighs and legs. The observer arranges himself so that the best possible observations can be made. The patient then walks to and fro in front of the observer, who carefully notes any changes in the size of the veins as compared with their size in the standing position. After the patient has passed in review several times in this fashion, a tourniquet is tied around the upper third of the thigh, sufficiently tight to compress the superficial veins. The patient again walks to and fro several times, and the observer notes any changes in the prominence of the varicosities. The procedure is carried out with the tourniquet in the mid-thigh and lower third of the thigh. Observations and comparisons being made with previous findings. In instances in which the greatest improvement is seen when the tourniquet is around the lower third of the thigh, some variable must account for the fact that the improvement is greater under this condition than when the tourniquet is around the upper third of the thigh. This further improvement indicates not only that the retrograde flow through the saphenous vein comes through the main opening into the femoral vein but that there is a back-

ward flow below the highest application of the tourniquet which is caught when the tourniquet is moved lower. This backward flow is undoubtedly through incompetent communicating veins between the superficial and the deep system of the thigh. It seems therefore according to these observers, that if there is incompetency not only of the valves of the long saphenous and the femoral vein, the lower the ligation in the thigh the more improvement in the condition can be expected.

TREATMENT

The literature dealing with the injection treatment of varicose veins with sclerosing solutions has become quite enormous, and for that reason my discussion will be limited to the injection treatment of varicosities and solutions used within the past decade.

Until 1927 the solutions of choice for injection therapy of varicose veins were sodium citrate, quinine solutions, sodium salicylate 25% and sodium chloride 10%. During the same year McPheeters recommended the use of sodium chloride 20%. (48). In 1929 Colt (10), reported good results with the use of sodium salicylate, with the exception of pain radiating down the extremity which lasted rarely more than a minute following injection. Kilbourne (33), advocated the use of strong solutions of sodium salicylate or quinine

and urethane solution in doses not larger than 2 c.c..

He states that the sclerosing agent is very toxic and must be injected slowly. At this same time Kilbourne made a survey to determine the mortality of surgical treatment in comparison to injection treatment. He reports the mortality by injection cannot be so accurately determined, but a study of about 50,000 cases shows that it is less than one in four-thousand as compared to one in every two-hundred fifty cases treated by surgical methods. Recurrences after operation average 30% and following injection therapy only, 6%. Schmier (65), recommended the use of sodium chloride 20-40% strength. Although the injections were quite painful and the danger of slough formation was more marked than with other solutions. In 104 cases treated by this method, 417 injections were given, averaging 4 injections per case. One case required 24 injections to effect a cure in both limbs. Rogers (60), states that he first prepared sodium morrhuate in 1919 in Calcutta for use in leprosy and tubercle, and found in strengths over 3% it caused a strictly localized mild inflammation of the vein wall, followed by firm fibrous occlusion of the vessel; just as did the intravenous injection of sodium hydncarpate and gynocardate which he reported in 1916. Kittel (36), while using sodium morrhuate for intravenous injections for therapuetic purposes other than varicosities noted its action upon the vein injected and advocated its use in treatment of varicosities. After

careful observation and experimentation over a prolonged period he obtained the following statistics; 1) sodium morrhuate has no toxicity, and amounts up to 10-12 c.c. of the 10% solution have been given at one time, 2) no general symptoms occurred in any of these treated with sodium morrhuate, 3) the effect on the injected vein is usually quite prompt and striking, 4) vein at the site of injection becomes hard within a few moments for a distance up to an inch, 5) on withdrawal of the needle, the puncture seals itself quickly and subsequent extravasation does not occur, 6) sodium morrhuate for practical purposes is innocuous to the subcutaneous tissues, 7) reactions on the vein injected produces very little discomfort. Kittel states, that during there series of 187 cases there were no instances of necrosis and there were only 13 known instances of periphlebitis. Zimmerman (76), although advocating the use of sodium morrhuate states that some individuals are sensitive to this type of therapy. At the same time Kittel published his statistics on sodium morrhuate, Winchester (74), reported a case of unconsciousness following intravenous use of sodium morrhuate and requiring the use of stimulants to produce consciousness. He states that the sclerosing effect of the substance was most satisfactory, but feels inclined to doubt the safety of the drug after his recent experience. During 1931 Cattell (7), recommended the use of quinine and urethane solution in

treatment of varicosities, or varicosities complicated by ulcer formation. Lewis (38), also believes the solution to be superior to other solutions used because of ease of administration and the small quantity required to give results. According to Johnson (30), quinine-urethane solutions became more popular in European clinics while hypertonic solutions of dextrose and sodium chloride were found to be more popular in America. He does believe the quinine solutions have some advantages such as, formation of a firm thrombus following the use of small amounts of the material, but were over-shadowed by its disadvantages, toxicity, danger of sloughing as a result of escape of fluid into the surrounding tissues, and pain caused by injection. The disadvantages were somewhat reduced by the addition of urethane to the solution. In 1932 Tunick and Nach (70), reported 200 cases which they treated with sodium morrhuate and obtained excellent results. In all cases a firm obliteration of the vein was produced with little phlebitis, no toxic symptoms were noted, and no complaints of cramps or pain following injection were made by their patients. During the same year, Kilbourne, Dodson and Zeiler (34), carried out a number of experiments to determine the toxicity, slough producing qualities, and bactericidal powers as related to phlebitis and embolism of various solutions used in the treatment of varicosities. They concluded that mercury bichloride was too toxic being found to be fatal in

three cases; metaphen, less toxic and not likely to cause a slough. Sugar derivatives, and sodium chloride, are non-toxic and relatively painless. Unlike quinine-urethane they are not self sterilizing or bactericidal. Sloughs they produce are less serious than the salicylates and quinine sloughs. Sodium salicylate is efficient as a sclerosing agent, bactericidal, and causes painful cramps following injection and produces a more serious slough than those following sugar derivatives and sodium chloride. Sodium morrhuate is not toxic, sloughs are not as serious as the salicylates and quinine sloughs, but it is not bactericidal or self sterilizing. They believe the sclerosing agent of choice is quinine-urethane because of its bactericidal action. Because of the many cases being reported in the literature concerning the toxicity of sodium morrhuate, Praver and Becker (57), made studies of the sensitization following the injection of sodium morrhuate and reported seven out of one hundred-seventy-five patients receiving 783 injections showed sensitization reactions to the solution. During the same year Barker(3), states that although sodium morrhuate is thought to be more toxic than other sclerosing agents, it is still the solution of choice at the Mayo clinic. The search still continued for the ideal sclerosing agent and it has centered mainly around the solutions of fatty acids or the salts of these acids. Postlethwaite (56), recommended the use of sodium ricinoleate 2% solution, instead of the 5% solution which had been

used by Froehlich. He states that the 2% strength is sufficiently active to produce sclerosis without the danger of recanalization and less likely to cause the appearance of toxic symptoms. Johnston (31), used 5% sodium ricinoleate in combination with ligation of the great saphenous vein, and obtained good results. Biegeleisen (4), in 1937 presented four new solutions which are supposed to be the active ingredients found in older preparations used as sclerosing agents in treatment of varicosities. All contain fatty acids:

1. Moru-quin. Combination of sodium morrhuate and quinine. The morrhuate being present in the greater concentration and is therefore the more important ingredient.

2. Oleate quinine. Composed of 5% potassium oleate, 2% quinine alkaloid and 2% Benzl alcohol in water.

3. Sylnasol. Composed of salts of fatty acids derived from the psyllium seed oil.

4. Monoethanolamine Oleate. Composed of organic base combined with oleic acid. Biegeleisen, believes all solutions to be less toxic than sodium morrhuate and are good sclerosing agents, more so the latter one mentioned. Using Monoethanolamine oleate for 500 injections, patients have not complained of toxic symptoms, no pain or cramping on injection and but slight discomfort due to perivascular injection; sloughing was not observed in the total number of injections. Meyer (50), because of the allergic reactions

occurring with the use of sodium morrhuate advocates the use of a new synthesized sclerosing agent, Monoethanolamine oleate. In a clinical trial on 43 cases, a total of 345 injections were given. In every case a good thrombus could be produced either at first or subsequently on injection. There were no cases of slough or any evidence of allergic reaction. Meyer, believes this agent superior to sodium morrhuate because it is of known standard composition, more stable in solution, and has less tendency to produce allergic reactions. Schwartz and Wolfort (66), have used three different solutions at the Jewish Hospital of Brooklyn, with more than 3000 injections. There results show that 30% saline produced the most uniform results, 5% sodium morrhuate second, and a solution of 30% saline and 50% glucose was third.

The treatment of varicosities during pregnancy has brought about several disputable questions, mainly, what solution should be used. Quinine-urethane has been stated by many to be contra-indicated for use as sclerosing agent during pregnancy. Solomons (67), in a study of sixty cases of pregnant women treated with quinine-urethane, obtained satisfactory results in 97% of the cases with no serious complications occurring. He also found that the use of quinine-urethane during pregnancy does not affect the uterus.

Although good results have been reported in the use

of sclerosing agents alone in the treatment of varicosities the trend of treatment during 1937 and 1938 began to shift to the combination of ligation and injection treatment as practiced by Par'le in 1579 and Howe in 1797.

Johnston (31), recommends the combined ligation and injection therapy especially when the valves at the sapheno-femoral junction are impaired. Although he does not state how many cases have been treated by this method, he does state that no reoccurrences have occurred. Johnston, recommends the use of sodium ricinoleate in this type of treatment. Zimmerman (75), Hendrick and Owers (27), Rosenbaum (61), recommend the combination ligation and injection treatment of varicosities using sodium morrhuate 5% as the sclerosing agent. Mahorner and Ochsner (42), believe the greater number of permanent results will be obtained by the combined ligation and injection treatment of varicose veins. Faxon and Barrow (21), found in 367 cases treated by the combined ligation and injection treatment, 55% showed perfect results, 25% satisfactory and 20% failures. The failures they believe due to faulty operative technique. They recommend the use of quinine-urethane as the sclerosing agent. Veal and Van Werden (71), carried out a number of experiments on twenty-one patients which were to be treated for varicosities by high ligation. They found following high ligation of the saphenous vein, 1) the rate of blood flow is slowed, 2) blood flow ceases entirely

in the upper segment of the ligated vein, 3) at the point of injection the flow is both upward and downward, 4) below the knee the flow is downward and the rate is slower than before ligation. Other studies were made, by which they showed that there is a rapid readjustment of the venous pressure in the varicosities, seems to indicate that pressure changes play no part in the beneficial results obtained by the ligation of the saphenous vein. Horgan (29), recommends the use of sclerosing agents, especially sodium morrhuate, ligation plus stripping in the treatment of varicosities. Clarkson (9), recommends the use of sclerosing agents preferably sodium morrhuate, only in cases where the vein in which the valvular deficiency does not extend to the valve at the sapheno-femoral junction. He believes that ligation therapy should accompany injection therapy when the valve at the sapheno-femoral junction is incompetent. During 1938 Verovitz (72), completed ten years of experimental work with various solutions used in the treatment of varicosities. In seventy-five cases he found that quinine-urethane used as a sclerosing agent was too toxic, caused considerable pain following injection, much slough, and does produce cinchonism on patients having an idiosyncrasy to the drug. Sodium salicylate in 450 cases gave the most marked sclerosing, but also the most marked cramping. The drug is very toxic and patients complain of headaches and ring-

ing in the ears (salicylism). Varisol (NaCl 10%) does not contain the necessary qualifications to make it an ideal sclerosing solution, although many patients have been satisfied with its use. Sodium morrhuate was found to be dissatisfactory only because of allergic sensitivity to the solution by many individuals. Verovitz, believes the solution of choice to be, Moru-quin. In 1500 cases, he found its sclerosing action to be quiet rapid and positive, cramping of muscles was reduced to the minimum, little tendency to produce gangrene or sloughing and is relatively non-toxic. Sarma (62), reports good results in 958 cases following ligation and injection treatment of varicosities. He believes the solution of choice is sodium morrhuate or monoethanolamine oleate. Glasser (22), advocates the use of monolate, a new sclerosing solution which has been used in 550 injections without untoward reactions. Monolate is composed of monoethanolamine oleate 5% with benzl alcohol.

TECHNIQUE OF INJECTING SCLEROSING AGENTS

Before any attempt is made to inject a sclerosing solution those veins to be injected should be determined. This may be done by having the patient stand. The varicose veins will become distended, as occurs during daily work. Then the sites for the injections into the varicosed seg-

ments are selected and marked with an applicator with 5% merurochrome. (47). The patient is placed in a prone position, or the leg only may be held in a horizontal position. In this position the blood is the most stationary and relaxation of the calf muscles permits the injected fluid to stay in place for a longer period of time.(17). This position furthermore is preferable for it permits as little blood as possible in the vein, thereby preventing unnecessary dilution of the hypertonic solution and insuring better contact of the irritant fluid with the intima.(17)(30). After the selected site of injection is gently rubbed with alcohol, an intravenous needle, with short bevel preferably of rustless steel and on a 5 or 10 c.c. Luer-Lok syringe is inserted into the vein.(17). The use of too small a needle slows up injection and causes unnecessary dilution of the solution.(30). As soon as blood can be aspirated into the syringe, the second and third fingers of the left hand gently strip the vein proximally and distally from the inserted needle, and maintain compression on the segment to be injected. Thus the vein is emptied as much as possible before the injection is made. Following injection of the sclerosing solution the needle is withdrawn, a dental pad or piece of sterile gauze is placed over the site of injection and is pressed against the vein with a wide adhesive tape or elastic pressure bandage. McPheeters, states it is no longer necessary that veins be kept coll-

apsed after injection, for a better obliteration follows a full thrombus. (30). There is no restriction as regards to work. Patients may assume their regular duties.

COMPLICATIONS ASSOCIATED WITH VARICES

The most common condition associated with varices is the development of an infectious thrombophlebitis. (19)(47). This occurs in the superficial and deep group of veins in the lower extremity. Large varices of the superficial system predispose toward the development of a thrombophlebitis of the deep system, and a deep thrombophlebitis is thus more liable to develop with large varices of the superficial system present than otherwise. The blood of the large varices of the superficial system is either stagnated or flows in the reverse direction. With this concept in mind it is easy to understand the blood is more poorly oxygenated than any other blood in the system and consequently more susceptible to infection. The infection may arise from some distant foci of infection followed by the formation of a hard clot or thrombus and the sacculated veins becoming very painful and tender. Edwards (19), divides thrombophlebitis into two types. First, "ulcerating phlebitis", which he refers to as thrombophlebitis of the surface veins at the ankle and on the foot. In these cases, the skin is invariably adherent to the super-

ficial veins and sloughs occur, forming ulcers which are resistant to treatment. Second, "chronic sclerosing phlebitis" is a spontaneous chronic inflammation of the surface veins of the leg which goes on for months or years and ultimately cripples or destroys the valves of the saphenous system.

Congestion of the skin associated with the presences of varices at times causes a very intense dermatitis, and later on an eczema, which may be of the most extensive, moist and oozing type. (47). Rarely is there made mention in the literature of hemorrhagic varices. This condition occurs quiet frequently as a result of light trauma or spontaneous rupture. Probably the most severe and extreme condition which develops as a complication associated with varicose veins is varicose ulcer. (59). Circulatory disturbances resulting from either experimentally produced venous stasis or obstruction of the arterial blood supply have been claimed to produce the changes of chronic arthritis. McMasters (46), presented a study of 30 cases of varicose veins of long standing in which definite and prolonged edema of the ankles and feet had existed. In 21 cases chronic arthritis of the joints of the ankles or foot could not be demonstrated roentgenographically. Nine of the 30 cases showed roentgenographic evidence of chronic arthritis of the joints of the ankle and foot, but in each there was associated ulceration of

the leg or near the ankle joint in addition to the passive congestion from existing varicose veins. Ossifying periostitis of either the tibia or the fibula or both did not occur from venous stasis alone, but did occur in seven cases in which ulcerous lesions existed with the varicose veins. Oldham (55), reported a case of chronic ulceration of the leg for a duration of twenty years accompanied by arthritis of the leg and elbow joint. Following intensive treatment of the ulcer, the arthritis cleared up with limitation of movement. Edwards (19), states if the course of inflammation is allowed to progress in the superficial veins, by way of the perforators the deep veins are involved and pulmonary emboli are formed. Following the injection of sclerosing solutions, Probststein (58), reports 5 cases which resulted fatally in the production of pulmonary emboli. He believes the emboli do not occur so frequently in the bedridden patient and states the cooperation of the patient after injection in discontinuing the routine daily activities will lessen the frequency of pulmonary emboli. Westerborn (73), found among 30,000 cases treated by injection of quinine-urethane solution, death occurred in eleven and severe pulmonary embolism with recovery in five. Mortality rate being .037%. Several cases have been reported wherein the use of sodium morrhuate as a sclerosing agent has resulted in allergic reactions.(25)(45)(12).

CONTRAINDICATIONS TO INJECTION TREATMENT

Certain contraindications to injection treatment of varicosities must be observed, or severe complications may develop. Extreme disability should be a contraindication to extensive injection treatment. It is sometimes justifiable, however, to obliterate those veins directly causing symptoms. This is particularly true in the case of ulcers. (30). Patients with the history of white leg, or in whom the deep veins have become occluded by infection, must not be treated by injection, so that it is essential to ascertain whether the varicose superficial veins are acting only as a means of compensation, but a history of old phlebitis is not necessarily a contraindication as the deep circulation may be effective. Johnson, is of the opinion that the chief contraindication to any type of therapy is thrombophlebitis. The presences of inadequate arterial circulation should be noted, since the tissues will only withstand the mildest reaction. (67). If the deep circulation has been the site of extensive thrombophlebitis in the past, it is unlikely that any type of therapy will be of any benefit, and it may do great harm. De-Takats, beleives if the injection is carried out the inflammatory process may be activated and emboli may be formed. (16). Some authorities on varicosities beleive that arterial diseases may be activated following injection treat-

ment. (76). One of the greatest drawbacks to injection treatment is the simplicity and ease of doing it. For this reason many unexperienced in its use will have numerous accidents. Christopher (8), strongly advises against injection of varicose veins in, 1) cases of senile arteriosclerosis of the leg with lack of pulsation in the dorsalis pedis and posterior tibialis arteries, 2) cases with past history of phlebitis, 3) having subacute pelvic infections or acute pharyngitis.

The Varicose Vein Committee of the American Medical Association at its exhibit on varicose veins at the 1930 meeting gave the following as contraindications to the injection treatment of varicose veins:

1. Systemic diseases.

- a). Hyperthyroidism (requires immediate arrest of the disease; precedes in importance any other intervention).
- b). Active Tuberculosis. Subfebrile patients with slight pulmonary changes may flare up after the use of tissue irritants.
- c). Acute colds, infections. These conditions may be seen in office patients and may be overlooked or neglected.

2. Local conditions.

- a). Impairment of arterial circulation.
- b). Lack of patency in the deep veins. Determin-

ed by Perthes test.

- c). Thrombophlebitis, edema with history of deep phlebitis.
- d). Acute or subsiding superficial phlebitis.

SUMMARY AND CONCLUSIONS

In summary, it may be said that the modern or present day treatment of varicose veins consists of occluding them by the injection of sclerosing solutions. The combination of this method with ligation of the saphenous or incompetent communicating veins, where indicated is the treatment of choice. At present 5% sodium morrhuate and monoethanolamine oleate seem to be the solutions of choice. Other new sclerosing agents such as Monolate have been introduced into the profession and may prove to be more satisfactory than either of the two sclerosing agents mentioned.

BIBLIGRAPHY

1. Adams, Francis : translation "Works of Hippocrates",
Wm Wood Co, New York. 1886 Vol.2
Page 305.
2. Aegeneta, Paulus : New Sydenham Series 1846 2:406
3. Barker, N.W. : Diseases of Veins. M. Clinic of
North America 19:535-43, 1935.
4. Biegeleisen, H. : Fatty Acid Solutions for Injection
Treatment of Varicose Veins. Eval-
uation of Four New Solutions.
Annals of Surgery 105:610-615,
1937.
5. Borchardes, W.A. : Treatment of Varicose Veins by
Organic Arsenic Injections.
British Med. J. 1:375, 1927.
6. Brodie, Sir. B. : Lectures illustrative of Various
Subjects in Pathology and Surgery.
London: Longman, Brown, Green and
Longman, 1846.
7. Cattell, R.B. : Treatment of Varicose Ulcer. Surgical
Clinic of North America 11:291-303,
1931.
8. Christopher, Frederick : Text-book of Minor Surgery,
page 172. Published by W.B.
Saunders Co. 3rd Ed.
9. Clarkson, Patrick : Modern Classified Treatment of
Varicose Veins. Lancet 2:69-73,
July 9, 1938.
10. Colt, G.H. : Modern Treatment of Varicose Veins.
British Medical J. 525-28, Sept. 22, 1928.
11. Cunningham, D.J. : Text-book of Anatomy. "Veins of the
Lower Extremity", 2nd Ed. Published
by Wm Wood and Company.
12. Dale, Maurice L. : Complication- Sodium Morrhuate In-
jections. J.A.M.A. Feb'y 1937.
13. Dawkins, Alec. L. : Varicose Veins and Ulcers, their
Treatment and Etiology.
M.J. Australia 1:603-09, 1933.

14. DeLee, Joseph B. : Varicosities in Pregnancy.
Text-book, 5th Ed. Published by
W.B. Saunders Company. 1930.
15. deTakats, G. : The Impairment of Circulation in the
Varicose Extremity. Arch. Surg. 18:
671, Feb'y 1929.
16. deTakats, G. : "Resting Infection" in Varicose Veins.
Diagnosis and Treatment.
American J.M. Sc. 184:57-66, 1932.
17. deTakats, G. and Quint, Harold ; Injection Treatment
of Varicose Veins. S.G.&O.50:545-
561, 1930.
18. deTakats, G. : Causes of Failures in the Treatment of
Varicose Veins. J.A.M.A. 96:1111, 1931.
19. Edwards, Edw. A. : Thrombophlebitis. S.G.&O. 66:236 -
245, Feb'y 1938.
20. Edwards, Edw. A. : Treatment of Varicose Veins.
S.G.&O. 59:916-928, 1934.
21. Faxon, Henry H. and Barrow, David W. ; The End-Results
of High Ligation and Injection in
Treatment of Varicose Veins.
Surgery 3:518-27, April 1938.
22. Glasser, Thomas S. : A New Sclerosing Drug for Varicose
Veins. "Monolate".
Am.J. Surgery 39: 120, Jan. 1938.
23. Gray, Henry : Anatomy of the Human Body. Text-book.
Veins of the Lower Extremity. 22nd Ed.
Published by Lea and Febiger.
24. Harper, J.W. : Etiology and Treatment of Varicose Veins.
Tri-State Med. J. May 1936 P.1645.
25. Hatcher, Milford B. and Long, Harold W. ; Complications
of Varicose Veins. J.M.A. Georgia
26:427-28. August 1937.
26. Hawks, Geo. : Varicose Veins. Penn.Med.J. 1931-34 P.859.
27. Hendrick, J.A. and Owers, Albert : Present Treatment of
Varicose Veins of the Lower Extremity.
Tri-State M.J. 9:1874-75. July 1937.

28. Hill, L. : Royal Society of London 57:192, 1895.
quoted by Starling.
29. Horgan, Edmund : Varicose Veins with Special Reference to Treatment by Ligation, Stripping and Injection. Surgery 3:528-33. April 1938.
30. Johnson, G.S. : Recent Advances in Treatment of Varicose Veins. Surgery 2:943-66. December 1937.
31. Johnston, C. Harlan : Combined Ligation and Injection Treatment of the Varicosed Great Saphenous Vein. J.A.M.A. 109 No.17 Page 1359 Oct. 1937.
32. Keller, Wm. L. : New Method of Extirpating the Internal Saphenous and Similar Veins in Varicose Conditions. Preliminary Report, New York M.J. & Philadelphia M.J. 82:385, 1905.
33. Kilbourne, Norman J. : Treatment of Varicose Veins of the Leg. J.A.M.A. 92:1320. April 1929.
34. Kilbourne, Norman J., Dodson, Wm, and Zeiler, A.H. : Varicose Vein Solutions. S.G.&O. 54:640-49, 1932.
35. Kilbourne, Norman J. : Varicose Veins, Indications & contraindications to Injection. Annals of Surg. 93:691. March 1931.
36. Kittel, P.B. : Use of Sodium Morrhuate in Treatment of Varicose Veins by Injection. Lancet 1:68-69. 1930.
37. Klotz, K. : Etiology of Varicose Veins. quoted by McPheeters.
38. Lewis, Kenneth M. : Injection Treatment of Varicose Veins. Annals of Surg. 95:727-733. 1932.
39. Macleod, J.J.R. : Physiology of Venous Flow. Physiology of Modern Medicine. Text-book. 7th Ed. 1935.
40. Madelung : Verhandl. d. deutsch. Gesellsch. f. Chir. 13:114, 1884. quoted by G.S. Johnson.

41. Mayo, C.H. : Treatment of Varicose Veins.
S.G.&.O. 2:385, 1906.
42. Mahorner, Howard R. and Ochsner, Alton : Modern Treatment of Varicose Veins.
Annals of Surg. 107:927-51. 1938.
43. Mahorner, Howard R. and Ochsner, Alton : A New Test for Evaluating Circulation in the Venous System of the Lower Extremity Affected by Varicosities. Arch. of Surg. 33:479-92. 1936.
44. Maximow, Alexander A. and Bloom, Wm. : Histology of Veins, Text-book of Histology. Published by W.B. Saunders Company. 1930.
45. McCastor, J.T.N., and McCastor, Mary Cousen : Reaction of Sodium Morrhuate Injection.
J.A.M.A. 109: 1799-1800. 1937
46. McMaster, Paul E. : Influence of Venous Stasis on the Production of Chronic Arthritis. Arch. of Surg. 35:833-40. 1937.
47. McPheeters, H.O. : Varicose Veins with Special Reference to the Injection Treatment. Text-book 3rd Ed. Published by F.A. Davis Company 1931.
48. McPheeters, H.O. ; Injection Treatment of Varicose Veins by the Use of Sclerosing Solution s.
S.G.&.O. 45:541-47. 1927.
49. Meisen, V. : Varicose Veins and Hemorrhoids and their Treatment. 616.14 M47 1932 University Library.
50. Meyer, Nathaniel E. : Monoethanolamine Oleate.
Am. J. Surg. 40:628-29. 1938.
51. Nicholson, Berlin B. : Etiology and Treatment of Varicose Veins. Arch. Surg. 15:351-76. 1927.
52. Miller, Robert T., Jr. : The Results of Operative Treatment of Varicose Veins of the Legs by the Methods of Schede, Trendelenburg and Bull. John Hopkins Hosp. 17:289, 1906.
53. Nobl, G. : Der Varicöse Symptomenkomplex. Berlin & Wien. 1918. quoted by Meisen.

54. Nobl, G. : Artificial Obliteration of Veins showing Varicose Degeneration. Wien. Klin. Wchnschr 1926 xxxix Supp xlv 1-16.
55. Oldham, J.B. : "Acute Suppurative Arthritis as Complication of Varicose Ulceration". Lancet 2:576. 1937.
56. Postlethwaite, F.M. : Treatment of Varicose Veins with 2% Sodium Ricinoleate. J. Missouri M.A. 33:346-49. 1936.
57. Praver, L.L. and Becker, S.W. : Sensitization Phenomena Following Use of Sodium Morrhuate for Chemical Obliteration of Varicose Veins. J.A.M.A. 194: 997. 1935.
58. Probststein, J.G. : Complications of Varicose Veins. J. Missouri M.A. 33: 349-352. 1936.
59. Robb, Douglas : Varicose Veins and Complications. Australian & New Zealand J. Surg. 7:291-309. 1938.
60. Rogers, Leonard : Intravenous Sclerosing Solutions. British M.J. P.120 July 19, 1930.
61. Rosenbaum, Carl A. : Treatment of Varicose Veins. Arkansas Med. Soc. 35:59-60. 1938.
62. Sarma, P.J. : Clinic. Saphenous Vein Ligation. Surg. Clinic of North America 18:129-39. 1938.
63. Schede, M. : Ueber die operative Behandlung der unter-scherkelvaricen. Berl. Klin. Wchnschr. 14:85. 1877. quoted by G.S. Johnson.
64. Schiassi, B. : Semaine Me'd. 28:601. 1908. quoted by Meisen.
65. Schmier, A.A. : Sclerosing Solutions in Injection of Varices of the Lower Extremity. J.A.M.A. 94:1222-26. 1930.
66. Schwartz, Wm. A. and Wolford, B.E. : Ambulatory Treatment of Varicose Veins. J.A.M. Inst. Homeopathy. 30:214-17. 1937.
67. Solomons, Edw. : Treatment of Varicose Veins in Pregnancy. J. Ob. & Gyn. Brit. Emp. 44:650-58. 1937.

68. Starling, Ernest H. : Physiology of Venous Flow in the Lower Extremity. Text-book. P.788. 7th Ed. 1936.
69. Trendelenburg, : Über die Unterbindung der Saphena magna beim Unterschenkelvaricen. Beitr. zur Klin. Chir. 7:197, 1891. quoted by Meisen.
70. Tunick, Isidor S. and Nach, Robert : Sodium Morrhuate as a Sclerosing Agent in Treatment of Varicose Veins. Annals of Surg. 95:734-37. 1932.
71. Veal, J. Ross, and Van Werden, Benjamin Dekalb : Physiologic Basis for Ligation of the Great Saphenous Vein in Treatment of Varicose Veins. Am. J. Surg. 40:426-431. 1938.
72. Varovitz, C.H. : The Results of Ten Years Experimentation with Various Solutions used in the Injection Treatment of Varicose Veins and Ulcers of the Legs. Ohio State M.J. 34: 37-46. 1938.
73. Westerborn, A. : Fatal Pulmonary Embolism in Sweden following Injection Treatment of Varicose Veins. Int. Abstract of Surg. 64:495. 1937.
74. Winchester, A.H. : Letter to the British Med. Journ. July 19, 1930 P.120-121.
75. Zimmerman, Leo. H. : Modern Management of Varicose Veins. Ill. M.J. 71:444-47. 1937.
76. Zimmerman, Leo. H. : Allergic-like Reaction from Sodium Morrhuate. J.A.M.A. 102:1216-17. 1934.