Peripheral vascular disease: with particular stress on the early diagnosis and conservative non-operative treatment

Don. Blume
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PERIPHERAL VASCULAR DISEASE: WITH
PARTICULAR STRESS ON THE EARLY DIAGNOSIS
AND CONSERVATIVE NON-OPERATIVE TREATMENT

DON BLUME

SENIOR THESIS
Presented to the College of Medicine,
University of Nebraska, Omaha.
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INTRODUCTION
This paper deals primarily with the early diagnosis and the conservative, non-operative treatment of peripheral vascular diseases. The surgical treatment, especially that of the sympathetic nervous system has been purposefully avoided, because as yet, according to the literature, it isn't established on a sound physiological basis. Furthermore, as many authors state, in this group of diseases one is dealing with a local manifestation of a generalized systemic disease, and by the use of sympathetic surgery we are in no way aiding the individual in combatting this disease.

Interest in this group of diseases was stimulated by seeing several such cases in the wards. Since then from reading the literature on these conditions, it has become apparent that many people are afflicted, with very little attention paid to pains which come and go until severe complications have developed, necessitating amputation to save life or to secure comfort from excruciating pain.

It also is apparent from the literature that peripheral vascular diseases often go unrecognized by the medical profession. Although all other body systems are thoroughly checked and rechecked, the peripheral vascular system is never investigated. Patients may come to one's office with characteristic symptoms and signs which get
passed over by being called rheumatic or neuritic pains.

Another factor which stimulated interest is that the life span has increased a number of years, and since infectious diseases are no longer taking the toll of life they used to, their place in medicine is being taken by the degenerative types of disease. Peripheral vascular disease, especially the obliterative types, falls in this category. Therefore, one must look for preventative and curative measures to combat them.

In reviewing the literature in preparation for this paper, only the more recent literature was studied. Most stress has been put on the obliterative types of the disease while little attention is paid to the vasospastic or vasodilatating types, because the former are more commonly seen and carry with them the more severe consequences if not treated early and properly.
Peripheral Vascular Disease has existed for a great many years. Although it has been recognized, it had never been treated with any vigor until about ten years ago. Reisman (62) states, "Almost before we were aware of it, a striking innovation appeared in medical nasography and medical practice. A new specialty has developed which was hardly dreamed of three or four years ago—a specialty dealing with diseases of the blood vessels.

"In our textbooks the subject of these diseases, particularly those concerning the arteries, is dealt with largely as static—uninterestingly and briefly. But, within a very short period of time, diseases of the blood vessels have become a dynamic active branch of medicine with a rapidly growing literature of its own. Some may decry such intensive specialization upon one field, but it cannot be denied that concentration upon one field broadens one's knowledge, though it may narrow the broadeners of the particular disease. The new specialty, which might be called 'angiology', has already a large number of devotees in this country and abroad, and is bringing under its aegis diseases that previously did not seem to have any connection with it. In a number of hospitals special vascular clinics have been created and the men in these clinics are taking
their places beside the cardiologists and the allergists.

"When we look into the history of the subject, we find, as in nearly every other phase or department of medicine or science, that its roots go far back and that we are by no means the pioneers that we may fondly think ourselves. As is pointed out so wonderfully, in Thomas Mann's 'Joseph and His Brothers', when we come to what seems to be the beginning though want of knowledge may make it seem so. Therefore, when we start in 1773 with Stephen Hale's 'Haemodynamics', it is in implied recognition of Mann's Thesis. Hale's was seemingly the first to advance the notion that the arteries were contractile. With plain water he perfused an aorta and its mesenteric vessels at a constant pressure head and noted the outflow to be greater when the fluid was warm. Investigating also the effect of alcohol and extract of cinchona bark, he was led to conclude that some drugs caused contraction and some dilation.

"Weber appears to have been the first to assume a nervous control of contraction, advancing the hypothesis to explain blanching and pallor on one side and blushing on the other. Perhaps before Weber, Allen Burns in 1809 explained Angina Pectoris on the basis of a spasmatic contraction of the coronary arteries—a very
ingenuous and fertile thought. The muscular cost of the arteries was not described until 1840 when Henle reported its existence and then Bernard in 1831 noted the effect of cutting the sympathetic nerve on the vessels of a rabbit's ear and the effect of stimulation of the nerve. With these cumulative observations, the relation of the sympathetic nervous system to the caliber of the blood vessels become firmly established.

"The earliest clinical observation is probably that of Charcot in 1858 on Intermittent Claudication, a condition described as occurring in horses by Boulay in 1831. Four years after Charcot's publication, there appeared what is still the most important essay in the entire field of vascular disease, namely Raynaud's classical thesis on 'Local Asphyxia of Symmetrical Gangrene of the Extremities'. Galtz in 1847 suggested the existence of a vasomotor mechanism in the peripheral vessels, in the ganglion cells of vasomotor nerves.

"The next milestone is represented by Pal's epoch making monograph on Vascular Crisis. After the lapse of a dozen years Buerger's masterly article on Thrombo-Angiitis Obliterans appeared and marks another milestone. Since then the literature has grown so fast that it is impossible to do it justice. Other outstanding contributions are: Krogh's pioneer work on the capillaries;
that of L'eriche, the father of Sympathectomy; that of Cannon on the sympathetic nervous system and the endocrine glands; that of Sir Thomas Lewis and his associates on the capillaries; that of Brown, Adson, and other members of the Mayo Clinic on various phases of vascular disease; the work of Lechtwitz, Alice Bernhein, Starr, Landis, Scott, Kramer, Herrmann, Bastar, Dagliotti, and many others."
INCIDENCE
The incidence of Peripheral Vascular Diseases is much higher than is generally thought. de Takats (21) believes there are thousands of individuals who are unconscious or only mildly conscious of a progressive interference with their peripheral circulation. These individuals may have pulseless arteries in their feet, but they still remain in a compensated stage whereby their collateral circulation is well enough established to carry on adequate circulation, but their margin of safety is minimal. Their "rheumatic" pains come and go with changes in the weather, mechanical stress, or emotional load. Occasional numbness or tingling of the extremities is disregarded. In many instances these individuals undergo an annual or semi-annual physical examination in which the peripheral circulation is ignored, although other body systems are thoroughly checked and rechecked. These are the individuals who should have their peripheral pulses palpated.

As a result of this disregard of the peripheral circulation, many middle-aged wage earners, insured policy holders, or railroad and street car conductors suddenly develop a serious interference with their peripheral blood flow. "The question may then be asked; 'Did this really come out of a clear sky?'; in most instances this was surely not the case."—de Takats (21). The lesion
more than likely had existed for a considerable time and was probably caused by a sudden aggravation of a chronic progressive arterial obstruction. These patients are in many instances first seen by the general practitioner, or are encountered by internists, orthopedic surgeons, traumatic and industrial surgeons, neurologists, and dermatologists, whose special fields of interest lie apart from the problems of peripheral circulation.

Brown (15) saw a patient suffering from a peripheral vascular disease, who had worn as many as fifteen different types of arch preservers to aid and cure the "rheumatic" pains in his feet and legs. Finally this individual developed a small ulcer on his toe before the peripheral arteries were investigated and found to be diseased.

The foregoing example and the statements of de Takats show that peripheral vascular disease is very much in evidence if one will spend the time in looking for it.

A very practical statement is made by Kaplin (34): "Let it not be said of us 'They have hands and feel not; eyes and see not.'" In other words, this is a challenge to the medical profession to become aware of the fact that the incidence of vascular disease is very high and should be looked for in every patient who is given a physical examination.
CLASSIFICATION
According to Metcalf, Plank, and Ritterspach (56), a classification of Peripheral Vascular Disease, to be of value, should give information from both a therapeutic and a prognostic standpoint.

The classification must consist of both gross types of the disease, which are (a) spastic and (b) organic. The spastic group is divided into local vaso constricting type, as Raynaud's disease, and the vaso dilating type, as erythromelalgia; then, there is the general vaso constricting type, as primary hypertension, and vaso dilating type, as primary hypotension. The organic type is likewise divided into local and general distribution. Under the local type one considers (a) Thrombs Angiitis Obliterans, (b) Thromboarteriosclerosis Obliterans, (c) Simple Thrombosis and Embolism, (d) Arteriovenous Communication, and (e) Aneurysm, with or without Thrombosis. The general group of organic types is made up of primary and secondary arteriosclerotic conditions.

The classification of the Peripheral Vascular Diseases will be attempted only from the clinical standpoint, and that used will be taken directly from Brown (15), Metcalf, Plank, and Ritterspach (56) and Allen (4).
Functional or Vasomotor Type

Organic Type

1. Vasoconstricting type - Raynaud's Disease
2. Vasodilating type - Erythromelalgia

1. Vasoconstricting type - Primary or essential hypertension, early stages
2. Vasodilating type - Primary or essential hypotension

1. Arteriosclerotic disease - Senile gangrene, Diabetic gangrene
2. Thrombo-Angiitis Obliterans
3. Simple Thrombosis - Embolism
4. Arteriovenous communications - either congenital or acquired
5. Aneurysm with or without Thrombosis

1. Arteriosclerosis
   a. Primary
   b. Secondary types, due to hypertension, lead, etc.
DIAGNOSIS
In the diagnosis of Peripheral Vascular Diseases, Herrmann (30) writes: "The vast majority of patients with obliterative arterial diseases of the extremities are seen or diagnosed only after some serious complication, such as gangrene or infection, has appeared, this should lead to a determined effort on the part of physicians and surgeons to make an early diagnosis and to institute proper treatment in order to prevent the disease from progressing to a stage when amputation of the extremity is inevitable. The routine examination of all peripheral arteries would result in a much earlier diagnosis; and the true nature of a disease, erroneously being treated for weeks, months, and even years, as fallen arches, rheumatism, or sprained ankles, would thus be established. If, in addition, we were to make a practice of counting the rate of the heart by palpation of the pulse in the dorsalis pedis artery rather than in the radial artery, many more cases of early vascular disease would be detected."

Other reasons why Peripheral Vascular Diseases were undiagnosed are aptly put by MC Laughlin (50), who states that, previously, the practitioner thought he had neither the time nor the facilities to study such cases because of the complicated diagnostic and therapeutic apparatus used. This, however, is not the case, for now a patient
with an inadequate peripheral circulation may be studied easily in one's office with a moderate expenditure of time and limited equipment.

In the following will be given the general accepted methods of studying and diagnosing vascular diseases:

First, a very careful history must be taken; Brown (15) states that a good history will bring out the symptoms which will be pathognomonic of the disease, and from this one may be able to get some idea as to treatment and prognosis of the existing condition.

The following outline for the investigation of a case presenting itself as an inadequate peripheral circulation has been given by McC Laughlin (50):

(A) General medical history, including the patient's occupation, habits, and if he is a user of tobacco.

(B) The onset and course of the symptoms referable to the extremities.

1. Pain and cramps; at night, at rest.
2. Intermittent claudications; pain or cramps with exercise.
3. Numbness and tingling.
4. Cold extremities.
5. Previous frostbite or ulceration.
6. Effect of hot and cold weather on the extremities.
7- History of a wandering superficial phlebitis.
8- Color changes previously noted in the limbs.

Each of the foregoing phases must be entered into before a history concerning Peripheral Vascular Disease can be considered complete.

Pain is the most common symptom of which the patient complains and its type and character must be carefully investigated. The age of the patient may assist one in grouping the cases, with the exception of Thrombo Angitis Obliterans; in younger individuals one is more apt to see a vaso spastic condition, while in the older patient the occlusive arterial diseases, either senile arteriosclerosis alone or that complicated by diabetes, are discerned. A history of a migratory superficial phlebitis is important in diagnosing Thrombo Angitis Obliterans. Patients with an inadequate peripheral circulation usually complain of having more difficulty in the fall and winter than in the summer, because the cold produces a greater spasm of the vessels and thus adds to the pre-existing vascular disorder.

Another important factor in classing these disorders is age correlated with sex. According to Riesman (62), one usually sees Thrombo Angitis Obliterans in males between the ages of twenty-five and fifty years while above the age of fifty Arteriosclerosis Obliterans prevails;
Raynaud's disease is seen most often in females of a nervous disposition between the ages of fifteen and thirty-five years.

Brown (15) states that one most often sees Buerger's disease or Thrombo Angiitis Obliterans in Jews, (45%), and 55% in the other races. This author has observed three cases in which the disease has occurred in full-blood negroes.

After obtaining a complete history, the next very important step in diagnosis is the physical examination, which is a general one with particular attention on the heart (Mc Laughlin (50)). After this a careful and thorough examination of the extremities must be made—Pratt (59), Riesman (62), Brown (15) Mc Laughlin (50), Kaplin (34), and many others—on inspection one sees the condition of the skin whether rough, scaly, fissured, atrophic, or ulcerated; then any color changes are noted, which may be pale, waxy, or cadaveric on elevation, or hyperemic or subcyanotic when the extremity is in the dependent position. There has been a color chart devised by Lewis (41) on which one may determine or base the amount of impairment which exists in the extremity.

The next step in the physical examination is palpation of the peripheral arteries, which apparently is of utmost importance, for every author whose work I have
read has stressed this point: de Takats (21), Elliot and Evans (25), Pratt (59), Brown (15), Bierman (13), and many others. In the upper extremities one can usually palpate three arteries without much difficulty, which are the axillary, brachial, and radial; and in the lower extremities one has five arteries he can palpate if they are patent, namely the femoral, popliteal, posterior and anterior tibial, and the dorsalis pedis. Gay and Hardesty (27) caution that it should be remembered that the dorsalis pedis is absent in 4% of all cases, and in 8% of cases it is located lateral to its usual anatomical position; so these abnormalities must be kept in mind when one is palpating for this artery.

Kaplin (34) gives some valuable information on where the arteries of the lower extremities may be found, stating that the femoral artery may be palpated midway between the symphysis pubis and the anterior iliac crest; and the popliteal artery is found deep in the popliteal fossa where firm pressure must be applied to discern its presence. To locate the posterior tibial, the palm of the hand is placed on the dorsum of the foot with the fingers bent over the ankle joint so that their tips are behind the internal malleolus and between it and the achilles tendon. The anterior tibial is best felt on the anterior aspect of the foot, which is situated approxi-
mately one to two inches above the malleolus somewhat lateral from the mid line. For the dorsalis pedis artery, one usually finds it best between the first and second metatarsus, by palpating with the palmar surfaces of the index and middle fingers. It may be difficult at first to feel the arterial pulse in these locations, but with some experience and persistence one can become quite apt at locating them.

Again it must be emphasized (de Takats (21)) that if one were to practice taking the patient's pulse on the dorsalis pedis instead of the radial artery, many peripheral vascular diseases would be diagnosed at an earlier time.

For the rest of the methods of examination the one presented by de Takats (21), with a few additions by other authors, will be used, although all authors read have presented practically the same manner of examination. The methods of examination as put forth by de Takats are mostly for the general practitioner, who, he believes, is the first to see these patients.

After one has gone through the foregoing part of the examination, he may then proceed to determine if there are any postural color changes, which are, briefly: pallor on elevation, and rubor when the extremity is in the dependent position. When either of these exist, one
can conclude that there exists some impairment of peripheral circulation.

While determining postural color changes of the extremities, one should determine the optimal level at which the color of the skin appears normal. This level is usually from three to six inches below the level of the heart when the patient is lying in the horizontal position. This optimal level should be determined in every case, because it is the level at which the extremity gets just the proper amount of blood to carry on its normal physiological functions. There are cases where the patient has already determined this level by himself as this is the level at which he is most comfortable.

Next, one may resort to the cutaneous histamine reaction, for which the acid phosphate salt of histamine is used in a 1:1000 solution, and of this 0.1 cc is injected intradermally. In five minutes a characteristic flare is produced, which presents a wheal in the center. The flare is absent when "(1) the head pressure is too low to fill up the arterioles dilated by histamine, (2) when there is an existing spasm that the histamine can not overcome, (3) when the sensory nerves of the skin have degenerated following peripheral nerve injury."

The cutaneous histamine reaction is important and gives the following information concerning an extremity:
"(1) In patients with frank gangrene, it determines the lowest level at which one may safely amputate the extremity. At the lowest place where a flare can be detected, one can also consider that the circulation to the bone is also affected at the same level. (2) During the course of conservative treatment with drugs or physical agents the improvement of the collateral circulation can be visualized." (21)

Mc Laughlin (50) uses another method of producing the reaction with histamine other than by injecting it, which he believes gives just as satisfactory results as does the intradermal injection. The method described is thus: After thoroughly cleansing the skin, drops of 1:1000 acid phosphate of histamine are placed at different sites along the extremity to be tested, in the lower extremity it being best to test above the knee, at mid leg, and on the dorsum of the foot; then by using a hypodermic needle, the skin is scratched through the histamine as one does a vaccination.

Mc Laughlin (50) states that there soon develops a red spot, succeeded by a wheal surrounded by a flare. This reaction is accompanied by itching, and normally, will develop in five minutes if the superficial circulation is adequate. However, when the circulation is abnormal; the wheal and flare may develop very slowly,
may be almost invisible, or may not appear at all. The author has advanced this system of gradation of the reactions: "It is considered normal if a wheal one centimeter in diameter is surrounded by a flare two centimeters in diameter, this is represented as 111 (normal), this however must appear within ten minutes to be considered normal; then lesser reactions have been graded 11, 1, and 0."

Sir Thomas Lewis—MC Laughlin (50)—has shown that the appearance of the wheal is due to an increased permisibility of the minute vessels of the skin, and the flare is the result of a wide spread dilatation of the neighboring arched arterioles, brought about through a local nerve reflex or an axion reflex producing a hyperemia:

The next procedure that may be resorted to in the physical examination in diagnosis is the determination of blood pressure in the extremities, which too, gives information concerning the presence or absence of occlusion. The ocellometer is a sensitive and accurate instrument in determining the level of vascular obstruction. Elliot, Evans, Stone, and Gray (25) state that this instrument can show that pulsations still exist in arteries which fail to show pulsations by palpation. However, it does not determine what type of occlusion is present,
nor tell whether it is due to an organic or a spastic condition.

Metcalf and co-workers (56) have listed some normal readings for the occillometer in regard to the different arteries, which are: brachial artery--6, radial ulnar artery--3, femoral artery--6, tibial arteries, anterior and posterior,--3.

It is very essential that the previously described examinations should be done in a room in which the temperature is constantly maintained at about twenty-two degrees Centigrade or seventy degrees Fahrenheit, and with a humidity of approximately fifty per cent. The patient, with all of the extremities exposed, should be placed in this constant environment from a half to one hour, so that the body and extremities may assume a constant temperature before any diagnostic procedures are performed --Herrmann (30), de Takats (21), Scott and Morton (64).

One may produce the pain of claudication with the circulation free or with it occluded. Often this pain is confused with the pains of arch strain, rheumatism, neuritis, etc. The procedure as described by Elliot and co-workers (25) follows: The patient lies on a bed with the feet elevated by two pillows, and in time to a metronome, the feet are flexed and extended once per second--normal individuals develop pain in the anterior tibial
muscles in one minute, but these normal individuals are able to continue the exercise longer before being stopped by pain or fatigue. The patient with a diseased peripheral circulation is unable to proceed with exercise as long as the normal individual; pain is felt in both the anterior and posterior tibial groups of muscle long before the minute is up; these pains are identical with those experienced in walking. The patient with inadequate circulation is unable to continue the exercise after the first appearance of the pain because it is too excruciating. This test is very valuable in duplicating the characteristic pain of claudication so that the patient may describe it, and also for the physician to differentiate it from the pains of arch strain, rheumatism, etc.

The flushing time of arteries is a valuable procedure in making an early diagnosis of Thrombo Angitis Obliterans when just the digital arteries show the disease. This procedure has been described by Elliot and co-workers (25): The patient's ankles and feet are immersed in water at a temperature of forty-five degrees centigrade for ten minutes, during which stage the toes turn pink; this happens whether the arteries are badly diseased or not. Then upon removal of the feet, they are wrapped in woolen blankets to maintain their warmth and color. Following this the patient is put in a horizontal position, one
foot is uncovered, and a compression is put high on the thigh so that the femoral artery is compressed close to the pelvic ring. When this is completed, the leg is elevated to about forty degrees above the horizontal, and the foot is allowed to become blanched and pale. The compression is then released from the femoral artery, and with a stop clock the length of time is determined that it takes for the toes of the elevated extremity to assume the color of the other extremity, which has remained in the horizontal position and which has in the meantime been unwrapped. In normal extremities forty-six seconds are required for this to take place, while in diseased arteries the time is longer, depending on the degree and extent of the disease process present. In correlation with the oscillograph this procedure gives an excellent idea of the extent and location of a vascular lesion.

Taking of the skin temperature is also a valuable procedure in diagnosis; this is usually taken with a Dermotherm, which is a very sensitive and accurate instrument. An ordinary clinical thermometer may be used, however, but for accurate work it registers too slowly to be of much value. Some authors state that one can become so proficient that by touch he may determine a difference of temperature in the extremities to within one degree.
Elliot and co-workers (25) state that the skin temperature depends on the amount of blood brought to the extremity and the speed with which it circulates, and upon the loss of heat by radiation, conduction, and convection. Scuphon and de Takats (65) also state that the skin temperature will vary according to what structure the temperature is taken over, that is, muscle, bone, vein or artery.

Skin temperature, however, doesn't tell whether the vascular disease is spastic or organic in character, so, one must resort to methods of determining which type exists. A number of authors have described different tests which are of diagnostic importance in these conditions:

(1) Lewis and Pickering--Metcalf and co-workers (56) have suggested a heat cabinet. The patient is placed in a chamber heated by electric lights and the extremities are permitted to protrude; in this manner the general body temperature rises and by taking occasional temperatures of the extremities, one is able to ascertain the ability of the arteries to dilate, and hence gauge the activity of the sympathetic nervous system.

(2) Brown's (14) fever test causes an increase in both body temperature and the temperature of the extremities if the vessels are normal or vasospastic. The test is done by first taking the mouth and skin temper-
atures and recording them, then twenty-five to fifty millions killed typhoid bacilli are injected intravenously; then during the height of the fever produced, again the temperatures are taken. The rise of the peripheral skin temperature is greater than that of the mouth. The increase in mouth temperature is then subtracted from the increase in skin temperature and this figure is divided by the increase in mouth temperature to give a figure which represents the vasomotor index. Any case having an index of 2.5 is considered favorable for sympathectomy. The following is the formula given:

\[
\text{Rise in peripheral skin temperature} \quad \text{minus rise of mouth temperature} = \text{vasomotor index} \\
\text{Rise of mouth temperature}
\]

(3) Landis and Gibbon (38) recommend the following test: both arms are immersed for thirty-five minutes in water from forty-three to forty-five degrees Centigrade. If the peripheral temperature reaches thirty-one and five tenths degrees Centigrade, there is no organic occlusion present, but if the temperature reaches only twenty-six degrees Centigrade, there is moderate organic occlusion and good results may be expected from treatment.

(4) Maddock and Coller (45) recommend wrapping the patient in blankets and then recording the skin temperature to see if an increase has occurred.

(5) Scott and Morton (64) have used a local nerve
block with novocain to produce a rise in skin temperature. If there is just an existing spasm, the peripheral skin temperature may reach as high as thirty-two degrees Centigrade. These same authors have found that spinal and general anaesthesia and lumbar ganglion block give the same results. However, many object to these methods because they are hospital procedures, and as good results may be obtained with simpler procedures.

Another procedure used in diagnosis is arteriographic studies—Allen and Camp (3), Yater (76)—which were first performed in 1923. Since then a variety of substances have been used, such as iodides and bromides of sodium, stromium, potassium and calcium, proteinated silver salts, iodized oil, and thorium dioxide. The last named is in most use now. This is injected directly into the artery to be studied, followed immediately by x-ray plates.

Yater (76), however, states that thorium dioxide for use in arteriographic study is a drug not accepted by the Council on Pharmacy and Chemistry in the American Medical Association, because of the lack of knowledge of its latent radioactivity. Allen and Camp (3) in 1933, stated they had not seen any obvious or immediate injurious effects on the blood, blood vessels, or on the body as a whole from using this compound.

The information obtained from such a measure is the
type of lesion that exists, for instance, in Buerger's disease one sees patchiness of the obliteratorive process and extensive collateral circulation formation; in arteriosclerosis the rather shaggy outline of the arteries, evidence of calcium plaques, and the narrowing of the lumen are characteristic--(3). Perhaps the most important and practical use of arteriography is to aid in selecting the best site for amputation when gangrene has supervened--(76).

Arteriography should be considered an adjunct rather than an absolute necessity to diagnosis, and should not be resorted to unless all other methods of diagnosis have failed--(3).

Other less important diagnostic procedures may be employed, such as calorimetric determinations--Brown (15), maximum possible increase blood flow--Elliot and co-workers (25), reactive hyperemia, and blood volume--Gay and Hardesty (27).

In diagnosing peripheral vascular diseases, a differential diagnosis of these diseases should be considered, for which Metcalf, Plank, and Ritterspach (56) have prepared the following chart:
<table>
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<tr>
<th></th>
<th>Thrombo-Angiitis</th>
<th>Arterio-Obliterans</th>
<th>Raynaud's Disease</th>
<th>Primary Erythromelalgia</th>
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</thead>
<tbody>
<tr>
<td>2. Sex</td>
<td>Males 99%</td>
<td>Males 90%</td>
<td>Females 90%</td>
<td>Females 90%</td>
</tr>
<tr>
<td>3. Race</td>
<td>Jewish 42%</td>
<td>Any</td>
<td>Any</td>
<td>Any</td>
</tr>
<tr>
<td>4. Pulsation of arteries</td>
<td>Pulseless 50%</td>
<td>Pulseless 50%</td>
<td>Normal 50%</td>
<td>Normal 50%</td>
</tr>
<tr>
<td></td>
<td>Diminished 45%</td>
<td>Diminished 45%</td>
<td>Normal 45%</td>
<td>Normal 45%</td>
</tr>
<tr>
<td></td>
<td>Normal 5%</td>
<td>Normal 5%</td>
<td>Normal 5%</td>
<td>Normal 5%</td>
</tr>
<tr>
<td>5. Claudication</td>
<td>Usually present</td>
<td>Usually present</td>
<td>Absent</td>
<td>Absent</td>
</tr>
<tr>
<td>6. Excessive rubor with dependency</td>
<td>Present</td>
<td>Present</td>
<td>Absent</td>
<td>Absent</td>
</tr>
<tr>
<td>7. Gangrene</td>
<td>Common</td>
<td>Common</td>
<td>Rare, of minor degree</td>
<td>Never</td>
</tr>
<tr>
<td>8. Rest pain</td>
<td>Usually very severe</td>
<td>Usually mild</td>
<td>Usually absent</td>
<td>Mild to severe</td>
</tr>
<tr>
<td>9. Type of rest pain</td>
<td>Sharp stinging</td>
<td>Aching</td>
<td>Absent</td>
<td>Burning</td>
</tr>
<tr>
<td>10. Appearance of gangrenous ulcers</td>
<td>Moist, inflamed, dry</td>
<td>Usually dry</td>
<td>Small punched-out areas</td>
<td>None</td>
</tr>
<tr>
<td></td>
<td>and discharging</td>
<td></td>
<td>on the skin</td>
<td></td>
</tr>
<tr>
<td>11. Superficial phlebitis</td>
<td>30% of cases</td>
<td>Absent</td>
<td>Absent</td>
<td>Absent</td>
</tr>
<tr>
<td>12. X-ray of arteries</td>
<td>Usually negative for sclerosis</td>
<td>Usually positive for sclerosis</td>
<td>Negative</td>
<td>Negative</td>
</tr>
</tbody>
</table>
13. Color changes following exposure

<table>
<thead>
<tr>
<th>Color change</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>30%</td>
<td>15 - 20%</td>
</tr>
<tr>
<td>100%</td>
<td>Always</td>
</tr>
<tr>
<td>Never</td>
<td></td>
</tr>
</tbody>
</table>

14. Temperature

<table>
<thead>
<tr>
<th>Temperature</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>Low</td>
</tr>
<tr>
<td>High</td>
<td></td>
</tr>
<tr>
<td>during attack</td>
<td></td>
</tr>
</tbody>
</table>

15. Edema

<table>
<thead>
<tr>
<th>Edema</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frequently</td>
<td>Infrequently</td>
</tr>
<tr>
<td>Absent</td>
<td>Absent</td>
</tr>
</tbody>
</table>
TREATMENT
To treat a patient who presents himself with a peripheral vascular disease, an early diagnosis must be made to prevent serious sequelae, for the loss of one or more limbs, or even life, is surely important enough to merit the most serious consideration of any preventative or therapeutic measures known to medicine—Pratt (59), Brown (15). Herrmann (30) warns, however, against treating these unfortunate individuals by the use of medical means when only heroic surgical procedures can save a life. As much as the dislike for amputation of a limb for arterial deficiency, one must still accept the end result of a process, in which the rate of obliteration of arterial supply exceeds that of the development of collateral circulation, as amenable only to surgical intervention.

Another thought to bear in mind when treating these deficient circulatory conditions has been aptly stated by Herrmann (30), Reid (61), Theis (74), Buerger (16), McC Laughlin (52), and many others—this condition is a local manifestation of a generalized systemic disease, and that by treating it one must only expect to halt the progress and not to cure it, and that most all preliminary treatment is aimed at relieving pain and helping the body to establish new collateral arterial pathways through the involved extremities.

Barker (10) has stressed prophylactic measures stat-
ing that the vulnerability of the toes in people with a
deficient circulation hasn't been sufficiently stressed.
According to him, gangrene is produced by the most trivial
type of injury; in a series of one hundred seventy-one
cases, thirty-five per cent showed gangrene following var-
ious therapeutic measures, while in another series of
one hundred fifteen cases of arteriosclerosis with gang-
rene, thirty-nine per cent were caused by therapeutic
measures. He recommends that no surgical or medical
treatment of the toes be instituted until the arterial
supply has been proved adequate. Kittrick (48) has
also shown that many cases of arteriosclerotic gangrene
can be postponed for many years if gradual rehabilita-
tion by regular graded active exercise, careful foot
hygiene, and living within circulatory possibilities are
prescribed.

The first methods to be considered in the treatment
of peripheral vascular diseases are the general measures
and general management, or the conservative treatment,
the aims of which are, briefly:

(1) Control of infection
(2) Relief of pain
(3) Stimulation of the development of collateral
circulation
(4) Release of vasomotor spasm
Scott and Morton (64) have pointed out that treatment should always be directed toward preventing ischemia from doing any preventable harm. General measures have been stressed by Reid (61), Pratt (59), Buerger (16), Herrmann (30), Allen (1), Sibert (67), and many others. These measures are routinely applied by all men regardless of the type of specific therapy advocated. Reid (61) pointed out that these general measures are often forgotten and disregarded in the excitement of the development of new discoveries and ideas with respect to etiology, diagnosis, and treatment. Reid also believes that these measures, along with remissions that are common to many conditions, are the bases for the very good results given to many of the new procedures. The general measures which have been advocated by the foregoing authors are as follows:

(1) Importance of active cooperation.

In clinical practice it is difficult to make most patients realize the importance of the many necessary precautions and even more difficult to get them to respond in an intelligent manner; but in many instances experience has taught that the fault frequently rests with the doctor, because he has not taken the time nor had the patience to explain the basic reasons for such a regime. These patients could readily understand the explanation
that a reduction in the peripheral circulation means definite impairment of the nutrition to the tissues and that instructions given are efforts to keep the nourishment of the tissues of the extremities at a maximum level to enable them to combat infection in a normal manner. After this advice has been clarified to the patient, the performance of these duties by him must be checked and re-checked until they have become habitual.

Reid (61) and Pratt (59) have suggested commendation as being helpful in securing the best interests and cooperation of patients. Interest can frequently be kept active until the details become a matter of fixed routine by use of the following expressions: "The feet are cold; you had better wear two pairs of woolen socks during this cold weather"; "The skin is somewhat rough about the heel and I think you can grease that part a little more thoroughly"; "The seam of your sock is making a groove on your toe or foot, you had better have some seamless ones knitted"; "You should drink not less than three quarts of water in twenty-four hours"; "These shoes are too tight, you must get larger ones". It has been found by these authors that a good index of success along these lines is the development of ideas and the offering of suggestions on the part of the patient, for when he makes contributions toward his own condition, one can be certain that his

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interest has been definitely aroused. If the patients are allowed to take an active role in the treatment, they frequently adapt themselves to their tasks and one can usually be assured of success.

(2) Optimum resting level.

This level should be determined for every patient, for if the extremity is maintained at a too elevated position, the existing ischemia may result in severe consequences.

Reviewing: on elevation the extremity is pale and cadaveric, while in the dependent position there exists congestion rubor; in both of these extreme positions the extremity is not receiving the maximum amount of nourishment, and somewhere between these two is found the position where the skin color is a normal pink and appears to be getting a maximum amount of nourishing blood.

The optimum level can be determined by first placing the extremity in the dependent position until the veins become fully distended, and then slowly raising the extremity until this distension leaves the superficial veins; this is the optimum level, which is usually from three to six inches below the level of the heart when the patient is in the horizontal position. When the optimal level is established, the superficial veins will carry a quantity of blood which neither distends nor retracts the
skin overlying the superficial veins.

(3) Prevention of trauma.

Regarding trauma, the patient must be warned against sustaining any injuries; however when such is the case, he should be advised first to use all known aseptic measures to prevent infection, and then see a physician or surgeon and have these apparently harmless, but potentially malignant, injuries treated.

For the cutting of toe nails, trimming of corns and calli, treating of blisters, etc, patients should be advised to seek professional aid.

Any seemingly harmless injury must be considered a potential site of gangrene formation, and of a severe generalized infection. Because of the diminished blood supply and already diminished local resistance, one can see the possibilities of danger.

(4) Fluid intake.

The fluid intake in these patients should be maintained at a very high level, at least three or four quarts daily. It has been shown that there is an increased viscosity of the blood--Silbert (67)--and therefore, that fluid must be taken to decrease this viscosity so that circulation will be more efficient to the extremities.

Too get the patient to take enough water one can
suggest charting the amount consumed, and thus he will establish a routine of taking large quantities.

(5) Effect of cold.

It is noted that patients suffer more in cold weather, so it is advised that they wear woolen socks in the winter, two pairs if necessary. Reid (61) reports that he has insisted on patients wearing fleece-lined boots, and if need be for comfort and protection, fur-lined leggings.

When deficient circulation exists, the tissues are more prone to freezing which may easily lead to gangrene and severe infection.

Another point to remember is that if the feet can be made to perspire, it improves the texture of the skin and the nourishment of the tissue beneath it.

(6) Protection of the skin.

When rough, dry, fissured, dull, lifeless skin exists, a softening ointment should be applied to the extremity involved. For this, ordinary cocoa butter, lanolin, vaseline, or olive oil may be used. This ointment prevents greatly the chances of infection because the unhealthy skin is more prone to injury and has less local resistance to combat infection than does a soft, healthy, pink skin.

One should insist on scrupulous cleanliness of the
feet, using soap and water at least once a day followed by a bland, softening ointment.

(7) Eradication of face of infection.

This is very essential in Buerger's disease because it is believed, although it is still unproved, that this may be a factor in the etiology of the disease. So it is a wise procedure to check teeth, tonsils, sinuses, appendix, etc. for infection, and if it is present the affected part should be removed.

At times this problem is often regarded too lightly and patients are allowed to expose themselves to unnecessary risk, injury, or infection during the active phase of their disease.

(8) Active graded exercise.

For this the patient may be taught either the exercises laid down by Buerger or the modifications of these procedures advanced by Allen. The technique of Buerger's exercises is, briefly:

(a) The patient, lying prone, elevates the limbs to ninety degrees and rests them in this position on a suitable support for three minutes.

(b) The extremities are then lowered and allowed to hang over the side of the bed for three minutes, during which time the feet are put through the movements of flexion, extension, inversion, and eversion.
Following this, the patient again lies prone in bed for three minutes with the feet wrapped in a woolen blanket. This exercise should be performed at least one-half to one hour three times a day.

The modified Allen treatment is:

(a) With the patient lying prone, the limbs are elevated with support to an angle of sixty or ninety degrees until ischemia or pallor appears.

(b) The limbs are then lowered and allowed to hang over the edge of the bed until one minute after the appearance of the reactionary rubor.

(c) Following this, the limbs rest in the horizontal position from three to five minutes. In this method the time allowed for each position is determined periodically by the physician in charge.

Saunders (63) has developed a new procedure whereby the entire bed upon which the patient rests is slowly rotated by an electrically driven device, so that each of the positions suggested by Buerger may be assumed without expenditure of effort on the part of the patient.

Most authors deem it advisable for the patient to be hospitalized for a short period to teach him the technique of either Buerger's or Allen's procedures, and also to explain to him the benefits afforded to the poor circulation of his extremities.
In using active graded exercise in conservative treatment, one must remember that there are contra indications to its use, which must be investigated thoroughly before such treatment is instituted; these contra indications are the presence of a lymphangitis or a spreading infection. This sort of treatment seems to further exaggerate any existing contra indications.

(9) Abstinence in the use of tobacco.

According to Silbert (67) tobacco is the most important contributing cause of Thrombo Angiitis Obliterans; he has shown that most patients who suffer from remissions are those who started smoking again after they had shown marked improvement. Many of his cases with this disease who have had to have amputations are those who didn't stop smoking or who started smoking again after some improvement had followed treatment.

Tobacco abstinence has been shown to be a rational procedure in some interesting work done in the past few years by Maddock and Coller (46) and Barker (8); they found in 1932 that smoking produces a marked vaso spasm which is determined by taking the skin temperature and noting a marked drop. Friedlander and co-workers (26) found that the injection of denicotinized tobacco extract, in Ringer's solution, intra-peritoneally into rats, caused gangrene of the toes of the male rats in from five to
twelve weeks, where as the female rats failed to show any change whatever. Maddock and co-workers (47) have concluded that the smoking of two cigarettes by women resulted in a marked drop in the skin temperatures of the fingers and toes, and an increase in their blood pressure and pulse rates similar to those observed in men. Cigaret smoking by Jewish males caused a greater drop in the skin temperatures of their fingers and toes than occurred in Gentile males. This fact may be significant in accounting for the greater evidence of Thrombo Angiitis Obliterans among Jews than among the other elements of the population. Brown (14), to contradict this tobacco factor, states he has seen true, proven Thrombo Angiitis Obliterans in a small number of cases which have never smoked in their lives.

It has been shown by Karkovv and co-workers (35) and Sulzberger (72) that patients suffering from Thrombo Angiitis Obliterans show a marked skin hypersensitivity to tobacco, which is also suggestive that tobacco may be an etiological factor in Buerger's disease.

(10) Thyroid extract.

Reid (61) and Perlow (57) have advocated that thyroid extract may be given to elevate the blood pressure and accelerate the circulation. Reid also states that many people with Thrombo Angiitis Obliterans have a low basal metabolic rate.
(11) Contrast baths.

This procedure is done by immersing the affected limbs alternately for one and one-half to two minutes in warm water at 110° to 115° Fahrenheit, and then immersing them in cold water at 45° to 50° Fahrenheit for the same length of time. This treatment may be continued for thirty minutes at a time and should be done two to three times a day, or more if necessary. The progress is slow with this treatment but beneficial results are seen. This procedure exercises the toneless musculature of the vessels and thus helps to establish a better circulation.

The use of drugs has not offered much aid in relieving pain or producing vasodilatation. Many authors state that morphine, codeine, or any opiate should not be used to alleviate the pain, for, due to the chronicity of the disease, the opiate habit might be instigated. Instead of these, if drugs must be used, aspirin, phenacetin, and amidopyrine are suggested, or the use of some other physical agent such as contrast baths, vascular exercise (passive), Buerger's exercises, or alcohol injection of the main sensory nerves--Mc Laughlin (53), Theis (74).

Regarding vasodilating drugs, Allen and Crisler (7) state that the effect of these drugs is very short lived, and frequently cannot be given orally, intravenously, or
intramuscularly in amounts sufficient to produce marked dilatation, because the general systemic effects are too great. Therefore, direct intra-arterial injection must be resorted to.

de Takats (21) and MC Laughlin (51) have suggested the use of theobromine sodium acetate, 2.6 to 4 gm. to be given, which produces a short period of dilatation which may tide an individual over a critical period. Perlow (57) has advised acetylcholine for the same purpose.

This drug is injected either intramuscularly or subcutaneously in doses of 0.1 gm. or 0.2 gm. It will increase the skin temperature one to three degrees depending on the spasticity present, and this rise in temperature usually occurs from four to eight hours after the injection. The author describes this drug as a powerful vasodilator, and for this reason it acts best where marked spasticity exists.

Other drugs which have been used are histamine phosphate in doses of 0.1 to 0.15 mgm. and acetyl B--methylecholine in doses of 0.5 to 2.0 mgm. (7).

de Takats (24) has found papaverine, an opiate, to show excellent results in acute arterial occlusion; this has also been reported on favorably by other authors.

Quoting from Allen and Crisler (7), "These drugs cannot be 'fixed' in an extremity to any degree", thus
making drug therapy a difficult procedure, and in comparing the upper with the lower extremity for suitability to drug therapy, they state that the former is relatively very refractory, because only moderate temperature increase was noted following the use of vasodilating drugs.

There is also in the literature evidence that tissue extracts of many types have been used to produce vasodilatation (57), (52); these too are injected either intramuscularly or subcutaneously. This type of therapy acts very similar to the foreign protein or typhoid vaccine reaction, (to be discussed later) but not so violently.

The treatment by repeated injections of hypertonic salt solution has met with some success. Success is attributed to the fact that hypertonic salt decreases the viscosity of the blood, thus allowing for better circulation to the affected extremities—(66). Silbert (66) explains the method: Five per cent solution of sodium chloride is used; this solution should be fresh and should be prepared with distilled water, filtered and immediately sterilized, because bacteria grow rapidly in this mixture and it is very important to avoid contamination. If injections are followed by chills or fever, the cause is usually found to be in the failure to follow the foregoing set rules. After the preparation of the
solution, the injection is given by gravity into the superficial veins at the elbow; the initial dose is 150 cc, and all subsequent injections are boosted to 300 cc; this solution is allowed to run in slowly, ten minutes being taken. The patient is kept lying flat on his back while he is receiving this injection. During this procedure the patient often becomes thirsty, and many experience a warm sensation over the body, due probably to the blood taking up more fluid and thereby increasing its volume. In the beginning the treatment is given an alternate days, three times weekly, later twice weekly, and then the length of intervals is further increased as the patient improves. Total duration of treatment may last from six months to two years, depending on the severity of the individual case. The chief advantage of this treatment is that immediately following the therapy the patient is allowed to get up and go directly to his work without inconveniencing him.

MC Laughlin (53) has gathered some facts from literature concerning the foregoing treatment; he reports that in a series of five hundred twenty-four cases with thirty-five thousand injections without a fatality, eighty-three per cent showed marked improvement; from another group of facts by Samuel, MC Laughlin (53) states that there was a reduction in the number of cases requiring
amputation from seventy-seven per cent to less than ten per cent following hypertonic salt solution injection.

There are however some complications and contraindications from hypertonic saline treatment. McC Laughlin (53) states that a moderate amount of anemia may develop, but not severe enough to make one hesitate to use the treatment, and Silbert (67) states that the contraindications are:

(1) Don't use in patients over sixty years of age, nor those who show signs of myocardial damage;
(2) Don't use where there is poor renal function;
(3) Don't use when there is obstruction of the circulation due to embolism from cardiac disease or other sources;
(4) Raynaud's and other vasomotor neurosis don't respond to this treatment;
(5) Only satisfactory results are obtained when smoking is stopped, consequently absolute abstinence from tobacco is necessary.

Phillips and Tunich (58) have reported the use of x-ray in the treatment of Thrombo Angiitis Obliterans; this treatment was discovered accidently by them. They noted in a patient who was being irradiated over the lower pelvis for hypertrophied prostate, and at the same had Buerger's disease, that the vascular lesions showed
marked improvement following this irradiation. These men, by further study, found that by using stimulating doses of x-ray over the tenth dorsal to the fifth lumbar vertebrae in the lower extremity affections, and over the cervical and upper dorsal segments in the upper extremity disturbances, the following results were noted:

1. Relief of pain in two to three weeks, the exception being ten per cent uniform and progressive relief.
2. Resumption of work in five to six weeks.
3. Intermittent claudications reduced in all and completely cleared in fifty per cent of the cases in six weeks.
4. Improvement in circulatory and trophic disturbances noticeable in from one month to six weeks.
5. Phlebitis and inflammation showed improvement after the first treatment.
6. In a series of ten ulcer cases, all were healed in from six to eight weeks.
7. Marked general improvement due to reduction of pain was noted.

Foreign protein has been used quite extensively in the treatment of peripheral vascular diseases, especially in the occlusive types.

Many different substances have been used to produce a febrile reaction, but at the present Typhoid vaccine is
used mostly. At first the ordinary T. A. B. (Bacillus Typhosis B, and Paratyphosis A and B) was used, and later the "H" antigen was added. By the addition of the "H" antigen, a more sure reaction is produced and it tends to produce less chill and malaise for the amount of fever produced—Barker (9).

The injection of Typhoid vaccine results in vaso dilatation, with an increase in the flow of blood during the febrile reaction. At the same time, this febrile reaction relieves the pain of claudication and the rest pains which are usually felt. These beneficial reactions last for about twenty-four hours after the vaso dilatation has subsided. According to Barker (9) the initial dose of intravenous Typhoid vaccine is from fifteen to thirty million killed organisms, but Allen and Smithwick (2) advocate one hundred twenty-five millions as the initial dosage, to be repeated once a week, but never to exceed more than three hundred million bacilli at a single dose.

Injections have been given as often as every day with as many as eighteen injections to a course without any severe consequences. In continued long treatment with Typhoid vaccine, the dose usually has to be increased by twenty-five million organisms each time, and as many as five hundred million organisms have been given at the
end of a course--(9). Usually the dose has to be in-
creased with each injection to produce a reaction, for
patients vary considerably in their tolerance. The num-
ber of injections depends on the patient's response in
the relief of pain and the healing of ulcers, but if the
treatment is to be prolonged for any length of time, it
is usually well to give a period of rest of a month or so
after each twelve injections. Such treatment is very
severe on the human organism due to the febrile reactions
produced.

Cohn (17) states that when giving typhoid vaccine
intravenously as a therapeutic measure, one should be
aware of the reactions which are characteristic. First,
there is a slowing of the peripheral circulation during
the first hour following the injection, and associated
with this, there is a decrease in the surface temperature
with a subsequent chill. Secondly, the general body
temperature increases three to six degrees, for each de-
gree of which, the peripheral temperature rises three
degrees, and at times this rise in temperature may be
maintained for several days. Allen and Smithwick (2)
have reported an increase in the peripheral temperature
of from five to fifteen degrees, and the old normal or old
level wasn't reached for as long a period as six to eight
days.
Cohn (17) also gives some advice in the use of typhoid vaccine:
(1) It shouldn't be used in arteriosclerotic patients who show degenerative change to any degree;
(2) It should never be used until the extremity has been heated for at least one-half hour by electric pads or other heating devices;
(3) The initial dose should be small, preferably twenty-five millions of the mixed organisms;
(4) The vaccine should be given intravenously and not around the vein;
(5) The vaccine should be given slowly;
(6) The patient should be hospitalized at least during the febrile reaction period.

Barker (9) gives some contra indications for this therapeutic measure, which are:
(1) Elderly asthenic, cachectic patients,
(2) Arteriosclerotic or anemic patients,
(3) Individuals with cardiac disease, particularly those with known coronary disease,
(4) Patients with an obvious, latent, or subacute infection.

It is obvious that Typhoid vaccine therapy therefore is not without grave danger—(17), (9), and if it is used, the technique and precautions cited must be followed very
closely if good results are expected.

One common complication which accompanies this treat-
ment is thrombosis of vessels during the chills with an
immediate exaggeration of the presenting symptoms due to
the sudden vascular occlusion-(9). Another phenomenon
noted is a primary vaso constriction just preceding the
chill, which also causes an exaggeration of the symptoms
--(12).

There exists some controversy over this treatment.
Beirman (12) and Johnson and co-workers (33) believe that
the physical means of raising body temperature is better
than by using Typhoid vaccine, the initial vaso constric-
tion which develops before the extremity increases its
temperature being omitted by the physical means; and they
believe a body temperature of one hundred to one hundred
two degrees Fahrenheit is sufficient to cause vaso di-
latation, because at a higher temperature, which Typhoid
vaccine produces, the vaso dilating system is no longer
stable, and therefore not a reliable system.

Conclusions regarding Typhoid vaccine therapy are--
(9), (2) -- that it tends to relieve pain and give an in-
creased blood supply to the extremity by establishing new
collateral blood channels, and with the newly established
collateral circulation there is an acceleration of the
healing of open lesions; the best results are seen in
patients who complain of rest pain and have existing ulcerations or limited gangrene on their extremities. It must be remembered that good results cannot be expected if other simpler measures are not also carried on at the same time.

Intramuscular foreign protein injections have been very disappointing, because the febrile reaction produced is so slight and the residual soreness at the site of injection is so severe, that it is deemed advisable not to use them. Sulphur in oil has been used with some success, but the local reaction is so severe, it too has been discarded—(9), (75).

Since 1933 the change of atmospheric pressure has been used quite extensively in treatment of peripheral vascular disease. The principle of this procedure is to use alternating positive and negative pressure to increase the blood flow to the extremities. Landis and Gibbon (40) in 1933 reported on this therapeutic measure which dates back to Nathan Smith in 1798. Shortly after Landis, Herrmann and Reid (32) of Cincinnati presented their work on the same measure. These authors were working independently of each other—(38), (31), (39), (37), (32), (30).

The complete history of the development of this method of treatment is well written in Herrmann's monograph on "Passive Vascular Exercise"—(30), and its historical
development will not be discussed in this paper.

All authors read believe this treatment is based on sound physiological reasoning. Landis and Gibbon (40) suggest that the sudden exchange of extreme degrees of suction and pressure as a means of increasing the flow of blood to an extremity through rigid or diseased arteries is in accordance with Poiseuille's law, which is that the amount of blood flowing along a capillary tube depends on the fall of pressure along the rigid tube. This has been verified by all subsequent workers.

The name "Pavaex" was given to this treatment by Herrmann, and Reid (32). This contracture was derived by using the first two letters of each word in "Passive Vascular Exercise."

When "Pavaex" was first used, Landis and Gibbon (40) advocated that 120 mm. of mercury pressure, both positive and negative, be used, but Herrmann and Reid (32) state that best results are obtained by using 80 mm. mercury negative pressure and 20 mm. mercury positive pressure, never exceeding 40 mm. mercury positive pressure.

The readers are referred to Herrmann's monograph on "Passive Vascular Exercise" (30) for the technique and procedure of using this type of treatment.

In instituting this treatment in average cases the suction varies from 60 to 80 mm. mercury, negative pressure;
and a positive pressure of 20 mm. mercury. Two to four such cycles are done each minute and this is done for two and a half hours each morning and evening, but some men--de Takats (22)--believe that longer applications produce much better results. The patient is kept in bed with the extremity resting at the optimal circulatory level. It is thought that twenty hours of treatment a week is sufficient for less urgent cases, but if there is a crisis, treatment may be continuous over a great many hours without fear of producing severe consequences--(56).

It has been suggested by Freeman in Metcalf and co-worker's (56) article that hot air of one hundred four degrees Fahrenheit be introduced into the boot during "Pavaex" treatment. He has stated that better results are obtained because with the alternating positive and negative pressure, the heat aids in producing vaso dilatation. Many other authors have confirmed this procedure and have also gained more satisfactory results with it.

This treatment has caused a rise in the peripheral temperature of some patients to as high as 7.1°C Centigrade above the pre-existing abnormal low temperature, and this rise has persisted for as long as seventy-two hours, whereas in other patients, the temperature has diminished and sunk to the old level in as short a time as
twelve hours--(32). On this same subject, Landis (37) states that the hyperemia produced is maintained for several hours after treatment has been discontinued and the dilating effect becomes more lasting as the treatment is continued.

Theis and Freeland (73) and Herrmann and Reid state that they haven't observed a great increase in skin temperature and that its beneficial effects are not obtained by vaso dilatation, because with the addition of heat to the arms a greater increase in skin temperature was reached. Both Herrmann and Landis, as well as Freeland, have advocated the use of some form of heat in conjunction with the alternating negative and positive pressure treatment to produce a maximum reflex heat vaso dilatation with the increased circulation. This has been proved by determining oxygen and carbon dioxide content of the venous blood. Therefore, reflex dilatation and pressure produces a greater clinical improvement than either treatment produces alone.

Herrmann (29) has shown by different methods of study that there is marked improvement in patients after using "Pavaex" treatment. By doing arteriographic studies on patients, he has shown an enormous increase in the size and number of useful collateral arteries in the distal parts of the extremity which had been treated inten-
sively. He states that one hundred hours of exercise, five hours a day, is sufficient to stimulate the development of an adequate collateral arterial circulation in most patients.

Herrmann, in the same article, showed that the degree to which the collateral circulation can be developed by this procedure depends largely on the actual number of arteriolar and smaller arterial pathways that are patent and unaffected by the disease process which exists. Therefore, the most striking clinical benefits will be observed in patients with sudden obliteration of the major arterial pathways by trauma or disease, and the least striking clinical results are to be expected in patients with extensive arteriolar obliterations in the distal parts of the extremities, that is, in patients with long existing Buerger's disease and arteriosclerosis obliterans. He believes that pressure produces its greatest effect on the circulation, while heat has a definite influence on the local metabolism of the extremity.

de Takats (22) gives some contra-indications to this treatment, "On theoretical grounds, infection and venous thrombosis, appearing separately or jointly should constitute a serious warning against the use of the machine. Particularly in the infectious type of diabetic gangrene with osteomyolitis of the toe, it would seem unwise to
use negative pressure."

de Takats (22) further states that a recent soft clot may readily be mobilized by this treatment, and thus result in severe consequences and even death. One should also think of certain acute venous thromboses which produce a temporary arterial spasm and exhibit cold, cyanotic, numb, and tingling toes and may mislead the physician to apply the apparatus for an arterial embolus. Therefore, the differential diagnosis of an arterial embolism, arterial thrombosis, and venous thrombosis is important before the use of the machine is instituted. Other contraindications are superficial migrating phlebitis and infection.

Metcalf and co-workers (56) gave a report by Conway on fifty-one cases on whom he used "Pavaex": in thirty-six patients with arteriosclerosis obliterans there was definite improvement in eighty per cent, in ten cases of sudden vascular occlusion the treatment was sufficient in nine cases to prevent the loss of a limb by amputation, and in four cases of thromboangiitis obliterans no improvement was noted.

Concluding on "Pavaex" treatment the following points are agreed upon by all authors--(22), (73), (29), (38), (31), (36), (5), (39), (32), (30):

(1) Indolent ulcers may heal as a result of treatment.
(2) Rest pain is usually relieved while the patient is receiving treatment, but it frequently returns.

(3) In some cases the pain disappears more or less permanently.

(4) Intermittent claudication is usually benefitted.

(5) Gangrene can be avoided in cases of sudden arterial occlusion if the patients are treated soon after the occlusions took place.

(6) It relieves pain of ischemic neuritis.

As yet there is much disagreement as to the results; many authors get good results while others obtain bad results in treating the same types of patients with the same disease. So, it seems as if there is much experimental work to be done in this field before treatment will be established on an absolute sound basis.

Within the last two years there has been developed another type of treatment—the use of intermittent venous occlusion. Collins and Wilensky (19) and de Takats and co-workers (23) have advanced it.

De Takats and co-workers (23) state that the phenomena of reddening of the toes, filling of the veins, rise of the surface temperature, and increased mobility of the toes are observed as objective changes produced by "Pavaex" and can be reproduced by intermittent venous compression or occlusion.
In Germany Beir (11) established the following facts about venous occlusion, based on numerous experimental and clinical observations:

1. Venous hyperemia produces a reactive hyperemia independent of nervous impulses.

2. Mild venous stasis maintained for one hour produces more beneficial results than arterial constriction of the same duration.

3. Reactive hyperemia may be produced when the vessels are occluded or cut, as in pedicled flaps whose pedicle has just been severed.

4. Reactive hyperemia ensues through the accumulation of metabolites and the filling and stretching of minute vessels.

The procedure of producing intermittent venous occlusion as given by Collins and Wilensky (19) is, "Apply to the proximal portion of an extremity a pneumatic cuff, which is inflated to a pressure approximating the diastolic level of the arterial pressure. This results in the creation of reactive hyperemia." The apparatus which the above authors have designed creates alternating periods of venous congestion and release of this congestion.

Lewis and Grant (42) show that during the release of venous congestion, an increase in arterial flow of as much as six hundred per cent develops, depending on the degree
and duration of application of venous congestion. They also showed that this increase in arterial flow is the result of an active vasodilatation which occurs in the arterioles. In applying the pressure, the above authors used 90 mm. of mercury pressure for fifteen minutes while Collins and Wilensky (19) used 60 to 80 mm. mercury pressure in alternating periods of two hours.

de Takats and co-workers (23) state that it is thought that a slowly diffusible histamine-like substance accumulates in the tissue spaces when the arterial supply to the limbs is occluded, causing an active dilatation of all the vessels, and that the longer the occlusion and the higher the environmental temperature, the more vasodilatation is produced.

It has been observed that the hyperemia following vascular occlusion was maximal after one hundred twenty seconds and that the longer the occlusion was maintained the more the desired reaction was diminished, so it is concluded that one hundred twenty seconds is the desirable length of time to produce occlusion to get the full benefit from the procedure. Another point stressed is that occlusions must not follow one another too closely, because the hyperemia won't reach its maximum if this is done, the vessels seeming to lie in a latent stage and enough time doesn't elapse for this latent stage to pass--
(23).

The practical applications of this procedure are given by de Takats and co-workers (23): any blood pressure apparatus may be used to produce the intermittent venous hyperemia, but a wide eight inch cuff, conically shaped to fit the thigh is preferable, for the pressure is distributed over a larger surface, and the same amount of pressure that is painful when exerted by a narrow cuff is comfortable with the larger cuff. The amount of pressure used is not to exceed the diastolic pressure at the level applied; it may vary between 60 and 90 mm. of mercury pressure in an extremity on which the toes are not edematous, cyanotic, ulcerated, or gangrenous. When the foregoing conditions exist, 40 mm. mercury pressure should not be exceeded at first, although with subsequent treatment the pressure may gradually be increased. The duration of the venous compression is determined by the appearance of a definite rubor, which occurs in one to two minutes when the pressure of 60 to 90 mm. mercury is used. The duration of the release should exceed that of the compression; together with the one minute of elevation, which can be kept constant, it should last twice as long as the compression. Thus, two minutes of compression require four minutes of release, of which three minutes should be spent in the horizontal position and
one minute in the elevated position. The elevation can
be active, but it is preferable to lift the leg with the
aid of a pulley. Thus, in the average case a cycle is
completed in six minutes—two minutes compression, three
minutes release, and one minute in elevation. When the
circulatory embarrassment is more pronounced however, one
minute compression will readily produce a rubor and this
is then followed by one minute of release and one minute
in the elevated position, making the cycle cover only
three minutes.

According to the above authors, thirty minutes of
this vascular exercise in the morning and the same in the
evening is sufficient, but the method is flexible and
readily adaptable to the patient's needs. If it should
be painful or uncomfortable to the patient, either the
pressure or the duration of the individual cycle has to
be adjusted to obtain maximum benefits.

Several points in favor of this treatment over that
of "Pavaex" are:

(1) It can be used at home with comparatively lit-
tle cost, while "Pavaex" requires hospitalization.

(2) It is available to a larger mass of people.

(3) It has a more logical cycle of constriction and
release, and is readily adaptable to the circulatory
embarrassment of the individual patient.
(4) This method of treatment does everything that "Pavaex" does with less cost and a smaller amount of expensive apparatus--(23).

In Buerger's disease, the outstanding results obtained were the complete and rapid relief of pain and the ability of ulcers to heal. In one case cited, all other methods were used without avail, but by venous occlusion the ulcer healed readily. In a series of twenty-three cases of arteriosclerotic obliterans, both diabetic and non-diabetic, ulcers healed in five cases while in several the treatment hastened amputation, consequently there exists some rationale regarding the use of this method of treatment--(19).

The contra indications for this treatment are the same as with the use of "Pavaex", that is, spreading infection, thrombo phlebitis, and wide spread arteriolar obstruction--(23).

There will be included in the medical treatment of peripheral vascular disease a minor surgical procedure, which is often an adjunct to good medical treatment to prevent amputation for pain only. Silbert (68) introduced a method which he describes as "the injection of the posterior tibial nerves at the papliteal spaces, for the relief of pain"; he performed this minor surgical procedure on five patients, under local anaesthesia, with excel-
lent results. The nerves were injected with procaine followed by a pure alcohol injection.

Smithwick and White (70) have drawn the following conclusions regarding this type of treatment:

(1) Pain in the lower leg and foot, secondary to obliterative vascular disease, can be relieved by alcohol injection of peripheral nerves.

(2) Alcohol injection can be done without paralysis of any of the important muscles of the leg or foot.

(3) Sloughing of the tissues may result from spilling alcohol on them.

(4) Depending on the length of the nerve trunk injected, the anaesthesia produced may last but a few months or may be permanent.

(5) Sacrificing a leg should never be necessary because of pain.

(6) Careful operative technique and scrupulous asepsis are essential to success.

(7) The incision should be made above the lower third of the leg and should be vertical by preference.

(8) The relief of pain has been responsible for saving six out of eleven legs which were otherwise doomed to amputation.

(9) After an extremity had been desensitized by this procedure, the authors frequently noted that the foot
became drier and warmer and previous color changes were eliminated. It was also noted that the surface temperature would rise five degrees Fahrenheit, this being due possibly to elimination of the sympathetic constricting power along with relieving of pain by interrupting the course of the peripheral nerve to its peripheral distribution. The majority of sympathetic nerves course peripherally with sensory nerves.

(10) The results are more successful if the papliteal artery pulsates. In cases of arteriosclerosis with obliteration above the papliteal vessel, this procedure, even if done in two or three stages; may precipitate actual gangrene and hasten amputation. The authors, however, feel that in such a case, if amputation is necessary because of pain, one is justified in doing a desensitizing operation first to see if pain can be relieved.

(11) After desensitization, ulcerations which previously resisted all treatment will frequently heal.

Smithwick and White (71) have advised a new procedure, in which the nerves are simply crushed to an extent of a quarter of an inch if rapid regeneration is desired, or up to a half inch if prolonged anaesthesia is desired.

They conclude that this latter procedure is the better of the two methods suggested, because it is time saving, a shorter incision is necessary, one avoids the
danger of spilling alcohol on the tissues, and the nerves
tend to regenerate more rapidly than they do after alcohol
injection. They also suggest that this procedure is
much more valuable in Thrombo Angiitis Obliterans than in
Arteriosclerosis Obliterans.

Next to be considered in the treatment of peripheral
vascular disease are the major surgical procedures, but
they will be discussed very briefly in this paper.

First is the criteria for amputation. It must again
be stated that amputation is not to be avoided if it is
the only procedure left to save a life—(30).

Mc Kittrick (48) has reviewed the amputation criteria
by classifying those applicable to these three major con­
ditions: Buerger's disease, arteriosclerotic gangrene,
and diabetic gangrene. The following indications are
given for early operation:

(1) Buerger's disease.
   (a) Progressive extension of gangrene in spite
of conservative treatment.
   (b) Rapidly ascending infection.
   (c) Destruction of so much of a foot that in­
sufficient structure remains to insure an adequate weight­
bearing extremity.

(2) Arteriosclerotic obliterans.

Generally, unless actual gangrene involving the
deeper structures of a digit exists, most patients respond to the hospital routine of conservative measures. Undoubtedly the early response to treatment represents a readjustment of the circulatory needs of the extremity rather than a new development of collateral circulation. Many of these patients come to the hospital with severe, unbearable rest pain to become pain free within two weeks' time without other than simple measures.

(3) Diabetic gangrene.

Indications are not difficult if one remembers

(a) A diabetic patient is frequently as old as his age in years plus the duration of his diabetes.

(b) Beginning gangrene in a patient with diabetes usually accompanies serious change in other parts of the body and is the beginning of a big economic load and short expectancy.

(c) Treatment by trial and error is exceedingly dangerous and usually unsuccessful.

(d) Prolonged sepsis or pain undermines the already damaged heart and kidneys and lowers their morale.

(e) Once gangrenous, the chances for septicemia are much greater than for the development of a collateral circulation.

(f) If a patient comes with a pain that
is not relieved in two weeks with conservative measures, whether gangrene is present or not, surgery is indicated because it will be the eventual results.

It is stated, however, by M.C. Nealy and Shapero (55) that the primary element in an amputation decision is an estimate of the circulatory status of the limb. They reemphasize the importance of pre and post operative medical management to encourage the development of a good collateral circulation. They also stress the fact that amputation need not always be done at or above the knee in Buerger's disease: It is done at the lowest level compatible with an assurance of healing given by the circulatory tests. In arteriosclerosis also, careful study can save limb length.

M.C. Laughlin (77) in a personal communication suggests that amputation is done most extensively in obliterative arterial diseases principally to remove gangrenous digits and for the relief of excruciating pain.

According to the literature regarding sympathetic surgery, there seems to be much unrest and difference in opinion in the rationale of this procedure. Taking the opinion of Cohn (18), who is strongly against this type of surgery, one finds that the entire group of vascular diseases are generalized diseases and that by doing sympathectomies to combat the existence of the disease in
one extremity is useless. He states that the advocates of sympathetic nerve surgery have met with definite rebuff to their early enthusiasm, that Periarterial Sympathectomy has been shown to be ineffective, and ramisection and ganglioneectomy have no place in the treatment of cases where obliterative changes are present. He states that no amount of removal of vasoconstriction control can cause dilatation in arteries which have definite changes in their walls.

Cohn (18) goes further to state that patients with Raynaud's disease who have been subjected to ganglioneectomy have not only not been permanently relieved of their symptoms, but have later had to have an amputation performed. He also believes that better results may be obtained by use of the conservative measures in overcoming arterial spasm than by doing radical surgery. He contends that much study and experimental work are still necessary to make this an accepted method of treating vascular disorders.

On the other side of the question, Smithwick (69) has enumerated the values of sympathectomy in the treatment of vascular disorders:

(1) Recent advances in the knowledge of the anatomy and physiology of the sympathetic nervous system have been responsible for excellent clinical results.
(2) Preganglionic section exhibiting marked vascular spasm have resulted in satisfactory clinical results.

(3) Certain groups of Thrombo Angiitis Obliterans cases are suitable for sympathectomy if any marked degree of spasm exists.

Mc Laughlin (77) states that the field of sympathetic surgery finds its only field of usefulness in those cases in which there is a definite vasospastic element present, and this is primarily confined to (1) Raynaud's disease and (2) a few selected cases of Buerger's disease where it has been proved that vasospasm exists.
PERSONAL CONCLUSIONS
1. An early diagnosis must be made to prevent the development of severe sequelae.

2. Diagnostic procedures are not difficult nor too time-taking.

3. Always palpate peripheral pulse, and if absent, there is peripheral vascular disturbance.

4. Patients with a diseased peripheral circulation should be instructed thoroughly on how to rehabilitate themselves and how they can live within their vascular margin of safety.

5. All patients should be given advantage of the general measures to help relieve pain and help to establish an adequate collateral circulation.

6. Drugs haven't offered much aid in relieving spasm or producing vasodilatation; vasodilating drugs cannot be "fixed" in the vessels long enough to produce the desired effects; Papaverine has been proven useful in acute arterial occlusion.

7. Tissue extracts have been used with good results to produce vasodilatation.

8. Hypertonic saline solution produces its desired effect by decreasing the viscosity of the blood, thus allowing for better circulation to the affected extremity.

9. Typhoid vaccine therapy tends to relieve pain and give an increased blood supply by establishing a new
collateral circulation to the extremities; the best results are seen in patients complaining of rest pains and presenting ulceration or limited gangrene.

10. "Pavaex" treatment shows its best results in the treatment of indolent ulcers; rest pains are usually relieved while the patient is receiving treatment, but they frequently return; intermittent claudication is usually benefitted; pain of ischemic neuritis is relieved; gangrene can be avoided in cases of sudden arterial occlusion if the patients are treated soon enough after the accident has happened.

11. Intermittent venous occlusion brings about complete relief of rest pains in Buerger's disease and brings about the healing of ulcers; this procedure produces the same desired effects as does "Pavaex" with much less apparatus.

12. Section of sensory nerves or alcohol injection may be resorted to, in order to prevent amputation for the relief of pain; some vasodilatation results from section of the sensory nerve.

13. Amputation is resorted to in cases where only heroic surgical measures can save life; amputation is resorted to for the relief of excruciating pain.

14. Sympathetic surgery should only be resorted to where there is definite evidence of an existing vasospasm, such as is present in Raynaud's disease and in selected cases
of Buerger's disease where vasospasm has been proven to exist.
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