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Peripheral vascular diseases ; special reference to non-surgical treatment

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PERIPHERAL VASCULAR DISEASES;
Special Reference to Non-surgical
Treatment.

by

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1937

"It takes a good physician to save a leg but any
one can amputate one"... Scott and Morton (58)

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INTRODUCTION

This paper has been prepared with the sole purpose of becoming better acquainted with the modern trends of therapeutics in peripheral vascular disease. This age old problem was considered from this aspect with the thought in mind that such a view would have more practical value than attempting to discuss a theoretical problem such as etiology, since no original work was done to complete it. An attempt has been made to review the more recent literature, with occasional reference to an earlier work of an originator of some phase of the subject. The original idea was to discuss generally the therapeutic principles applied, but after reading several articles the impression gained was that there was considerable disagreement as to the effectiveness of these procedures. Therefore, an effort has been made to view the field generally but more particularly as to the efficacy of the methods in use. Since this paper deals primarily with treatment, many of the theoretical considerations of the various types of obliterative arterial diseases of the extremities and minimum requirements for a definite diagnosis, which have been outlined in detail by Allen (1), and many others, have been purposely omitted in this paper. The general conclusion reached by Herrmann (30), was, "from the standpoint of therapy alone, however, the

clinical name of the disturbance is of little importance and usually adds to the confusion rather than to the elucidation of the facts concerning the pathologic-physiology of the disease."

Interest in this subject was stimulated by the thought that with the increasing of the span of life, reduction of deaths by infectious diseases, and increasing number of degenerative diseases, would ultimately increase the incidence of the degenerative types of peripheral vascular disease. Therefore, this problem would gradually assume larger proportions of the medical practice, not only from the local standpoint but as deTakats and Scupham (21), have aptly expressed that it must be remembered that peripheral vascular diseases are only a local manifestation of a general disease. During my very meager clinical training the general impression which was conveyed, was that gangrene meant inevitable amputation, therefore interest gained impetus in an attempt to learn more about the accomplishments in this field of surgery.

The motto which is now coming into the fore in the medical field is one of prevention, or at least early diagnosis to prevent sequelae. This is directly applicable to peripheral vascular disease, and is therefore, a great responsibility of the physician to note early

a deficient circulation of the extremities. deTakats (18), summarized the situation at the present. He stated, "that it is no exaggeration to say that thousands of individuals are unconscious or mildly conscious of progressive interference with their peripheral circulation. Their margin of safety is minimal. Their rheumatic pains come and go with changes of the weather, mechanical stress or emotional load. An occasional numbness or tingling of the extremities is disregarded. They undergo an annual or semiannual physical examination during which chest plates are taken and electrocardiograms are read. Insurance examinations may be made or physical examination when they apply for a new job, but nobody palpates pedal pulses. As a result, the middle aged wage earner, the insured policyholder, or the railroad or street car conductor suddenly develops a serious interference with the peripheral blood flow. This did not come on suddenly but was just part of a chronic progressive arterial obstruction which is present in many patients going through the better clinics which is present in many patients going through the better clinics and is not recognized." Therefore, interest in this subject should be universally developed.

HISTORY

It is difficult to say how long peripheral vascular disease has existed, but it is quite inconceivable to believe that the race of the past could have reached the senile period without degenerative changes occurring in the peripheral arteries. It is possible that some of the presenile types of gangrene may not have existed since the beginning of the human race but this is not very likely.

It has been only about a century and a half since members of our profession began to suspect that certain ills of man might be due to deterioration in the functioning of blood vessels. Herrman (30) found the first description of a definite cause and effect relationship between organic arterial diseases and gangrene, was presented in the monograph written by Francois Quesnay in 1749, entitled "Traite' de la Gangrene." However it was not until 1817 that Hebreard and, two years later, Avisard, presented ample pathologic evidence to support Quesnay's clinical observations.

According to Reid (54) many great physicians were interested during the sixteenth and seventeenth centuries, in ossified and bone like arteries but it was not until the last quarter of the eighteenth century that Margagni and Fothergill suspected the casual

relation-ship between degenerative changes of the coronary arteries and the clinical condition of angina pectoris. In 1837 Carswell and Cruveilhier (1829-1842) attributed peripheral gangrene to an obliteration of the peripheral arteries and thus dispelled the old idea that it was due to a lack of innate heat.

In 1829-1833 Lobstein gave us the term arterio-sclerosis and very soon it was used to denote all forms of arterial disease. The blood vessels have gradually come to their own and full realization of their importance by the medical profession has been accomplished. A matter of particular interest to surgeons has been the study and treatment of peripheral vascular diseases.

There has been a gradual differentiation of this large class called peripheral vascular disease. Raynaud described the disease which now bears his name in 1862. The general entity erythromelalgia was outlined by Weir Mitchell in 1878. In 1879 Winiwarter wrote about thrombo-angiitis obliterans which was later (1908) so clearly presented by Buerger (11).

Since these original descriptions a great deal of clinical and experimental work has been done in an attempt to improve diagnostic and therapeutic procedures. In reviewing the literature little could be found as to specific therapeutic measures in use before the beginning

of the twentieth century. The only methods in use up to this time which, however, must not be minimized are general measures and amputation. In the last three decades much has been done to find additional measures of value and especially in the last ten years. The origin of these will be given as they are discussed.

INCIDENCE

Since there are so many individuals who go about their regular work entirely unconscious of the narrow margin of safety which exists in regard to the distribution of arterial blood in the distal portions of their extremities, it is extremely difficult to give the incidence of organic disease of the extremities. According to Herrmann (30) who analyzed patients in the fourth, fifth, and sixth decades of life, who complained of "painful feet or legs" revealed that in seventy six per cent of them, there was evidence of extensive arterial disease of the arteriosclerotic type. A recent survey made by our federal government in regard to the proposed "old age pension" showed that there are more than 7,500,000 men and women living in the United States at the present time who are sixty five years of age or older; and it has been estimated that there are more than 10,000,000 people in this country alone who have some form of circulatory disturbance in the extremities which is responsible for partial or complete disability for the usual type of physical work.

CLASSIFICATION

There has been few additions to classification of peripheral lesions since Collins (13) made an attempt to classify them in 1914. A great deal of clinical and experimental research has been performed since that time in an attempt to isolate specific etiological agents for each definite entity, with many pertinent observations which have been helpful in good logical therapeutics.

Allen(1) suggests that since the specific etiology of the many conditions is not known a good pathological anatomical classification is very helpful. He has given a very simple classification which may be briefly summarized as follows:

A. Primarily Spastic Conditions

B. Primarily Organic Conditions

1. Congenital (these have been aptly described by deTakats in 1932).
2. Inflammatory.
3. Traumatic including thermal and drugs.
4. Degenerative.
 - a. arteriosclerotic
 - b. diabetic
 - c. Monckeberg's sclerosis

Brown (10) as early as 1926 pointed out the importance of recognizing the spastic element in the true occlusive diseases. He suggested that there

were four types of lesions generally which were in some cases distinct and in others a combination of several or all. These were:

- 1) Major arterial occlusion
- 2) Major arterial spasm
- 3) Minor arterial occlusion
- 4) Minor arterial spasm.

DIAGNOSIS

A few diagnostic features common to all vascular diseases of the extremities will next receive consideration. The diagnosis of vascular disorders may now be made early due to the numerous new apparatus available and methods devised, though occasionally no instruments are required. Gutman (27) emphasized the point that it is especially important to diagnose the conditions in their early stages as simple procedures at this time may prevent subsequent gangrene. deTakats and Mackenzie (20) pointed out that progress in the field of peripheral vascular diseases can be expected only when adequate methods for testing peripheral circulation are systematically employed and when the value of various therapeutic procedures can be estimated, not only by the subjective impressions of the patients, but by the objective findings measured by diagnostic procedures. Such diagnoses may be established by a complete history, careful inspection and palpation of limbs under suspicion, the search for metabolic disorders, infections, and central and peripheral nervous diseases as well as by careful study of the cardiac apparatus and arteries.

Suggestions are given by Allen (1) whereby a good and adequate history may be obtained. He concludes that the majority of cases that present themselves for

treatment have many characteristics in common, regardless of their age, sex, nationality, or type of arterial obliteration; such symptoms as pain, intermittent claudication, insomnia, and lowered tolerance for cold, may be complained of by all. The history should take into consideration the duration of symptoms, the extent and period of disability, the type of work, injury or previous inflammatory process such as phlebitis, the amount of generalized arteriosclerosis, stability of the nervous system, and habits. Any or all of these may throw considerable light on the diagnosis and prognosis.

deTakats (18), Buerger (11), Gutman (27), and many others give the following clinical diagnostic objective signs of impaired circulation of the extremities due to arterial disease: local pallor, determined by holding the extremity above the level of the heart, indicating that the superficial vessels are emptied; coldness due to such impelled absence of blood; rapid cyanosis occurring when the limb is suddenly changed to a pendant position; rubor due to dilatation of capillaries and small vessels of the skin; local cyanosis due to stasis of toneless superficial vessels when the limb is in a pendant position. Landis and Gibbon (34) advise a room of 70 degrees F. with a good natural light during the examination.

Allen (1) suggested that all of the extremities be exposed so that a comparison may be made.

In addition to inspection there is touch and palpation. Palpation of the dorsalis pedis, posterior tibial, or other arteries of the upper and lower extremities may disclose absent or decreased pulsation. This procedure should not be difficult but as Reich (52) has found that in 4% of cases the dorsalis pedis pulse is absent and that in another 8% the artery is in a lateral position from the customary site (normal), this should be remembered. He also warned that the absence of pedal pulses is not infrequently found in older male patients who have no complaints. Their feet are warm and of good color; the slow gradual occlusion of the main vessels has permitted the development of an adequate collateral circulation. An absent pulse wave, therefore, does not always mean complete occlusion because blood may trickly through.

Gutman (27) gives a good review of the modern laboratory tests which are dependable. Pachon oscillometry is considered a valuable means of determining patency of arteries. A comparison of the shape and height of oscillometric readings taken at several similar levels of the two extremities offers a fairly accurate idea of an occlusion; with the exception of instances where

extensive collateral circulation exists, oscillometry is one of the most precise methods of determining the circulation of an extremity particularly of the larger vessels.

deTakats (19) in 1931 described the histamine test which is also useful for the determining of collateral circulation. He injected .1cc. of 1:1000 solution of acid phosphate of histamine, which is a powerful vasodilator, into the extremity held in the horizontal position. This produces a characteristic flare with a central wheal. The flare is absent when there is insufficient head pressure in the artery, arterial spasm which cannot be overcome, or when peripheral nerves have degenerated. Its use also extends to the therapeutic field for it may be used to tell the lowest level of safe amputation when bony prominences are avoided, and a little leeway for increased bone destruction over areas with good skin circulation is considered. It may also be used to note improvement of collateral circulation under conservative treatment.

Touch enters the diagnostic field in that differences in surface temperature of an extremity may be determined by the hands which can appreciate a difference of 1 degree F.. Differences of temperature of an extremity may vary to the extent of three degrees or more.

However, where doubt exists a special mercury skin thermometer or the thermoelectric couple may be used. This is an indication of the amount of blood reaching the extremity. As Brown (10) pointed out in 1926, it is very important to determine whether this is due to spasm or occlusion. Many laboratory procedures have been devised since that time in order to make this differential diagnosis. Brown (10) first suggested the use of typhoid vaccine which increased the skin temperature, during the reaction of fever, thereby produced a dilatation of spastically contracted vessels. He called this the "fever test for spasm". deTakats (19) describes a method whereby the posterior tibial nerve is anaesthetized by novacaine injections at the inner ankle. The skin temperature of the plantar surface of the big toe is determined before and ten minutes after injection. If the condition is spastic there will be a rise within that length of time to the normal vasodilatation level of 33-35 degree C. Landis and Gibbon (34) devised a simpler method for general practitioners. The examination should be made in a room of 70 degrees F.. The temperature of the big toe is determined with a skin thermometer, for which even an ordinary fever thermometer can be used. Then the hands and arms of the patient are immersed in hot water

(113 degrees F.) for twenty minutes. This produces a reflex vasodilatation on the lower extremities. The rise in temperature, measured on the big toes is the index of the amount of vasoconstriction that the reflex heat overcomes. When the normal vasodilatation level of 91.4 degrees F. is obtained, the test has demonstrated a sufficient vascular bed to overcome organic obstruction. However, as frequently occurs in older, arteriosclerotic individuals, should the rise in temperature not be sufficient to reach the normal vasodilatation level, one must assume a deficiency of the available collaterals, a diminution of safety factors. This then not only reveals the element of spasm in a given patient but has a prognostic value as it measures available collaterals.

Gutman (27) also suggests another simple procedure which may be of some aid. This is the reaction hyperemia following blood vessel compression, as determined by the sphygmomanometer, which is delayed in arterial disorders. In the normal, the blood reaches the digit in less than 15 seconds as a full flush of maximum intensity in obliterating diseases of an extremity, the hyperemia is delayed to a minute or more and presents a mottled or patchy appearance. deTakats (18) points out that the dial type of sphygmomanometer might be

used as an oscillometer in general practice.

Arteriography is another means of determining the circulation of the extremity. An ordinary radiogram may reveal the presence and extent of calcification of an artery, but offers no conception as to the efficacy of the circulation in the calcified vessel, as concluded by Landis and Gibbon (34). In arteriography, which is still in the experimental stages, sodium dioxide is used as an opaque medium. In the normal limb, the vessels are numerous; the involved arteries show a patchy distribution of lesions in various locations, an irregularity of course and contour of their lamina with a reduction in size and often divided, as by a knife, at points of occlusion in arteriosclerosis, marked tortuosity and narrowing of the lumen with conspicuous absence of collateral circulation are the prominent features Gutman (27) redescrined.

Some diagnostic procedures which are not routinely to be established but which may add additional information in some diagnostic problems are used by deTakats and MacKenzie (20). These are the electrocardiogram, blood volume and viscosity, ophthalmoscopy, and plethysmograph. Biopsies of smaller arteries in muscle tissue may be taken for indication of general pathological change.

The differential diagnosis of peripheral vascular

diseases presents difficulties and not infrequently the first impression is incorrect. Some are border line cases and occasionally remain as such, a definite diagnosis being impossible until the microscopical examination of a pathological specimen is made. However, the following generalizations made by Allen (10) are used by most men in this field:

Findings	Vasomotor Disturbances	Thrombo-angiitis Obliterans	Monckeberg's	Arterio-sclerosis
Average age	30	40	50	60
Sex	female	male	male	all
Nationality	all	Hebrew	all	all
Duration	years	years	months	months
Extremity	upper	lower	lower	lower
Symmetry	bilateral	one side at a time	unilateral	unilateral
Gangrene	late	late	early	early
Pulsating Vessels	no	no	no	yes
Vessels by X-ray	no	no	no	yes
Response to Foreign Protein	marked	marked	slight	slight
Response to Novocaine block	rapid and marked	slow and mild	to be determined	slight
Development Collateral Circulation	none	good	slight	fair

TREATMENT

Since this paper is concerned primarily with the non-surgical treatment the first aim is to formulate the indications for such treatment. However, as Buerger (11) and many others have concluded medical treatment should be instituted first if only to improve the collateral circulation pre-operatively. Herrmann (30) however, warned against the use of medical treatment when only heroic surgical procedures can be life saving. As much as the dislike for amputation of a limb for arterial deficiency, we 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 vessels, as amenable only to surgical removal. The question therefore arises as to what are the indication for amputation.

McKittrick (42) reviewed the amputation criteria by classifying those applicable to three major conditions i. e. thrombo-angiitis obliterans, arteriosclerotic, and diabetic gangren. The following indications are given for early operation:

1. Thrombo*angiitis obliterans.
 - a. Progressive extension of gangrene in spite of conservative measures
 - b. Rapidly ascending infection.
 - c. Destruction of so much of a foot that in-

sufficient structures remain to insure adequate weight bearing should complete healing take place.

2. Arteriosclerotic.

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.

Indications not difficult if one remembers:

- 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 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 gangrene the chances for septicemia

are a lot greater than that for collateral circulation.

f. If a patient comes in with a pain that is not relieved in two weeks with conservative measures whether gangrene is present or not, surgery is indicated as this will be the eventual result.

McNealy and Shapiro (43) stated that the primary element in the amputation decision is an estimate of the circulatory status of the limb. They re-emphasized the importance of pre-operative and post operative medical management to encourage collateral circulation. Stress is placed on 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 the assurance of healing given by the circulatory tests. In arteriosclerosis also careful circulatory study can save limb length. Not all diabetic gangrenes are to be handled alike since one group is essentially infectious. Diabetes is common to both only as a complication, and the proper amputation level in the infectious type is much lower. Dodd (22) concluded the situation quite appropriately by stating that a wider clinical experience is necessary for the development of unfailing criteria measuring the indications for and the nature of the surgical approach to this great problem.

What is therefore the aim of conservative measures?

McKittrick (42) and Herrmann (30) summarized these aims very shortly as follows:

1. Control infection.
2. Relieve pain.
3. Stimulate the development of collateral circulation.
4. Release vasomotor spasm.

Scott and Morton (58) pointed out that treatment should always be directed first toward preventing the ischemia from doing more harm than necessary, regardless of the cause. Recent advances to accomplish this aim have been the correlation and crystallization of ideas and the application of the various methods more definite to each type of disease according to deTakats and Scupham (21). Some of these procedures now in use will be presented.

Barker (8) pleaded for prophylactic treatment when he asserted that in spite of the many warnings the vulnerability of the toes of patients with occlusive arterial disease has not been sufficiently emphasized. Gangrene is induced by the most trivial type of injury. In 35% of a series of one hundred and seventy one cases of thrombo-angiitis obliterans with gangrene, this condition followed various therapeutic procedures, while in 39% of one hundred and fifteen cases of arteriosclerosis with gangrene, therapeutic procedures were the cause. He recommended that no local surgical or medical treatment

of the toes be instituted in any case until the arterial blood supply has been proved adequate. McKittrick (42) found that in many cases of arteriosclerosis gangrene can be postponed for many years if gradual rehabilitation by regular graded active exercises, careful foot hygiene, and living within circulatory possibilities is prescribed.

First, in the medical treatment of peripheral vascular diseases, the importance of general measures is stressed by Reid (53), Buerger (11), Allen (1), Silbert (61), and many other authors. These are routinely applied by all men regardless of the type of specific therapy they advocate. Reid (53) pointed out that these are often forgotten in the excitement of new ideas and discoveries with respect to etiology, diagnosis, and treatment. He also believed that these procedures along with remissions that are common to many conditions are the basis for the very good results given to many of the new procedures. The general measures which have been advocated by Allen (1), Reid (53), Buerger(11), and many others as useful are as follows:

1. In the management of the patients with peripheral vascular disease it is of utmost importance to secure and maintain the interest and active cooperation of patients. Fortunately, most of the therapy is reasonable and easily understood if only the time and patience are devoted to

explaining its significance.

2. The position of maximum circulation of the affected parts when at rest should be determined for each case. A simple method is to observe the fullness of the veins when the extremity is put at different levels with respect to the level of the heart. The best position is at the level where the veins are neither collapsed nor distended, when they are visible and apparently on the same level with the surface of the skin. This point is usually within three to six inches below the heart. The importance of not elevating above the heart or dependency must be stressed.

3. The effect of cold is evident from the height of incidence of complication during the winter months. The affected extremities should never be allowed to become cold. Moderate sweating improves the texture of the skin and the nourishment of the tissues beneath it.

4. By means of baths, oils, and greases the skin should be made as soft and delicate as possible.

5. The most trivial wounds and infections should be treated as a major complication until they are completely healed.

6. Any form of trauma to inflamed or diseased vessels should be avoided by both the patient and doctor. The possible dangers of the tourniquet and blood pressure

apparatus, as well as certain forms of exercise and passive massage should be avoided.

7. Buerger's (11) or Allen's (1) exercises should be taught the patient during which time a short period of hospitalization is desirable.

8. Amputations performed between two tourniquets for gangrenous and infected extremities probably reduce the incidence of infection of the stumps. If, for fear of damage to tissues and blood vessels, the use of a tourniquet is contraindicated, the distal tourniquet alone may be used.

9. The fluid intake should be established and maintained at a high level which should at first be measured. The total daily intake should not be below 4000 cc. per day.

10. In some cases the uses of thyroid extract may be of some help in improving the circulation.

11. Eradication of foci of infection especially in thrombo-angiitis obliterans and inflammatory lesions.

12. Abstinence from alcohol and tobacco.

Tobacco abstinence has been shown to be a rational procedure by some interesting work done in the past few years. Maddock and Collier (39) found in 1932 that smoking produces aggravated vessel spasm by measuring the skin temperatures. Friedland and co-workers (23) found that

the injection of denicotinized tobacco extract, in Ringer's solution, intraperitoneally, in rats caused gangrene of toes of the male rats in from five to twelve weeks whereas the female rats did not show this change. Maddock and co-workers (40) also concluded that the smoking of two cigarets by women resulted in a drop in the skin temperatures of their fingers and toes, and an increase in their blood pressures and pulse rates similar to those observed in men. Such 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 of significance in accounting for the greater incidence of thrombo-angiitis obliterans among Jews than among other elements of the population. Silbert (61) found that in 50% of the patients who required amputation out of 225 cases of proven thrombo-angiitis obliterans, continued to smoke in spite of repeated warnings. Recurrence of symptoms after the individual has been restored to good condition, was almost invariably traceable to the resumption of smoking.

Allens (1) modification of Buerger's (11) exercises are described as follows: "The first position should be last, theoretically as long as is necessary to blanch the skin of the extremity. This varies considerably but two minutes of elevation of 45 degree angle is usually

sufficient. The second position is carried out by the patient sitting on the side of the bed with feet hanging down. During this phase, which should also last two minutes, the patient should systematically dorsiflex and extend the feet, then invert and evert them, then flex and extend the toes. The third position is carried out with patient lying flat in bed with the feet on an electric pad covered with a light warm blanket, and should last five minutes. The three positions consist of a cycle and there should be from three to six cycles in a seance, with from two to four seances a day. These exercises should be carried out with accuracy, a time peice at the bedside or in the patient's hand being essential". He pointed out that these are very useful especially in the arteriosclerotic group. Sanders (56) reported the invention of a new type of oscillating bed so that these exercises may be performed by the patient without active motion. This is accomplished by change in position of the foot of the bed which operated electrically.

Another local general measure, which is advised by Perlow (49), is diathermy. This is used locally to the extremity for one hour twice a week with other general measures. Its action is though to be the causation of active arterial hyperemia and hyperlymphemia, local relief of pain by the heat acting on all the nerve endings,

antispasmodic action and bactericidal action. He concluded that the heat goes deeper in the tissues than ordinary local heat as it can not be dissipated as rapidly, therefore, it is of definite value in the treatment of peripheral circulatory disorders, especially in arteriosclerotic ischemia without gangrene.

Drugs have entered the field of therapy in the very recent years. The rationale of their use has been for the most part the relief of spasm. Much controversy still reigns as to their efficacy. Scupham (59) advocated, for the relief of vessel spasm, the use of large doses (from 40 to 60 grains, or 2.6 to 4 Gms.) of theobromine sodium acetate. Gutman (27) agrees that theobromine compounds are useful for pain, the pre-gangrenous state, and for more prolonged vasodilatation in intermittent claudication in arteriosclerotic and thrombo-angiitic obliteration. However, McGovern and co-workers (41) concluded that theobromine with sodium salicylate as a vasodilator is unreliable and too feeble to be useful.

Gutman (27) recommended the use of acetyl products, powerful vasodilators, for Raynaud's disease. Goldsmith (25) was in full agreement and ascribed to acetyl-B-methyl choline chloride three important actions. They are as follows: a parasympathetic stimulating effect, a vasodilating effect, and a nicotine like effect, which causes

a rise in the blood pressure when its other actions have been abolished by atropine. In her work she found that following oral administration the skin temperature rose, in hypertension and Raynaud's disease, to a much higher level. She advised 50 mg. for arteriosclerotics and 1,000 to 1,500 mgs. for thrombo-angiitis obliterans. Action began after fifteen minutes to two hours after oral administration and lasted from one to six hours but could be maintained for seven to eight hours if the dosage was repeated in three to four hours. There was no relief from pain but a marked temperature rise. Safety in its use was established.

deTakats (17) recommended the use of papaverine in acute arterial occlusion. In five cases marked improvement was noted. He pointed out that no stable solutions are available so it must be made up in ampules. He concluded that it is harmless and its principle effect is in combatting reflexive vessel spasm of arterial occlusion. Gutman (27) was in full agreement, and stressed the fact that it must be given within two to four hours after the attack. The method of administration is intravenously but where the first or second injections afforded no relief, treatment should be discontinued.

For the relief of pain, all authors universally agree that morphine and codeine should be avoided if poss-

ible, and that aspirin, phenacetin, and amidopyrine should be tried first.

With the search for new type of therapy Conwell (15) began the use of Parathormone. He reported the indications for its trial were: unsatisfactory results with other forms of treatment previously employed, unsatisfactory results with other forms of treatment on similar cases, and the presence of a hypocalcemia suggested a metabolic disturbance with possible vasocanstrictor hyperirritability. In two cases of intermittent claudication and two with thrombo-angiitis obliterans who were given .5cc. or 10 units of Colip's parathyroid extract every other day for ten injection improvement was relatively rapid and uniform. The attacks of intermittent claudication were controlled, permitting at least temporary return to normal activity. The circulatory changes in the patients with thrombo-angiitis obliterans were even more spectacular, i.e., fairly prompt and complete control of pain that had necessitated morphine, return of warmth, moisture, diffuse reddish color on elevation of the foot, loss of tenderness, improved sensation and motion of the toes, disappearance of the ecchymoses and deeper discoloration, and return of pulse in dorsalis pedis and posterior tibial arteries. There were no untoward reaction noted. Calcium gluconate was also given to two of the patients

but their response was equal to the two in which it was withheld.

The use of skeletal muscle extract, pancreatic extract, and adenosin phosphate has been used by many foreign workers for the relief of ischemic pain. Barker and co-workers (6) have summarized their work with also original work on the problem. They used all three types of substances first, a pancreatic extract, so called padutin, second, a skeletal muscle extract, the so called myoston, and third muscle adenosin phosphoric acid. The results in their experiments, which were always supplemented by controls, were encouraging. They found definite lengthening of the time necessary to produce intermittent claudication during a standard claudication test in 92% of a series of fifty five cases of thrombo-angiitis obliterans and arteriosclerosis obliterans, following intramuscular injection of padutin. Similar effects were noted in all of the series of eight cases of thrombo-angiitis obliterans after intramuscular injection of myoston. In only one of five patients with arteriosclerosis obliterans was an increase in claudication time noted after myoston had been given intramuscularly. In 75% of a series of eight cases of intermittent claudication which the patients received myoston orally an approximately equal more transient effect was noted. Definite, but

less striking increases in claudication time were noted in four cases in which patients received muscle adenosin phosphoric acid intramuscularly. They also found quite conclusively by measuring the amount of vasodilatation that this relief was not due to this factor for the relief was greater than from any of the vasodilating mechanisms. Schwartzman (57), however, believed that this is the cause and not the supplying of some absent metabolic substance to the ischemic muscle. He found that extract from diaphragmatic muscle was superior.

In 1925 Phillips and Tunick (51) reported the use of x-ray on Buerger's disease. This type of procedure was noted accidentally in a patient who was originally irradiated over the lower pelvis for hypertrophied prostate and at the same time had Buerger's disease. The vascular lesions showed improvement under this type of treatment. With the use of stimulating doses of x-ray over the tenth dorsal to the fifth lumbar vertebrae in the lower extremity affectations, and over the cervical and upper dorsal segments in upper extremity disturbances the following results were noted:

1. Relief of pain in two to three weeks time, the exception being 10%; uniform and progressive relief.
2. Resuming of work in five to six weeks.
3. Intermittent claudication reduced in all and and completely cleared in 50% in six weeks.

4. Improvement in circulatory and trophic disturbances noticeable in from one month to six weeks.

5. Phlebitis and inflammation shows improvement after the first treatment.

6. In ten ulcers in the series all were healed in from six to eight weeks.

7. Marked general improvement due to reduction of pain.

Pfhaler (50) in 1935 corroborated this work. He emphasized that local irradiation is contraindicated.

In 1923 Goodman and Gottesman (26) reported on the use of typhoid vaccine in Buerger's disease (four cases). This type of therapy was instituted since such marked improvement was noted in joint conditions and this was considered a chronic inflammatory lesion so decided that this type of therapy might be logical. Typhoid vaccine was used because of its convenience, safety, and ease of administration. Intramuscular doses were given weekly, gradually increasing the dose at each injection sufficient to produce mild symptomatic reaction. The most striking result obtained was the sustained relief of pain in all cases sufficiently complete to obviate any further necessity for medication with morphine or its derivatives.

Allen and Smithwick (2) reported on the use of typhoid

vaccine in all types of peripheral vascular disease. They found that there was a definite relief from pain and a beneficial change in the appearance of lesions. They advocated the combination of this type of treatment with general measures. They thought that the method of action was the enhancing the collateral circulation.

In 1930 Barker (5) of the Mayo Clinic brought into us an experimental product call typhoid 'H' antigen which is now in common useage. This was made by a fraction of the typhoid bacteria prepared by emulsification of the organisms in sodium chloride solution and subsequent killing with 5% phenol. He found that it was not as sure of productin a reaction, but it was less apt to cause a chill and malaise for the amount of fever produced. Barker (7) reported further observations on the use of foreign protein in thrombo-angiitis obliterans. He concluded that it has relatively little effect in cases in which there is claudication only or where there is extensive gangrene, but best results are secured in cases in which there is rest pain, with or without ulcers or limited gangrene.

Perlow (48) concluded that the cases with a high degree of vasospasticity will improve best on typhoid vaccine given intravenously, probably because of fever produced and the peripheral vasodilatation. He advised

the use of twenty five million killed bacteria (T.A.B.) and increase by fifteen to twenty five million at each dose until a good febrile reaction is reached. Injections were given every five to seven days for ten to twelve injections followed by a rest for four to six weeks. The contraindications to the use of typhoid vaccine intravenously, he found, were myocarditis, severe arteriosclerosis, hypertēnsion, and debility.

Waller and Allen (72) suggested a substitute for typhoid vaccine. They used two cc. of a 2% suspension of sulphur in olive oil deposited intramuscularly. A satisfactory rise in temperature was obtained, accompanied by a maximal vasodilatation. The average duration of the fever was fifty hours and no case showed permanent impairment as a result of its use. Chills only occasionally followed the injections and repeated injection continued to produce a fever. The chief objection found was the resulting pain at the site of injection which began in about two hours and continued as a dull aching pain for about 24 hours often severe enough to require a narcotic.

Administration of fluids to patients with thromboangiitis obliterans was first suggested by Koga in 1913 who used the subcutaneous method of giving one liter of normal salt solution daily. In 1917 MacArthur (38)

modified the Koga treatment when he advised the daily installation of up to one gallon of Locke's solution into the duodenum by a Rhesuss tube to get blood dilution. Ginsburg (24) first suggested the use of intravenous fluid in the form of sodium citrate solution which was followed by improvement in some cases. Steel (70) corroborated this work in 1921.

Silbert (63) used hypertonic saline solution intravenously as a method for increasing blood volume and decreasing blood viscosity. The technique employed was to give 150 cc. of 5% saline the first administration and 300 cc. with each subsequent injection. Injections were given with the patient lying down, into a superficial vein, over a period of ten minutes, and these were repeated three times a week gradually reducing with improvement. Silbert (63) noted improvement in 46 out of 66 cases of thrombo-angiitis obliterans treated. Signs of improvement were subjective increase of warmth and diminution of pain and objective increase of warmth, healing of ulcers, and return of pulse in vessels otherwise pulseless. He warned against dismissal of patients and advised constant observation. He found that excretion takes place through the urine within forty eight hours two thirds the first day, and the other third the second. Some blood destruction as a light amount of urobilin in the urine was noted.

He advised discontinuing treatment in the face of a mild anemia and monthly blood and urine examinations to note any changes which may occur. Silbert (61) concluded that this form of therapy is safe and efficient. The following contraindications were given: patients over sixty years old, those with poor renal function, those with poor myocardium, obstruction due to embolism, Raynaud's disease, and vasomotor neuroses. Perlow (48) listed the same contraindications. After ten years experience and treatment of 524 cases with gratifying results Silbert (65) had no essential change in his views on this type of treatment.

The use of changed atmospheric pressure as a therapeutic procedure was first introduced into the medical field in 1812 by Murray (46). This procedure and a similar type of apparatus was redescribed by Clanny (12) in 1835. He found it useful in gout, dropsy, rheumatism, and anomolous pains. According to McNealy and Shapiro (43) Junod in 1834 presented to the French Academy of Sciences his experience with the application of "thinned and thickened air " either to the entire body or to a single portion of it. The apparatus used consisted of a glass and copper cylinder or boot shaped to fit the foot and leg. A broad rubber ring was fastened about the extremity to shut off air. A manometer and thermom-

eter were supplied and the boot was attached to a suction syringe and, if needed, heated vapors were also applied. At that time the observation was made that "if the atmospheric pressure over an extremity is diminished the skin swells and becomes red. The inflowing blood spreads and unaccustomed warmth in it; the exerted moisture quickly evaporates and deposits on the walls of the cylinder". The work of Junod did not gain wide recognition and was forgotten.

In 1893 Bier (9) introduced the principle of hyperaemia as a therapeutic measure. His work was followed with great interest in his methods, although they were often modified, were widely used. He stated that, "if we accept the reactions of the body as useful efforts of nature, we must admit that hyperaemia is the most widespread of all autocurative agents". Bier (9) used a glass boot with a cuff of para paper for its attachment. The boot was hooked up to a bicycle pump and the valves changed so as to convert it into a suction pump. He noticed an increase of surface temperature following treatment. Experience taught him that dilatation of capillaries is associated with acceleration of blood current in the concerned part, provided the heart action remains the same. He also noted that in the development of collateral circulation by hyperaemia, produced by dil-

atation of the vessels, it was the capillaries that played the active role. Meyer and Schmeiden (45) used a slight modification of Bier's method. They advised conservative treatment of circulatory disturbances of the extremity before surgery. Stetten (71) in 1913 pleaded for conservative treatment for diabetic gangrene and advised Bier's hyperaemia treatment for improvement of circulation with which they obtained better results than any of the more radical procedures. In 1917 Sinkowitz and Gottlieb (66) reported on the use of Bier's hyperaemia treatment in four cases of thromboangiitis obliterans with excellent results.

This type of procedure was then more or less abandoned until 1933 when Landis and Gibbon (34) reported on the use of alternating positive and negative pressure applied to the normal limb. They noted an increase in the blood flow to the extremity by this method. Herrmann and Reid during the same year applied this method to diseased extremities as a type of therapy. The amount of pressure used was eighty mm. of negative pressure and twenty mm. of positive pressure. A complete description of the mechanics and principles of their machine may be obtained by referring to Herrmann's monograph (30) on "Passive Vascular Exercises". At the outset this type of therapy was applied to many conditions since there

was a great deal of enthusiasm. Shipley and Yeager (60) advised it for ununited fractures, arthritis (atrophic and hypertrophic), frostbite gangrene, and various circulatory disturbances that result from trauma. Recent work, however, has been done in an effort to isolate the conditions in which it is useful.

Herrmann and Reid (28) reported that the most startling results have been obtained among patients who are suffering from more or less sudden occlusion of a major arterial pathway to an extremity. They found that in every instance of acute obliteration of a major artery in which there was no obvious death of tissue, they were able to relieve the spasm and draw blood into the extremity in a short time, with quick relief from pain and prevention of gangrene. This they claimed, has been accomplished even when sensation in the extremity was absent or markedly diminished. The value of this method of therapy, in their experience, diminished when occlusion of the arterioles occurred unassociated with sudden increases in the pathologic process and consequently is not complicated by vasospasm. In cases of thrombo-angiitis obliterans the authors admitted that the method was much less effective, and thought that considerable care and judgment are necessary in its use for treatment of this condition. Landis and Hitzrot (35)

essentially agreed with Herrmann. They pointed out that the treatment should not be left in the hands of a technician but should be under the definite supervision of a physician.

Herrmann (32) found that feet that had been subjected to various degrees of freezing responded promptly, and serious sequelae were prevented in all the cases in which this method of treatment was given. Hyperthermia was also found to be valuable adjunct to this type of therapy. Herrmann (31) advised the supplying of preheated air to the interior of the boot at a temperature of 104 to 106 degrees F.. This was found to be especially useful in the presence of moist, spreading gangrene in which the arteriolar pathways of the extremities are impaired.

Allen and Brown (4) seemed less optimistic about this type of procedure. They commented that in their hands this method of treatment has not produced any results that they had not observed repeatedly following simpler methods. They pointed out that the need for a therapeutic procedure which will aid the older patients with occlusive arterial lesions, and that passive vascular exercises have not been of any help in this direction. Conway (14) supported this conclusion when he noted no improvement in more than 80% of cases of arteriosclerosis

obliterans and in four cases of thrombo-angiitis obliterans no benefit was derived. He concluded, however, that in no case did the method seem to be harmful in any way. Saltzstein and co-workers (55) are of the opposite opinion and stated that they believed this method of value to thousands who later in life, have only symptoms of pains in the feet and legs after walking short distances.

Contraindications are included in the articles of most authors but are well summarized by Korn and Feller (33) as follows:

1. Large pressure variations cannot be used indiscriminately without careful supervision.
2. Active cellulitis or suppurative processes because of danger of spread of infection.
3. Presence of osteomyelitis makes it unlikely that healing will ever occur.
4. Large varicose veins may cause embolism, although not reported.
5. Large gangrenous or sloughing areas present, only temporary relief can be expected so ^{no} more than lowering the amputation level can be obtained. Herrmann (28) and Saltzstein (55) advised against its use in livid cyanotic extremities with congested venous return.

Lehman (37) reported the use of elevation of environ-

mental temperature alone in one case of acute arterial spasm with remission. He concluded that this may be a definite therapeutic possibility.

There will be included in the medical treatment a minor surgical procedure which is often an adjunct to good medical treatment in order to prevent amputation for pain only. Silbert (64) introduced a method which he described as "the injection of the posterior tibial nerves at the popliteal spaces (best) in five patients for the relief of pain". He performed this operation under local anesthesia. The nerves were first injected with procaine and then with pure alcohol. His results were encouraging.

Smithwick and White (69), with this type of procedure, concluded:

1. Pain in the lower legs and feet secondary to obliterative vascular disease can be relieved by alcohol injection of peripheral nerves.
2. This can be accomplished without paralysis of any important muscles of the leg or foot.
3. Careful operative technique and scrupulous asepsis are essential to success.
4. A serious slough may be precipitated by spilling alcohol into the tissues.
5. Incision should be made above the lower third

of the leg and should be vertical by preference. They usually heal by first intention.

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

7. The relief of pain has been responsible for the saving of six out of eleven legs otherwise doomed to amputation.

8. It should never be necessary to sacrifice a leg because of pain.

9. After an extremity has been desensitized by this method we have noticed frequently that the foot becomes drier, warmer, and that previous color changes are eliminated. The surface temperature may rise five degrees F.. This is probably due to elimination of sympathetic stimulation both by relieving pain and by interrupting the course of the nerve fibers to their peripheral destinations. The majority of the sympathetic nerves course peripherally with sensory nerves.

10. The result is more apt to be successful if the popliteal artery pulsates. In cases of senile arteriosclerosis with arterial obliteration above the popliteal vessel, this procedure, even if done in two or three stages, may precipitate actual gangrene and hasten amputation. We feel, however, that in such a case if amputation

is necessary anyway because of pain, one is justified in desensitizing the extremity first.

11. After an extremity has been desensitized, ulcerations which previously resisted all methods of treatment will frequently heal.

Smithwick and White (68) devised a new technique in which the nerves are simply crushed with an instrument over an extent of one fourth of an inch if rapid regeneration is desired, or up to one half inch if prolonged anaesthesia is necessary. They concluded that this operation is better because it is time saving, shorter incision is necessary, avoids danger of spilling alcohol in the tissues, and the nerves tend to regenerate more rapidly than those injected with alcohol. They found that complications were due to faulty technique in most cases, poorly fitting shoes, and too extensive an operation at one sitting. Some of the complications encountered were delayed healing, infection of the wound, and ulceration of the anaesthetic skin. They also pointed out that this procedure is of more value in thromboangiitis obliterans than in the arteriosclerotic group and should be used only in the advance cases. Laskey and Silbert (36) advised the complete section of the nerves. The nerves which are blocked, crushed, or sectioned are the posterior tibial, deep peroneal, terminal

cutaneous trunk of the superficial peroneal nerve, deep and superficial peroneal nerves, sacral, internal saphenous, or the posterior and lateral femoral cutaneous nerves. Any of these may be blocked depending on the area involved. Their distribution may be obtained by referring to any standard text in anatomy.

SUMMARY and
CONCLUSIONS

In summarizing this paper the most striking fact is that the recent advances have been the correlation and crystallization of ideas and the application of the various methods more definite to each type of disease. It is also apparent that a great deal of work has been done in the last decade in an attempt to solve this perplexing problem. However, a more logical treatment may be devised only when the etiological agents are isolated, rather than merely attempting to improve the conditions as they exist. The following conclusions have been reached after a review of the literature:

1. Early diagnosis is important to prevent sequelae, therefore, routine examinations should include the peripheral vascular system.

2. Many new diagnostic methods have been devised, in order to make more definite and earlier diagnoses, which are useful.

3. Medical treatment is indicated in every case if merely to improve the circulation pre-operatively and postoperatively.

4. General measures should not be forgotten in the excitement of new ideas of therapy for they are of definite value.

5. Foreign protein (typhoid vaccine) treatment is of definite value in thrombo-angiitis obliterans.

6. Vasodilating drugs are still a subject of controversy as to their efficacy.

7. Tissue extracts may be prove to be of value but more experience is necessary.

8. X-ray therapy shows promise of being valuable.

9. Hypertonic saline solution has been proved to be of value in thrombo-angiitis obliterans.

10. Passive vascular exercises are of value in major arterial occlusion and frostbite. The results in other conditions are still controversial.

11. Nerve section (sensory) for relief of pain in the lower extremities due to obliterative arterial disease is of definite value in advanced cases especially thrombo-angiitis obliterans.

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