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1. PREFACE.

It may be said that the past decade has witnessed striking changes in the attitude of the physician to the patient afflicted with peripheral arterial disease.

Formerly, such a patient was considered a victim of a hopeless and incurable malady, condemned to operation, institutional life, and a slow death. It was not uncommon to see men in the prime of life severely mutilated by amputation performed as a prophylactic measure. The medical profession is indebted to such men as Maurice Raynaud, Weir Mitchell, and Leo Buerger for their classical description of certain peripheral vascular diseases. With their advent came classification and differentiation of the various forms of peripheral vascular disease and afterwards gradually the evolution of treatment other than amputation.

The purpose of this essay then is to review such treatment in the light of present-day experience. Particular reference is made to the form/
form of therapy known as intermittent venous occlusion.

I am greatly indebted to Professor D.M. Dunlop under whose auspices this work has been carried out, and to Dr. W. Melville Arnott for his continued advice and help.
11. DELIMITATION OF CONCEPT OF OBSTRUCTIVE VASCULAR DISEASE.

In discussing response to treatment of any condition it is necessary to standardise the condition under consideration. We have adopted for our title the term Obstructive Vascular Disease.

Literally, this gives rise to a conception of disease of the vessels whereby there is obstruction to the flow of blood and this is exactly the meaning we wish to convey. We define Obstructive Vascular Disease as that state of the vessels, including under the title vessels, arteries, arterioles, capillaries, venules and veins, whereby as a result of pathological changes in the vessel wall there is encroachment by the vessel wall on the lumen of the vessel to the extent that the normal flow of blood along the lumen suffers interference of a degree ranging from slight impairment to complete cessation or inhibition of flow.

The term Obstructive Vascular Disease, however, it must be realised, has suffered misapplication and therefore/
therefore misinterpretation, having been utilised as, for instance, has the term Bright's Disease, to cover a wide variety of dissimilar conditions.

In general, under the term Obstructive Vascular Disease, there has been included, not only pathological processes causing obstruction, but also any other condition causing obstruction. Considering the term in the latter sense we summarise below the causes of obstructive vascular disease (Buerger; Circulatory Disturbance of Extremities, 1926).

A. Organic Causes of Obstruction:

1. Arterio-sclerosis obliterans - senile diabctic.
2. Thrombosis.
3. Embolism.
4. Thrombo-angeitis Obliterans.
5. Endarteritis Obliterans (a) Tuberculous. 
   (b) Syphilitic.
6. Acute Arteritis.

B. Mechanical Causes of Obstruction:

1. Traumatic: (1) Bullet wounds.
   (ii) Dislocation of joints, and attempted reductions.
   (iii) Laceration due to severe muscle exertion or injury.
(iv) Severe general bodily concussion as after entombment under earth following explosive shells.

II. Ligation of vessel - operative.

III. Pressure from outside: (i) Tourniquet. (ii) Splinting.

IV. Pressure from inside: (i) Cervical rib. (ii) Tumour. (iii) Aneurysm.

G. Other Causes of Obstruction:

Neuropathic or local sensitivity embodying -

1. Raynaud's Phenomenon.

II. Erythralgia.

III. Aerocyanosis.

IV. Erythrocyanosis.

In our review of treatment we are concerned with organic vascular obstruction and have experience of the following types of cases:-

1. Arteriosclerosis Obliterans.

II. Thrombo-Angeitis Obliterans.

III. Embolism or Thrombosis.
111. REVIEW OF THE FUNCTION AND CONTROL OF THE CIRCULATION TO THE LIMBS, THE CLINICAL MANIFESTATIONS OF INTERFERENCE WITH THAT FUNCTION, AND THE CRITERIA EMPLOYED IN ASSESSING IMPROVEMENT OR REGRESSION IN THE FUNCTION OF THE CIRCULATION TO THE LIMBS.

Before proceeding to the consideration of treatment of Obstructive Vascular Disease it is necessary to review briefly (1) the present view as to the function and control of the circulation to the limbs; (2) The clinical manifestations of interference with (1) that function by obstructive vascular disease; (3) The criteria utilised in assessing improvement or regression in the function of the circulation to the limbs.

(i) The Function of the Circulation to the Limbs (after Lewis).

The circulation to the limbs often participates, actively or passively, in responses of the whole peripheral circulation; the mechanism and purpose of such general reactions only concern us incidently. The circulation to the limbs will be regarded mainly from the standpoint of its local functions.
Of these functions, the first to be named is that of transporting to or from the extremities the substances needed for or arising out of metabolism, and thus to ensure the proper nutrition of the tissues. This function is common to the circulation as a whole. The metabolic needs of most of the tissues of the limb, however, are not great; the blood-flow required to nourish skin, subcutaneous tissues, bones and resting muscle, is small; only the muscle in action makes large demands.

The second function is to be found in the mobilisation of the forces of inflammation in defence against various forms of injury experienced. This also is common to the circulation as a whole, though the limbs are particularly prone to damage, owing to the vigour and frequency of their movements.

A third function is the maintenance of temperature within safe bounds, so that the tissues, and especially the skin, may be guarded against damage from continued over-cooling or over-heating.

A fourth function, and the last that will be named, concerns the part played by the limbs in controlling body temperature. The surface of the limb actually/
actually forms about two-thirds of that of the whole body and, under conditions of civilised life, the limbs are amongst the most exposed parts. Thus the circulation to the limbs plays a dominant role in regulating heat loss.

**The Control of the Circulation to the Limbs. (After Lewis).**

1. **General Reactions and Nervous Control:**

Though the capacity of vessels of all orders, large and small arteries, arterioles, capillaries, minute venules, small and large veins, may affect it, the general rate of blood-flow is chiefly regulated by the state of the small arteries and of the arterioles. This is not only true of the limb as a whole but of the body generally. In the case of the limb, however, there is, in addition, a mechanism almost peculiar to it, - that of special sluice gates called arteriovenous anastomoses. These anastomoses, just visible to the naked eye when dissected, are present in great numbers in all the digits and in the palm of the hand and sole of the foot. Their walls are very muscular and are richly innervated. The anastomoses when open allow/
allow a veritable flood to pass from arterioles to venules, and provide an exceedingly effective mechanism for rapidly warming up the limbs from their very tips.

When the vessels of the limbs participate in general reactions of the peripheral circulation to cells regulating blood pressure, the small arteries, arterioles, and arteriolar-venous anastomoses of the skin and directly subjacent tissues are chiefly brought into or out of action. Precisely the same cutaneous vessels participate in the regulation of body temperature, in which the limbs play so large a part.

These general vascular reactions affect all the limbs, and all parts of them, together; and they are controlled by the central nervous system through the vasomotor nerves, distributed in the limbs by way of their mixed nerves. The sympathetic nervous action is reinforced by the simultaneous release of hormones, such as adrenaline, into the blood stream.

11. Local Reaction and Metabolite Control:
The nutritional requirements of the tissues fluctuate greatly from moment to moment and from place to place, and these are met by exchange through the walls/
walls of the minute blood vessels. This exchange calls for fine discrimination in the distribution of blood through these vessels, if the supply is to be economic. An economic system of distribution exists, and consists of fluctuations in the size of the appropriate vessels of the smallest orders. These fluctuations are mainly controlled automatically by metabolism itself, the products of local metabolism acting directly upon the requisite vessels keeping them in a state suited to the needs of the tissue at a given moment and given place. The circulation to muscles is chiefly regulated in this way, the supply varying with activity. A blood-flow debt to a given territory, accumulated during temporary and local arrest of circulation, is satisfied by an increased blood-flow after circulation is released, this compensation depending upon a similar mechanism. Fine adjustments of the circulation to suit local needs are made by similar responses of the smallest vessels in instances of injury, the substances being released by the actual injury and giving rise at once to vascular responses in the corresponding territory.
III. Local Control by Temperature: In addition to the two chief controls described there is a third, which assumes unusual importance in the case of limb vessels. Arteries, arterioles, capillaries and veins all react directly to temperature; they shrink when cooled. The metabolic need of tissues falls as their temperature falls, and the reaction of the vessels to cold is consequently appropriate from this standpoint. Vessels of the body that lie deeply, or that lie superficially in the trunk, are protected against large changes of temperature in circumstances of everyday life and their vessels are therefore unusually affected. The direct and considerable influence of temperature on the exposed blood vessels of the limbs contributes to the maintenance of body temperature; the closure of vessels in a cold limb limits the amount of cooled blood returning to the body.

This direct influence of temperature is also important from another standpoint, namely, in testing the vessels of the limbs. In drawing conclusions from the size of a vessel or from the extent of its pulsation, the temperature of the limb must/
must always be taken into account or must be controlled.

1. The Clinical Manifestations of Interference with the Function of the Circulation to the Limbs.

The Effects of Defective Circulation: The effect of obstruction of the circulation to the limb depends on:-

(i) The level of the obstruction.
(ii) The efficiency of the collateral circulation.

It is obvious that the larger and more proximal the artery obstructed the greater will be the area threatened with ischaemia and that a deficient collateral circulation will increase the effect of the obstruction.

Sudden obstruction of a large artery as by an embolus is immediately followed by a fall in skin temperature. This commences in the periphery and gradually spreads proximally. The rate of fall depends on the gradient between outside temperature and temperature of the part. A few seconds later changes in colour begin,—slight paling as blood drains out of the minute vessels into the veins; blueness as stagnation develops; full cyanosis in 2.5/
2.5 minutes, then the appearance of Bier's spots due to minute vessel contraction of unknown origin - growing in size and producing a mottling. Within fifteen minutes numbness is noted at the tips of the fingers and this spreads centripetally at 3 - 4 cm per minute. Within half-an-hour the whole of the ischaemic area is anaesthetised. This is followed by loss of power, cold and warmth. Marching hand in hand with loss of sensation is motor loss. If the arrest of circulation remains complete and no collateral circulation develops, then a sharp line of demarcation develops depending on the extent of blood flow. The limb distal to this becomes gangrenous. However, pathological reduction is more often a gradual process and shows itself in the vessels of the superficial tissues, those of the muscle vessels, or equally in both.

The skin in the absence of sufficient blood supply becomes glazed and dry and undergoes colour changes ranging from marked pallor to true cyanosis. The temperature is reduced relative to the normal side or to a normal limb, and perspiration is often diminished or absent. Nail growth is abnormal, being much/
much reduced. There is an increased susceptibility to trauma, and in the event of injury, great delay in healing. Ulceration is, therefore, common, and gangrene may appear. There is diminution or loss of superficial pulses. Muscle ischaemia is evidenced by the cramp-like pain, designated intermittent claudication. There is usually reduction in muscle bulk due to (1) disease; (ii) ischaemia.

Pain is a feature of ischaemia in all regions. It may occur as "resting pain" around the heel and dorsum of the foot, as pain of ulcer or gangrene, or as intermittent claudication.

Summary of Clinical Manifestation.

The clinical manifestation described above may be classified as follows:

A. Subjective:

1. Pain: (a) Pain of ulcer, or gangrene.
   (b) Rest pain.
   (c) Intermittent claudication.

II. Coldness.

III. Tingling.

IV. Paraesthesia.

V. Weakness.

B. Objective:

1. Temperature changes.

II. Trophic changes: Colour and skin condition—dryness; sweating.
   Ulcer.
   Gangrene.
III. Pulsation of vessels.

IV. Palpation of vessels.

V. Wasting.

The Pains of Obstructive Vascular Disease: These have been divided into:

i. Pain of rest.

ii. Intermittent claudication.

iii. Pain of trophic ischaemia.

Rest Pain: This type of pain occurs without exercise and is not easily explained. It occurs without gangrene or ulcer or without any trophic changes and is generally localised to the digits, or around the dorsum of the foot, or in the region of the heel or tendo-achilles. It is particularly troublesome at night. In character it is a continuous ache. Jablons attributed this pain to the increase in connective tissue around the nerve trunks, and Meleney and Miller to obliteration of the nutrient arteries of the nerves. Putman believed that true neuritis was present. Neurological evidence of true neuritis was present in some of a series investigated by Allen, Brown and Mahorne, but, in their opinion, not in sufficient evidence to serve as an explanation. Allen, Brown and/
and Mahorner believe, that though the above factors may play a part in the production, the pain is mostly due, directly or indirectly, to constant profound anoxaemia approaching the threshold of tissue death. Lewis, Pickering, have shown that in the pain of intermittent claudication oxygen lack per se is not the factor. In this condition they postulate the "P" factor, i.e. some unknown metabolites. It is not impossible that with further elucidation the "P" factor may be found to play some part in the production of rest pain.

Intermittent Claudication: Literally, intermittent "limping", the term first coined by Bouley, a French veterinary surgeon, in 1831 to describe a condition in horses. He gives a classic description of the syndrome in a brood mare 6 years old, which was able to trot some distance and then stopped. If forced to continue the animal would go a few paces, then fall down rolling its eyes and obviously in an extremity of pain. After a short time it appeared quite normal again and was able to progress for approximately the same distance when the same syndrome occurred. It was subsequently discovered/
discovered that the mare had a thrombosis in the common iliac artery, obstructing the blood flow.

In 1858 Charcot described a similar syndrome in man. Strangely enough, the site of the thrombosis corresponded to that in the mare, and more strangely still the etiology was trauma. An old bullet wound had damaged the adjacent tissues in this individual some years before.

Emb gave an illuminating description of the syndrome in 1892. Furthermore, Emb suggested the use of the term as applicable to a distinctive clinical entity - a designation for a complex of symptoms such as may be associated with a number of different pathological processes. In this sense, not indicative of any particular disease, it was used by Buerger and is still used at the present time.

The observations of the Emb type of intermittent claudication are complete, or almost complete, absence of pain and discomfort in a limb when at rest, commencement of disturbances, pains, tension, paraesthesia, weakness shortly after walking is begun, gradual intensification of these until walking/
walking is embarrassed, and finally impossible, and the disappearance of the disorder after a period of rest.

It is most common in the muscles of the calf and is generally taken as denoting a fairly severe degree of ischaemia. As has been stated, Lewis, Pickering and Pothschild recently demonstrated that oxygen lack is not a direct factor and have postulated an unknown metabolite, the "P" factor, as the direct factor.

Pain of Ulcer and Gangrene: Pain of ulcer and gangrene is again part of ischaemia with superadded direct pain of ulcer or gangrene which may or may not have the factor of infection superadded.

3. The Criteria utilised in assessing Improvement or Regression in the function of the Circulation to the Limbs.

As an index of response to treatment then the first criterion is improvement in the clinical syndrome outlined above. The factors generally quoted by writers are:

1. Colour.
2. Healing of ulcers.
3. Effect on gangrene.
4. Effect on pain.
5./
V. Skin temperature.

VI. Effect on pulsation of superficial vessels.

In addition, certain specific tests of blood flow are quoted. These are - I. Skin temperature recordings. II. Oscillometric readings.

IV. The Consideration of the Value of the criteria outlined above.

It is obvious that improvement in colour, the granulation of healing of ulcers, healing or delimitation of incipient or frank gangrene, reduction in pain, marked increase in skin temperature and genuine return of pulsation in arteries of the part is good enough evidence of improved circulation.

The word improved is stressed. It has become almost synonymous with the word increased, and the healing of ulcers, etc. attributed to increased blood flow.

While not denying that in certain instances methods of treatment presently to be described may bring about increased blood flow, we wish also to stress (1) an increased utilisation of existing blood flow, and (11) a diminished tissue requirement, as, for instance, during rest, whereby a previously deficient blood flow becomes temporarily at least, sufficient. The effect of such rest is often confused with the result/
result of some form of treatment. The kudos going to the treatment, the whole field of treatment of obstructive vascular disease is therefore rendered more secure. Increased utilisation or diminished need would certainly account for colour changes, healing of ulcers and gangrene. Increased skin temperature and increased pulsation of peripheral arteries could only mean increased blood flow to the part.

For a second time, while not denying the possibility of increased blood flow as a result of certain forms of treatment, we wish to deprecate the value of - (i) Skin temperature. (ii) Oscillometry.

not as diagnostic procedures, but as criteria of improvement or regression in circulation - i.e. of changes in blood flow.

Measurement of Skin Temperature.

Skin temperature may be measured by the hand which is sensitive to one degree centigrade. This method is of use as a diagnostic measure but some other method is required to give absolute recordings.
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Measurement of Skin Temperature.

Skin temperature may be measured by the hand which is sensitive to one degree centigrade. This method is of use as a diagnostic measure but some other method is required to give absolute recordings.
The method used is the thermo-couple method.

It is not considered necessary to say more of the principle of the thermo-couple than that it is comprised of two dissimilar metals set in contact. When subjected to change in temperature of the environment a potential difference is generated between those metals so that being connected by a wire a current is set up in that wire. Such a current may be recorded on a galvanometer and the galvanometer deflection calibrated in terms of degrees centigrade change in the region of the thermo-couple. In that one junction between the galvanometer terminal and the wire would comprise an extra thermo-couple and so upset the circuit, it is necessary to employ a "cold junction". Herein the wire, dissimilar to the terminal of the galvanometer, is joined to a wire similar to the galvanometer terminal and this is kept at a fixed temperature so that this thermo-couple gives no interference. The similar wire is then led to the galvanometer. The circuit is shown diagramatically below.
This method has been utilised by all observers. Those writers in assessing progress in their cases have used skin temperature as an index of blood flow,

(i) In the normal condition of the limb, i.e. without vaso-dilatation.

(ii) After vaso-dilatation has been induced.

We/
We will therefore investigate -

1. The evaluation of skin temperature in the limb without vaso-dilatation (a) in the normal limb; (b) in the limb of obstructive vascular disease.

2. The evaluation of skin temperature after vaso-dilatation has been induced (a) in the normal limb; (b) in the limb of obstructive vascular disease.

1. The Evaluation of Skin Temperature without vaso-dilatation.

1. The apparatus.

The apparatus is that shown in the accompanying photographs. The thermo-couple consists of constantan and copper wires. The copper wire goes direct to the galvanometer the terminals of which are copper; the constantan wire goes to the cold junction, in this case a thermos flask containing melting ice at 0°C.; there a constantan-copper junction is made and a lead of copper taken to the galvanometer. This galvanometer is the Cambridge Recording Galvanometer and is capable of reading temperatures from 0°C. - 40°C.
11. Technique.

To investigate the value of skin temperature in the above circumstances, two experiments were performed - (i) The skin temperature of four normal individuals was observed in controlled circumstances on six occasions; (ii) The skin temperature of three cases of obstructive vascular disease was observed in controlled circumstances on six occasions.

Skin temperature is dependent on the interplay between the internal and the external environment of the skin. The blood flow to the skin may be affected/
affected by general reflexes of the circulation as a whole and by hormonal influences or locally by temperature, humidity, and movement of the surrounding air. The latter factor may bring about its effect either by direct influence on the vessels, especially the arterioles, or by nervous reflexes, especially on arterio-venous shunts. It is, therefore, primarily essential to control both internal and external environments. Accordingly, investigations were carried out on normal individuals who had previously rested for half-an-hour in a room, thermostatically controlled and in which the humidity and movement of air was also as nearly as possible constant. As the fingers are the most accurate index of blood flow and changes of blood flow, the palmar surface of the distal phalanges of the first digit was used.

The patient was clad in everyday garb. He lay on a couch and constantly occupied exactly the same position, in full supination, and the arms by the side and the forearms and hands also supined. At the end of half-an-hour readings were taken. The room temperature was constant at 22°C. and a recording was taken on four normal subjects on six consecutive days.
Table and Graph of readings obtained demonstrate the results.

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</table>
III. Summary of Results.

1. The normal individual in environment of constant temperature and with humidity and currents of air controlled as far as possible, does not attain on every occasion a constant skin temperature.

2. It is, in point of fact, exceptional for this to occur.

3. There is a variation in skin temperature level in different individuals in the above circumstances.

4. There is a variation in the same individual varying from $1 - 3^\circ C$.

5. The average variation in six normal subjects varies from $1 - 3^\circ C$.

Exactly the same investigation was carried out in those patients suffering from obstructive intracranial vascular disease. Again a variation of several degrees centigrade was demonstrated. In this case the range was less, being $1 - 2.5^\circ C$.

IV. Conclusions.

14. Skin temperature is not dependable as a criterion.
criterion of change in blood flow, the result of treatment.

2. Before assessing improvement in circulation as the result of treatment, it is considered necessary to demonstrate a substantial rise in temperature of more than three degrees centigrade over a period of time of at least one week, recordings being taken always under the same conditions.

2. Evaluation of Skin Temperature after Vaso-dilatation.

i. In normal subject.
ii. In obstructive vascular disease subject.

It is first necessary to consider the rationale of vaso-dilatation, the methods available, the method utilised, the apparatus, and the technique.

It has been pointed out that blood flow to the skin is to a large extent dependent on the vaso-motor nerves. By abolishing this action a much more reliable criterion of blood flow to the part should, in theory, at any rate, be attained. In using skin temperature as a criterion of improvement or regression/
regression in blood flow many writers accordingly have first induced vaso-dilatation. Different methods are available to abolish vaso-motor tone. They may be summarised as follows:

i. Spinal anaesthesia.
ii. Local anaesthesia by nerve trunk injection.
iii. Fever therapy (Typhoid vaccine).
iv. Warming the blood (a) by application of the "Hot Chamber"; (b) by warming the extremities.

The majority of observers have utilised the last method, i.e. iv. (b). This is commonly known as the method of Landis and Gibbon, it being first introduced by them in 1933. The vaso-motor centre is very sensitive to change in blood temperature. By warming two similar limbs it is possible to raise blood temperature and abolish vaso-motor tone by central action. At the same time thermo-couple readings may be taken from the other two limbs.

The apparatus used is the same as that described above with the addition of a basin containing water at a temperature of 45 - 46°C. The method is shown in the photographs. Environmental factors are controlled as before. The method incidentally/
The Value of Vaso-dilatation as a Diagnostic Procedure.

From the above graphs the value of vaso-dilatation as a diagnostic procedure is clearly seen.

It must be noted that under standard conditions of environment and water temperature, vaso-dilatation does not always ensue at the same time. It may show a wide range of 6 - 26 minutes. This has been experienced in a large number of cases.

To investigate the value of skin temperature after vaso-dilatation, the following experiments were carried out:

1. A normal individual was heated upon 3 occasions under exactly the same conditions of environment and water temperature.
Results.

A. It is seen that the skin temperature reading varied over a range of three degrees centigrade.

B. Vasodilatation ensued at different times on each occasion.

2. Seven cases of obstructive vascular disease were heated up on three occasions before treatment under the same conditions on each occasion.
Results.

There is a wide range of variation as in the normal individual of again two to three degrees centigrade.

3. The Effect of prolonged heating on a case of obstructive vascular disease.
Results.

After two hours the obstructed limb is only two degrees centigrade below the normal limb. As the rise is gradual it is obviously due to gradual heating from narrowed blood vessels, and not to release of vaso-motor tone. It must be stated that this gradual progressive rise is not a constant factor. It seems to depend on the temperature of the water used in inducing vaso-dilatation and usually occurs at high temperature of the water (46 - 47°C). As vaso-dilatation varies in its time of onset it is obvious that this factor, being present, a different terminal level of temperature will be attained in the limb of obstructive vascular disease.

4. The Effect of the Temperature of the Water on the Temperature attained by the Skin.

The subjective sensation of the patient is often taken as a criterion of the temperature of water used in vaso-dilatation induction. It has been found that the temperature tolerated varies from time to time in the same individual. The graph demonstrates the effect of altering the water temperature.
Results.

A different skin temperature is attained when the temperature/
temperature of the water used is varied.

Conclusions.

1. Though in theory, with the abolition of vaso-motor tone, one would expect a steady skin temperature reading in the normal and in the case of obstructive vascular disease, this is not found in practice.

2. Experimental factors account for this fact to some extent - (a) Temperature of water used. (b) Duration of heating.

3. However, with all factors controlled, there is still a little variation.

4. Skin temperature after vaso-dilatation then is not a reliable method of gauging improvement or regression in blood flow, the result of treatment.

5. It is considered that a sustained rise of at least three degrees centigrade - over a period of one week - may be taken as evidence of increased blood flow.
OSCILLOMETRY.

The oscillometer was introduced by Pachon in 1909. Its purpose was to measure the amplitude of the peripheral pulse. Pachon's use of the oscillometer, however, was limited to the determination of systolic and diastolic blood pressure without the necessity of using a stethoscope.

Cawadias, in 1912, was the first to adapt the Pachon oscillometer to the study of the patency of the peripheral arteries. Further work in this field was done by Goyot, Jeanneny, Heitz and Others. It is interesting to note that although the oscillometer was used in the study of peripheral arterial diseases in France for a number of years it was practically unknown in this country until 1927, when Samuels described its value in the study of the circulatory disturbances of the extremities.

The original Pachon oscillometer is constructed as follows: E. is a rigid, air-tight metallic box containing an aneroid capsule, C. B is a rubber cuff to encircle the extremity under investigation. The interior of the cuff B communicates with the chamber, E/
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![Diagrammatic sketch of Pachon oscillometer.](image-url)
References.


PUTMAN: (quoted by Jablons).

ALLEN, BROWN & MAHORNER: Mayo Clinic Monographs, 1929, W.B. Saunders Co.


E, by way of the channel F. A hand pump, P, is used for inflating the entire system to any desired pressure, which is measured by the manometer M in centimetres of mercury. This pressure can be reduced at will by releasing the escape valve, V. It is thus seen that the pressure within the aneroid capsule, C, is at all times equal to the pressure within the main chamber, E, since C and E communicate through the channel F. The button, S, is a cut-off arrangement by means of which the system C, a, B, can be completely shut off from the large chamber system E. By depressing the button S, the variation in pressure set up in the cuff, B, by the rhythmic variations in volume of the segment of the limb under compression are transmitted only to the aneroid capsule. The capsule, in turn, transmits its variations to the indication needle L, which swings along a scale graduated in centimetres of water.

The oscillometer thus takes the place of the palpating finger in the examination of the peripheral arterial pulsations, yielding quantitative information concerning the amplitude of the pulses.
The following may be considered the normal range of readings at various levels of the extremities:— Axillary region, 4 to 20; brachial region, 2 to 12; wrist, 1 to 10; palm, 0.25 to 2. In the lower extremities the range is — upper portion of thigh, 4 to 16; above the knee, 4 to 14; below the knee, 3 to 12; calf, 3 to 10; supramalleolar, 1 to 10; pedal (plantar and tarsal) 0.25 to 4.
I. OSCILLOMETRY.

Investigation carried out.

Oscillometric readings were taken on a normal limb in the region of the ankle, and the cuff was applied (i) tightly, and (ii) loosely. The graph shows the result.

Results.

Difference in pulsations recorded of four divisions.

Conclusions.

Oscillometry is obviously an unreliable method of assessing the relatively slight changes in blood flow which are to be expected during treatment.
References.


V. REVIEW OF TREATMENT.

1. INTRODUCTION.

With the publication in 1924 of Leo Buerger's book "The Circulatory Disturbances of the Extremities" there was available a review of conservative treatment of obstructive vascular disease.

Buerger stresses the conservation of warmth, the enhancement of the circulation, the prevention of traumatism, and the treatment of local conditions, trophic disorders or gangrene, when these supervene. He makes particular reference to methods of enhancing the circulation and as such suggests his "Passive Vascular Exercises". Treatment by "Heat" at this time occupied a prominent position, - heat to be applied by means of an electric thermo-phore by a hot-air apparatus, or an incandescent apparatus containing one or more incandescent lamps, or a simple strong electric lamp with reflector. Diathermic treatment is referred to and advised according to the technique of H. Wolf. Finally, reference is made to the injection subcutaneously or intravenously, of solutions that might diminish the viscosity/
viscosity of the blood (after Mayesimm and Koga).

Prophylactic treatment was also well recognised at this time and according to Buerger "The agencies likely to upset the time balance between the tissue requirements and the permanently defective circulation are the following, - prolonged standing, walking, compressing forces that produce local anaemia, such as tight shoes, bands, etc., exposure to cold with its sequelae - ischaemia of the parts (or to cold moisture); mechanical insults that produce clean wounds or infection and thus call forth the need of an enhanced circulation".

Subsequent to 1924 there was the development of other forms of treatment and the continued use of previous forms, in particular, of "Infusion Therapy". Samuels and Silbert are the present day advocates of this method.

In 1925 Roentgen Rays were tried with very doubtful success. Vein ligation was used for gangrene or as an operative procedure in arterial ligation until three or four years ago, and as recently as 1934 was exploited as a treatment of peripheral vascular disease.

With/
With the realisation of the possibility of vaso-dilatation, dawned the vaso-dilator drugs - theo-bromine, ethyl alcohol, papaverine, acetyl choline - between 1930 and 1935, and allied to this "Fever Therapy" by typhoid vaccine, sulphur in oil, and the effect of tissue extracts, insulin-free pancreatic extract, myostan, etc.

In 1932, Herrmann and Reid instituted "Pavaex". The physiological basis being established by Landis in 1933, and finally in 1936, based chiefly on the investigation of Lewis and his workers, Collens and Wilensky introduced intermittent venous occlusion.

(For references see under specific headings.)
11. **ACTUAL TREATMENT.**

Treatment will be considered under the following headings:

1. Prophylactic measures.

11. Active measures.

1. **Prophylactic measures:**

   A. General.

   B. Relationship of tobacco.

11. **Active measures:**

   A. Miscellaneous

      1. Vein ligation.

      11 Infusion therapy.

      Relationship of blood findings to obstructive vascular disease.

     111 Roentgen Ray Therapy.

     1IV. Tissue extract.

   B. Measures designed to increase blood flow

      1. By releasing vaso-motor tone.

         (a) By drugs:

            1 Paraverine.

            2 Ethyl Alcohol.

            3 Theobromine.

            4 Acetyl B Methyl-Cholin

         (b) By non-specific protein therapy:

     11 Specific measures:

         (a) By local action:

            1 Balneo therapy.

            2 Diathermy.
(b) Special measures.
   1 Postural exercises.
   2 Payaex.
   3 Intermittent venous occlusion.
I. PROPHYLACTIC MEASURES.

A. General.

Absolute rest is essential in cases with severe trophic disturbance, that is, ulcer or gangrene, otherwise care of the extremities is the sine qua non of prophylactic treatment. At the first evidence of the disease they should at least be washed at least twice weekly with soap and water, dried thoroughly, and rubbed with hydrous lanolin as often as is necessary, to keep the skin soft, supple and free from scales. If the nails are brittle and dry, they should be softened by soaking in warm water half an hour each night and lanolin applied generously on, about, and under the nail. The nails should be cleaned with an orange stick and cut straight across to avoid any injury to the toes. Only shoes which do not bind or rub should be worn; new shoes should only be worn a half hour the first day, increasing half an hour each day until they are no longer irritating. As a result of the diminished circulation the extremities are particularly sensitive to cold, and woollen hose and felt or sheepskin shoes should be worn if the feet are exposed to cold over long periods; woollen mittens should/
should protect the hands. Every effort should be made to protect the extremities from trauma, since mild abrasions from falling boards and tools frequently initiate gangrene. "Corns" should not be trimmed except by chiropodists who understand the vascular condition and corn plasters should not be applied. The use of strong irritating ointments or tinctures must be avoided. Slight abrasions must be carefully treated by covering with sterile vaselin under a light sterile bandage. Minor surgical procedures, such as removal of toenails, incision of toes, and injections into veins of the feet have played an important part in the initiation of gangrene, since these procedures were causal in more than 30 per cent. of all cases of gangrene. These meddlesome measures cannot be too strongly condemned in the presence of arterial insufficiency.
B. RELATIONSHIP OF TOBACCO TO PERIPHERAL VASCULAR DISEASE.

For a generation or more there has been an accumulative mass of evidence, laboratory and clinical, which has been interpreted as indicating a causal relationship between the use of tobacco and organic circulatory disease. Though the excess use of tobacco has not been definitely established as an etiological agent in such disease there is sufficient evidence to interdict its use at any stage of the disease. There has been no control investigation of the effect of such interdiction alone, used as treatment. In all instances it has been done as a routine and along with some other form of treatment. In view of the evidence presented below such a practice is considered justified.

The evidence is considered under the following headings:

1. Experimental and Clinical Investigation of the chronic Circulatory Effects of Tobacco and Nicotine.

2. Relationship of tobacco to Thrombo-angeitis Obliterans.

   Experimental Investigation.
In 1902 Esser described degenerative changes in the vagus nerves of dogs chronically poisoned by nicotine salts. He failed to find degenerative changes in the heart muscle and concluded that the cardiac irregularities in heavy smokers reported by earlier writers were due to degenerative changes in the cardiac nerves. Several papers, however, appeared in the years 1906 and 1908, (Adler and Hensel; Baylec; Boveri; Goget; Guillon and Gy; Lee; Lesieur; and Zebrowski) reporting changes in the media of the aorta of rabbits given doses of nicotine tobacco infusion or solution of tobacco smoke. All these early writers mentioned degenerative changes in the media. Some described aneurysm of the aorta; Adler and Hensel, Boveri and Goget - atheromatous plaques; Baylec, Boveri and Goget - changes in the intima. Adler and Hensel described the pathology of the media as degenerative or calcareous. In 1921 general interest was again aroused in the vascular effects of chronic tobacco poisoning. Clinical opinion was divided as to an elevation of blood pressure in chronic smokers. Studies by Brigham, Earp, and W.M. Johnson/
Johnson showed no difference in blood pressure between smokers and non-smokers, but W.F. Dixon, the pharmacologist, affirmed that chronic smokers exhibit hypertension, and Knopi accepted the dogma that smoking augments cardiovascular disease.

Relationship of Tobacco to Thrombo-angeitis Obliterans.

Erb in 1904 stated that smoking was an important contributory cause of thrombo-angeitis obliterans. Dr. Howard Lilienthal noted this relationship in 1914, and more recently, Dr. Willy Meyer devoted a paper to the discussion of the importance of this factor. Parks Weber in England stated in 1916 that he had never seen a case of thrombo-angeitis obliterans in a patient who was not an habitual smoker. Schlesinger in Germany demands of patients complete cessation from smoking. Melleny and Miller in 1925 reported 60% incidence of smoking in twenty-five patients investigated. Jablons, in 1925, in a review of 200 cases, found eight only who did not smoke. Silbert, in 1927, investigated 350 cases, all of whom smoked. Barker, in 1931, had a series of 350 cases, of which only five were non-smokers, and Silbert in 1935 stated that in his/
his experience of one thousand patients, he had yet to encounter one who did not smoke. In our own experience of fifteen cases there were two non-smokers. In an investigation of thrombo-angeitis obliterans in women, Horton and Brown in ten cases reported three who smoked.
References.


EBB, : Munchen. med. Wchnschr., number 21, 1904.


References.


BARKER, N.W.: Proc. Staff Meet. of the Mayo Clinic,
vo1. 6, p. 66, 1931.

HORTON, BROWN, : Arch. Int. Med.,
II. ACTIVE MEASURES.

A. Miscellaneous.

I. VEIN LIGATION.

History and Clinical Experience.

The origination of the idea of purposeful occlusion of normal veins as a therapeutic measure in the treatment of arterial disease is usually ascribed to Sir George Makins who observed from experiences in the South African War that there was a smaller incidence of gangrene in those instances of arteriovenous fistula resulting from gun shot wounds which were treated by ligation of both the artery and vein, than in similar wounds treated by ligation of the artery alone. In a subsequent address Makins went further in his conclusions as to the application of venous occlusion as a therapeutic measure. In this address he advocated the possible value of ligature of the vein as a therapeutic measure in instances in which there is arterial occlusion but no fistula opening between the artery and the vein. Halstead, in 1921, discussed the subject of occlusion of healthy veins at some length. He expressed the belief that the first record of the idea is contained in a report of an operation by Von Oppel published in 1908. Von Oppel had reported six cases in 1913 of anaemia of the lower/
lower extremities treated by ligation of the popliteal vein with subsequent definite improvement. Makins refers to this report in his Hunterian oration of 1917 when he first advocated venous ligation as treatment of cases of arterial obstruction. The opinion of Makins, from a review of his experience, was - 1. In progressive arterial degenerative disease associated with arterial obstruction, ligation of the vein is at most a palliative measure, the beneficial effects of which only occasionally justify its employment.
2. In instances of sudden arterial occlusion, therapeutic venous ligation finds its most valuable application.
3. In arterial ligation, ligation of the vein is to be applied only in those instances in which gangrene would be expected.

In 1934, Brookes and Johnstone made a survey of 24 cases of deliberate ligation of a healthy vein in an endeavour to attain clinical improvement in cases of arterial obstruction due to -
1. Thrombo-angiitis obliterans - one case.
2. Arteriosclerosis obliterans - seven cases.
3. Arterial aneurysm and arteriovenous fistula - eight cases.
4. Arteriosclerosis obliterans - seven cases.
5. Arterial embolism - one case.

There/
There was no improvement in the case of thrombo-angiitis obliterans. In the fourteen instances of arterial obstruction due to arteriosclerosis results obtained were such as to suggest the possible beneficial effect in some instances. It was concluded that a favourable result could only be expected in a relatively small proportion of selected patients. In two instances of localised arterial obstruction with active process of gangrene the immediate marked improvement was considered to be the direct effect of venous occlusion. They concluded that ligation of the vein is a measure from which beneficial results can be expected only if there is a more or less abrupt and localised arterial occlusion which reduces the blood flow in an extremity to a dangerous level for a period of time only slightly in excess of that in which the anaemia would be tolerated, and if there is reason to believe that if the gangrene can be averted for this period, subsequent development of collateral circulation will take the extremity out of the danger zone.

Experimental Investigation.
The first experimental investigation of therapeutic value of occluding the concomitant vein of an obstructed artery was determined by observing the actual incidence of gangrene with and without venous occlusion. This was reported by Brooks and Martin. These investigators from that occlusion of the common and external iliac arteries in rabbits resulted in gangrene in fifteen out of twenty-one animals, but that the same arterial ligation coupled with ligation of the common iliac vein in 18 animals resulted in gangrene in only six instances. The above experiments were reported by Wilson in 1932-33. He performed a larger number of experiments (109) and found that simultaneous ligation of the concomitant vein did not influence favourably the incidence of gangrene. In 1935 these experiments were again repeated by Brooks, Johnson, and Kirkley in still larger numbers (200). A summary of the results obtained in this most recent study is shown in the following table.
A.

<table>
<thead>
<tr>
<th>Condition</th>
<th>Arteries alone ligated</th>
<th>Arteries and veins ligated</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total number of experiments</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>Slight muscle or temp. changes</td>
<td>33%</td>
<td>56%</td>
</tr>
<tr>
<td>Complete paralysis</td>
<td>66%</td>
<td>44%</td>
</tr>
<tr>
<td>Focal gangrene</td>
<td>17%</td>
<td>2%</td>
</tr>
<tr>
<td>Massive gangrene</td>
<td>29%</td>
<td>2%</td>
</tr>
<tr>
<td>Late ulceration</td>
<td>7%</td>
<td>6%</td>
</tr>
<tr>
<td>Contracture</td>
<td>15%</td>
<td>4%</td>
</tr>
</tbody>
</table>

The number of experiments performed and the relatively great difference in the incidence of gangrene occurring in these most recent experiments by Brooks, Johnson and Kirtley would seem to be as reliable statistical evidence as could be obtained for the belief that simultaneous ligation of the vein reduces the incidence of gangrene after ligation of an artery under the conditions prevailing in these experiments.

Physiological Basis for Venous Occlusion.

The physiological basis of venous occlusion was first investigated by Brooks and Martin. They studied the/
the immediate physiological effects of occluding the concomitant vein after arterial obstruction and found that this procedure caused an increase in intravascular tension in the circulatory bed in which the blood pressure had been diminished by arterial obstruction, but that the volume flow of blood through this circulatory bed was reduced to a lower level than had been previously produced by ligation of the artery.

Theis, utilising a cannula in the distal part of the artery, found a greater flow from the artery in proximal venous occlusion and wrongly concluded that this meant an increased volume flow. It was shown by Holman and Edwards, Pierse and Spurrell that after arterial occlusion, the calibre of the distal arteries was increased for some time by proximal venous occlusion and that the blood pressure therein is raised. Montgomery, Mulvihill and Harvey and Doroszka, while agreeing with the above findings, criticised Theis deductions and confirmed Brook's findings. Montgomery, by direct methods, measured the approximate total volume of blood flowing through the whole limb in unit time and/
found that proximal venous ligation caused a considerable reduction of volume flow.
References.


HALSTEAD, : Johns Hopkins Hospital Report, p. 21, 1921.


II. INFUSION THERAPY.

Historical Development, Physiological Basis, and Clinical Experience.

Saline therapy originated in the surgical clinic of Professor Ito of Kyoto, Japan. Koga, a pupil of Ito, published his paper "Zurtherapie der Spontangengaren an den Extremitaten" in 1913 giving therein a report of thirteen cases of thrombo-angiitis obliterans. All the patients were young and were treated by hypodermic infusion of saline (Ringer's solution); all were benefitted by this treatment. The explanation given by Koga was that the injections changed the viscosity of the blood.

Willy Myer, writing of Koga's work, uses the sentence - "In other words, in plain language, thick blood is made thin." Koga gave no information as to the instrument employed in estimating viscosity. It is presumed that he used the same instrument as his fellow worker, Mayesima. Mayesima, also an Assistant at Professor Ito's clinic, had, two years previously, in 1911, reported in an essay his findings on the question of blood viscosity in thrombo-angiitis obliterans. He was of the opinion that the blood in such/
such cases was increased in viscosity. He utilised the viscosimeter of Hess which permitted of reading the relative viscosity of the blood by comparing the quantity of the blood with the quantity of water running through the apparatus within a certain space of time. Two of Mayesima's conclusions read -

(1) Saline infusions reduce the viscosity of the blood. (ii) In spontaneous gangrene of the extremities the viscosity of the blood is more or less increased; if the increased viscosity is reduced by saline infusion the gangrene is influenced favourably.

It had been on the basis of this essay that Koga, at Professor Ito's suggestion, tried hypodermic infusion of saline in cases of thrombo-angiitis obliterans. The term, hypodermoclysis, was coined to denote this method of treatment.

In 1916 Willy Meyer, who had previously been using arteriovenous anastomoses in thrombo-angiitis obliterans with poor results, came across Koga's article. As the result of this and of personal communications with Professor Ito he decided to try hypodermoclysis therapy. Between 1913 and 1916 he treated "thirty odd" cases of thrombo-angiitis obliterans/
obliterans. All were given a series of hypoder-
moclysis sometimes repeatedly. He utilised Ringer's
solution and demanded absolute sterility in its
preparation, stating that with ordinary sterilised
water he had often seen infiltration and fever.
Twenty-four injections of 500 ccs. comprised a series.
The infraclavicular submammary connective tissue and
external aspects of the thighs were the places of
application. According to Meyer, the effect of this
treatment sometimes was remarkable: Often the
principal subjective symptom, the ever present
tormenting pain ceased as if by magic, usually after
the tenth to fifteenth injection and without any
other internal medication - left out on purpose.
Hand in hand with general improvement went the local.
Often the gangrene became localised and healthy
granulation sprang up. Ulcerations that had been
present for months began to heal slowly; return of
the pulse in the arteries of the affected limb was
seen very rarely. In some of the patients - the
minority - the improvement was lasting. In most of
them the symptoms, particularly the pain, returned
after a while though in milder form. Given a second
course/
course of treatment, results were often favourable. Meyer stated that although not in a position to report such uniform results as Koga, he was ready to say that this treatment deserved a permanent place among the means employed at that time, in the conservative treatment of thrombo-angiitis obliterans. He further gradually conceived the idea that the repeated hypodermic administration of this solution of important salts besides reducing the viscosity exerted a definite beneficial influence on the blood as such: In other words, that the quality of the blood was favourably affected. Starting from this premise he decided to try the effect of (1) blood transfusion; (2) repeated intravenous injection of a 2% watery solution of sodium citrate. The injection of sodium citrate was tried tentatively on the basis of the fact that it will keep blood in a fluid state in vitro for a number of days. He thought that the intravenous injection would accordingly delay coagulation in vivo. His associate, Garbat, tried blood transfusion in four cases. There are no published results, though on the whole the investigation appears to have been very unsatisfactory/
unsatisfactory. To get a suitable donor for one patient it required the examination of 38 volunteers; for another, the examination of 40, and for another that of 54 subjects. His results with intravenous injection of 2% sodium citrate were more encouraging. Four patients suffering from thrombo-angiitis obliterans were treated, getting approximately twelve grammes (100 cc.) of sodium citrate at weekly intervals over a period of ten weeks. His results were:

1. Alleviation of the pain suffered by the patient.
2. The blood which at first was very thick so that it flowed with difficulty through the salvarsan needle, came out much more easily.
3. One man, whose radial pulse had been obliterated, had a return of radial pulsation, and
4. As to harmful effects from the sodium citrate infusions there were none.

Ginsberg, in 1917, followed Garbat's report by treating four cases of thrombo-angiitis obliterans with 2% sodium citrate by the intravenous route. The first patient had 357 ccs., the second unspecified, the third, 200, and the fourth, 250. There was no beneficial effect in the first three cases. The fourth/
fourth patient had intense pain and died a few days later from suppression of urine. Ginsberg concluded that injection of sodium citrate from his experience was not very satisfactory.

Steel, in 1921, published the results of his experience of the treatment of six patients over a period of three years, his technique being as follows:— During the first month the patient is kept in bed with the legs constantly under a hot air electric light bath at 110°F. 250 cc. of 2% sodium citrate solution is given intravenously every second day. The second month the interval of injection is lengthened to every third or fourth day. Daily leg massage is given, and the patient is put in a wheelchair with the feet hanging down a short each day; or, if the case is not advanced, some walking is allowed. The intervals of injection are now gradually lengthened until at the end of a year the patient gets one every two weeks. Increased walking is permitted as the symptoms subside and evidence of a functional collateral circulation appear. Potassium iodide, 10 drops three times daily, is given during the whole course of treatment. The/
The iodide is always well borne. The length of treatment is regulated by the results obtained in establishing a functional collateral circulation.

The effects of this plan of treatment have been (i) relief of pain after the second injection; (ii) the checking of the gangrene and spontaneous amputation of the dead tissue; (iii) healing of indolent painful ulcers; and (iv) a slow but sure establishment of a collateral circulation, a shown by improved colour, warmth of the foot, swelling of the subcutaneous veins, and a strengthening of any existing pulse. In two cases there occurred a re-establishment of an anterior and posterior tibial pulse.

Silbert, in 1926, inaugurated treatment by sodium chloride. The reason given by him for using sodium chloride was "because it is the salt to which the body is accustomed and because 15 grammes can be administered without danger of toxicity." His technic is as follows:-
The solution is prepared in freshly-distilled water, filtered, and immediately sterilised. At the present time, 5 per cent. sodium chloride is used, 150 cc. for/
for the first injection and 300 cc. for all subsequent injections. The injections are at first given three times a week, later twice a week, and the length of interval further increased as the patient improves. The injection is given into a superficial vein in the usual manner by the gravity method, the fluid is allowed to run into the vein slowly during ten minutes, and the patient is kept flat on his back during this period. If care is taken, the superficial veins will not be injured or become thrombosed, so that the same vein can be punctured again and again. If the solution has been properly made, chills or fever should rarely, if ever, follow the injection.

During the injection, the blood volume is increased and the patients often state that they feel warm; the face becomes flushed and the superficial veins engorged. They often complain of thirst. The excretion of the 15 gm. of sodium chloride injected takes place through the urine within forty-eight hours.

On theoretical grounds, it would seem that the repeated/
repeated increase in the blood volume, necessarily stretching the vascular system, is responsible for the improved circulation and the development of the collateral blood supply that results. Another possible factor is the dilution of the blood with resulting decrease of viscosity.

Silbert's conclusions were -

1. Repeated intravenous injections of hypertonic salt solution have been used in the treatment of sixty-six cases of thrombo-angiitis obliterans.

2. Improvements have resulted in the majority of patients, those noted being cessation of pain, increased temperature of the extremity, growth of the nails, healing of ulcers, and re-opening of obliterated vessels.

3. No dangerous reactions or untoward results of any kind have been noted in more than 2,500 injections.

4. Four consecutive successful amputations below the knee have been done in four advanced cases after preliminary saline treatment.

5. If begun before the disease is too far advanced, treatment of thrombo-angiitis obliterans by repeated/
repeated injections of hypertonic sodium chloride solution will check the progress of the disease and will restore the patients to health and usefulness in the majority of instances.

Samuels, in 1934, reports his experience of the use of intravenous injections of hypertonic solutions in thrombo-angiitis obliterans. He used a solution of 2% sodium chloride in order to avoid annoying thrombosis of the vein at the site of the injection. He stated that there was a consistent increase in pulse amplitude and pressure following intravenous injections. To measure this he used a Paschon oscillometer. He concluded that saline therapy should be started as soon as the diagnosis of thrombo-angiitis obliterans is made. It is not to be considered as a specific for the disease but as a mechanical aid in the enhancement of collateral circulation in the extremities. Three hundred cubic centimetres is given every other day until gangrene and ulceration are healed. Later, the injections may be given at longer intervals, depending on the severity of the case. In cases with ulceration, clinical improvement is noted in improved nail growth, increased/
increased warmth of the extremities, and cessation of intermittent claudication.

In 1935 a further report appeared by Silbert. He gave a review of his experience of the past ten years, 524 patients with thrombo-angiitis obliterans having been treated, by means of repeated intravenous injections of 5% sodium chloride solution.

Improvement had resulted in 434, or 83 per cent of these cases, evidence by cessation of pain, improvement in walking, increase of oscillometer readings, increased temperature of extremities, healing of ulcerations and re-opening of obliterated vessels.

No dangerous reactions or untoward results have been noted in over 35,000 injections.

Seven and six tenths per cent of all patients treated have required amputation of an extremity.

Silbert further states that a discussion of the rationale of this method of treatment is purposely avoided as it rests on theoretical grounds, and the positive results obtained speak for themselves.

He says "It is only necessary to answer the criticism by Brown and Allen of the Mayo Clinic which appeared/
appeared in 1928, and that of Brown in 1934. It is probable that much of the relief which is obtained from various forms of intravenous solutions owe whatever effectiveness they may produce to certain contaminations and non-specific protein reactions. And Brown said in 1934 'Injections of hypertonic salt solutions have been used with good results'. In my opinion, their efficacy depends on the mild fever induced".

Silbert states that many of his patients have been treated for weeks and months in the hospital and temperatures have been recorded carefully. Any temperature reaction after injection was exceedingly rare. There were no chills, and nothing to indicate a foreign protein reaction. Evidence in support of the statements quoted above was, therefore, completely lacking in Silbert's experience.

Silbert has yet to discuss the theoretical grounds for the rationale of intravenous therapy. To date, he has made a reference to two factors - (i) reduction in blood volume, and (ii) increase in blood viscosity.

Relationship of Blood Findings to Obstructive Vascular Disease.

Following/
Following Kayesma's investigation in 1911, a paper appeared by Bernhard in 1920. In a study of 15 cases, he found no increase in blood viscosity as judged by the values for cholesterol, chlorides, and calcium. Heitz, and later Ssokoloff found normal values for blood cholesterol in cases of spontaneous gangrene of the extremities. Silbert, Kornzweig and Friedlander in a study of 69 cases of thromboangiitis obliterans found a reduced and increased concentration of the blood.

Normal and Allen in 49 cases of polycythemia vera found no instance of thrombo-angiitis obliterans. In 35 cases of relative polycythemia vera they reported five cases of thrombo-angiitis obliterans.

Friedlander and Silbert in 40 cases of thromboangiitis obliterans found an increase in the total ash content, in total protein, and calcium in serum and cholesterol in plasma. They showed subsequently that thyroid increased blood volume from 25% below normal to normal in thrombo-angiitis obliterans.

Roth, Maclay, and Allen investigated 105 cases of thrombo-angiitis obliterans, studying the blood volume and the value of protein, calcium urea, and inorganic phosphorus in the serum, and lecithin, cholesterol/
cholesterol and total fats in the plasma. They concluded as follows:– The values for serum calcium, serum protein, blood urea, serum lecithin, and serum phosphorus were found to be within normal limits in their study of the blood cases of thrombo-angiitis obliterans. In most instances the blood volume, hematocrit value and concentration of fatty acids and cholesterol in the plasma were found to be normal. In some instances the blood volume was slightly decreased and the hematocrit value and the concentration of fatty acids and cholesterol in the plasma were slightly increased. They doubted the significance of these findings since they were inconstant findings in thrombo-angiitis obliterans.
References.

III. ROENTGEN RAY THERAPY.

In 1925, Philips and Tunic, impressed by the excellent results obtained in the treatment of the after-effects of Polio-myelitis, decided to investigate its value in cases of obliterative vascular disease. Cases of polio-myelitis had shown remarkable relief of marked hyperaesthesia and improvement in trophic and circulatory disturbances of long duration.

It was felt that such improvement might be expected in cases of obstructive vascular disease.

Technique.

The doses of Roentgen Rays given were essentially stimulating ones and consisted of from 10 - 15 minutes exposure alternating at weekly intervals. They were directed over the mid-anterior and posterior aspects of the body from the tenth dorsal to the fifth lumbar vertebrae in affections of the lower extremities, and over the cervical and upper two dorsal segments in affections of the upper extremities. The following factors were used:

1. Current of 5 milli-amperes - 100,000 volts.
2./
2. Five millimetres aluminium filter.
3. Fifteen inch distance.

A series of fifty cases was treated. The type was not specified but most were cases of thrombo-angitis obliterans. The results of the radiation were as follows:

1. Relief of pain in two to three weeks and sometimes immediately. The relief was progressive and sustained in 90% of the cases.

2. Relief of intermittent claudication in one to two weeks.

There was complete cure in 50% of the cases.

3. Gradual improvement in colour and in warmth of limbs and commencement of healing of ulcers in one month to six weeks.

Interpretation of Results.

Phillips and Lunic stated that any reasons suggested for the above results could only be speculative and any explanation theoretical. They suggested two ways in which improvement might be brought about by Roentgen Rays:

i. An action on the prevertebral ganglia giving stimulation and therefore healing of diseased nerves.

ii. The promotion of an alteration in circulating cellular blood constituents of such a character as to increase phagocytic processes in the body. There would, therefore, be greater ability in combating infection.
References.

IV. TISSUE EXTRACTS.

The use and value of tissue extracts has been fully investigated by Barker, Brown and Roth.

History.

Interest in the therapeutic use of various tissue extracts for circulatory disease originated from the work of Frey and Kraut, in 1926, who isolated a substance from urine which lowered blood pressure when injected intravenously into animals. This substance was subsequently named Kallikrein (later, Padutin) and was found by Frey to inhibit the pain of angina pectoris and intermittent claudication, and to lower blood pressure in cases of hypertension when administered intramuscularly to human beings. Later, Frey found that the fluid from a pancreatic cyst had similar properties, and concluded that the effects of Kallikrein were attributable to a hormone present in many tissues but elaborated in the pancreas. Gley and Kistinios, and later, Wolfe, Findlay and Dessen, described extracts of pancreatic tissue which gave therapeutically/
therapeutically similar results. J.S. Schwarzmann prepared an extract of skeletal muscle, which he called myoston, and reported improvement in cases of angina pectoris after injecting it intramuscularly. M.S. Schwartzmann noted marked improvement in three cases of intermittent claudication after treatment with myoston. In a small series of cases in which there was occlusive disease of the arteries of the leg and intermittent claudication, pancreatic tissue extract has been reported to have increased the walking distance, but controlled tests before medication was used were not mentioned.

Rationale.

This effect on tolerance to exercise has been considered to be the result of vaso-dilatation. Experimental work in animals has shown that pancreatic extract and kallikrein produce a transient fall in blood pressure when injected intravenously, and cause dilatation of the coronary arteries when perfused into a rabbit's heart. However, when perfused through the arteries of the leg of a rabbit, Nazum and Elliot noted vaso-constriction. Topical applications of pancreatic tissue extract cause vaso-
vaso-dilatation in the frog's foot and inhibit the effect of ephedrin on dogs when injected intravenously. The physiological properties have been felt to be distinct from histamin and cholin, and from adenosin.

It is noteworthy, however, that both the pancreatic tissue extract and myoston are undoubtedly mixtures of various organic compounds, and that when used therapeutically they have been injected intramuscularly and not intravenously or by perfusion. Nuzem and Elliot were unable to demonstrate vaso-dilatation in animals after intramuscular or subcutaneous injections of kallikrein. Actual evidence is lacking that the therapeutic effects observed in cases of intermittent claudication are due to vaso-dilatation.

**Investigations of Barker, Brown and Roth.**

Barker, Brown and Roth studied the effects of pancreatic tissue extract, of two types of skeletal muscle extract, and of adenosin, on intermittent claudication. The cutaneous temperature of the digits was measured in a room of controlled temperature, to determine whether significant vaso-dilatation/
dilatation occurred.

In order to evaluate the effect of various tissue extracts, they used a standardised test for claudication. Their test was as follows:

After a rest of one half hour, the patient walks on a level floor, with one of us as a pace-maker, at the rate of 120 steps per minute, until sufficient distress occurs to cause him to stop. The time elapsed from the beginning of the walk until cessation of it is designated as the "claudication time". Although this involves a factor of subjective sensation in determining the end-point, objective evidence, such as limping, muscular weakness, or spasticity usually precedes this end-point. Sixteen patients with occlusive arterial disease were tested repeatedly on various days in the same environmental temperature and have shown an average variation of only 10% from their shortest claudication time. The maximal variation was 20%. The claudication time was determined and frequently verified two or three times before the extracts were given. The extract was then injected into the triceps muscle of the arm, hot moist towels were applied, and the muscle was gently massaged.

Preparations/
Preparations Used.

1. Pancreatic Tissue Extract: The first extract studied was the insulin-free pancreatic extracts which Wolffe previously had described and standardised by means of its power to neutralize epinephrin. The dose was arbitrarily fixed at 3 cc. as this seemed to give the maximal effect in the majority of cases. However, in a few instances a greater effect was noted after injection of 4 or 5 cc. Some variation was noted in the potency of the various lots of this extract.

Barker, Brown and Roth tested 55 patients. In the entire series of 55 cases, the diagnosis of arteriosclerosis obliterans had been established definitely in 20 cases, and thrombo-angeitis obliterans in 35 cases. All of the patients had typical intermittent claudication. The results were as follows:- Definite lengthening of claudication time was noted in 50 (92%) cases, and the average claudication time for the entire group was increased 1.85 times. The average results were slightly better in the group of cases of thrombo-angeitis obliterans than in the group of cases of arteriosclerosis. In the former, the increase, as compared with the control/
control test, was 1.98 times, and in the latter, 1.65 times. In 6 cases no claudication was produced after 20 minutes of standard walking. The poorest results were noted in which the control claudication time was short and in which marked degrees of arterial insufficiency of the legs were present. Generally, definite improvement was noted 1½ to 2 hours after the injection, but the maximal improvement usually occurred after 24 hours. The increased claudication time was maintained for from 2 to 7 days, usually 4 days, after which there was gradual return to the original claudication time.

II. Extract of Skeletal Muscle (Myoston): The skeletal muscle extract was prepared according to the method of J.S. Schwartzmann, and it was standardised on the basis of its content of adenosin phosphoric acid, 1 cc. containing 2.5 mg. Myoston was given intramuscularly by the same technique as that employed in giving pancreatic extract, to 13 patients, 5 of whom had arteriosclerosis obliterans and 8 thrombo-angiitis obliterans. All of them had constant intermittent claudication. The results were similar in effect and in duration of effect to those/
those following the use of the pancreatic extract in the cases of thrombo-angiitis obliterans. In all, there was definite lengthening of the claudication time; the average was 2.1 times the control average. However, in only 1 of the 5 cases of arteriosclerosis was any marked improvement noted.

Myoston was administered orally in amounts of from 5.3 to 16 cc., over periods of from 1 to 3 days, to 8 patients - two with arteriosclerosis obliterans and six with thrombo-angiitis obliterans. Definite increase of claudication time occurred in 75% of the cases, and the average claudication time was 1.8 times that of the control test. This effect did not last more than two days.

III. Muscle Adenosin Phosphoric Acid: Muscle adenosin phosphoric acid was obtained from the same source as myoston. This extract was administered intramuscularly in doses of 20 mg. in a 1% solution to four patients, two with arteriosclerosis obliterans and two with thromboangiitis obliterans. All of the patients had intermittent claudication. Definite lengthening of claudication time was noted in all the cases, but the average was only 1.6 times the/
the control claudication time.

Adenosin: It had been suggested that adenosin or adenosin phosphoric acid was the active portion of all these extracts. Barker, Brown and Roth tested the effect of pure adenosin given intramuscularly in physiologic solution of sodium chloride, in amounts of from 5 to 20 mg. It was given to 7 patients, 2 with arteriosclerosis obliterans and 5 with thromboangiitis obliterans. In two cases of the latter group lengthening of the claudication time did not appear. The average increase was 1.4 times that of the control claudication time. Thus, the average results with adenosin and muscle adenosin phosphoric acid were slightly inferior to those with pancreatic tissue extract, which has a very small content of adenosin phosphoric acid.

None of the patients tested with any of the extracts had untoward effects. There was usually moderate pain of short duration at the site of the injection, but there were no chills, fever or evidence of histamin-like or foreign protein reactions.

Effects of Surface Temperature: 1. Pancreatic Tissue: In three cases, temperatures of the skin were/
were observed for 24 hours, immediately before and after administration of 3 cc. of the extract. The curves were practically identical. In twelve other cases, in which the cutaneous temperatures were observed, during a control period, and for at least 2 hours after administration of the extract, the maximal rise was 0.8° C. In three cases, in which similar tests were made after intramuscular administration of myoston, the maximal rise was 1.6° C., and the average 0.3° C.

II. Adenosin Phosphoric Acid: In two of three cases following administration of muscle adenosin phosphoric acid, there was definitely vaso-dilatation, shown by a transient rise of 3.2° C. Barker, Brown and Roth thought this might have been due to the greater content of adenosin, for in three cases in which pure adenosin had been given, the rise in temperature was 4.6° to 8.2° C. This vaso-dilatation lasted only 1 to 2 hours and on the following day, when the cutaneous temperatures had returned to their basic levels, the claudication time was most greatly increased. In four cases in which repeated tests were made, both as to claudication time and cutaneous temperatures, each of the patients received several
or all of the different extracts, with definite increase in claudication time. There was absolutely no correlation between the claudication time and the cutaneous temperatures.

**Relationship of Skin Temperature and Relief of Intermittent Claudication.**

It has been the experience of Barker, Brown and Roth that definite vasodilatation does not significantly affect intermittent claudication. In two cases in which tests were made before and during artificially-induced fever there was no increase in claudication time. In both of these cases there was definite increase with the extracts. Even after extensive intravenous treatment with typhoid vaccine, little effect was noted on intermittent claudication. In one case, increase in claudication time was not noted either after 20 gr. (1.3 gm.) of theobromine, given orally, or later, after 0.2 gm. of theophyllin ethylenediamin, given intravenously, both of which produced definite vaso-dilatation. However, a 200% increase in claudication time was then noted after 16 cc. of myoston had been given by mouth over a period of two days. In 1 case, no difference in claudication/
Claudication time was noted during tests before, and four weeks after, lumbar sympathetic ganglionectomy, which caused a sharp increase in surface temperature, but there was a 100% increase after 3 cc. of pancreatic tissue extract had been given intramuscularly.

Conclusions of Barker, Brown and Roth.

Barker, Brown and Roth concluded (i) that pancreatic tissue extract and myoston, given intramuscularly, inhibits or delays intermittent claudication in the great majority of cases in which it occurs; (ii) that the exact component of the extracts responsible for the effect was not known, but must be common to both the pancreas and skeletal muscle; (iii) that the methods of action were obscure, but that the extracts had little or no effect on the pretrophic pain, or on the pain which results from the ulceration and gangrene which occurs in occlusive arterial disease. This seemed to exclude analgesia; (iv) That the therapeutic effect of these tissue extracts, when given intramuscularly, was not the result of vaso-dilatation; (v) That the explanation was to be found in the/
the supplying of some substance to the actively contracting muscle which it cannot obtain in sufficient concentration, with a restricted supply of arterial blood; (vi) That adenosin phosphoric acid may be the active substance; (vii) That from the practical standpoint the therapeutic value of the tissue extracts in peripheral arterial disease seemed to be restricted to those cases in which intermittent claudication was the chief symptom and trophic lesions were not present.
References.


B. Measures Designed to Increase Blood-flow.

1. By releasing vaso-motor tone.
   (a) By Drugs.

1. P A P A V E R I N E.

Allan and Maclean published in 1935 a review of the rationale of papaverine therapy and the explanation of the results following its use. They had noted the ischaemia following sudden arterial occlusion and felt that such profound ischaemia was not to be explained by simple occlusion of an artery. They thought it unreasonable that sudden occlusion of a popliteal artery, for example, should cause gangrene of a foot when individuals with chronic occlusive disease of the popliteal arteries were frequently seen who did not have any great degree of impairment of the circulation. They were not satisfied with this explanation of the cause of the pain in cases of acute arterial occlusion in which severe pain had begun suddenly, and began to think that the ischaemia and pain were largely due to widespread arterial spasm. The theory of spasm was supported by a number of other investigators. Seifert and others had observed arterial spasm during operation for the removal of an arterial embolus. After observations on/
on a patient with arterial embolism, Seifert con-
cluded that pain occurring at the onset of arterial
embolism was due to arterial spasm. He noted that
simple arterial ligation, which was frequently
necessary in the treatment of war wounds, did not
ordinarily provoke the type of pain which is
associated with arterial embolism.

In a study of experimentally-produced embolism, Gosset, Bertrand and Patel observed that an embolus was fixed at the point of lodgment by arterial spasm. They observed likewise that the lowered temperature of an extremity in which a main artery had been occluded by an embolus was replaced gradually by a normal temperature a few hours afterwards. This was indirect evidence that the original diminution in warmth was caused by wide-
spread arterial spasm that relaxed in the course of a few hours to allow re-establishment of circulation. Excellent experiments have been reported by Mulvihill and Harvey who ligated the external iliac arteries of dogs. The temperature of the extremities was reduced to that of the room in from two to six hours. This lowered temperature persisted for several/
hours, when there was a gradual or rapid increase in temperature so that in an average period of about thirteen hours after ligation of the artery, the corresponding extremity was again about as warm as before operation. If sympathectomy were performed when the temperature of the foot was decreased as a result of arterial ligation, there was an immediate increase to the approximate level of warmth before the iliac artery was ligated. If sympathectomy was performed before ligation, no change in the temperature of the extremity resulted from ligation. This is obviously a criticism of Seifert's work.
11. ETHYL ALCOHOL.

Cock and Brown, in 1932, investigated the use of ethyl alcohol in the treatment of obstructive vascular disease. They base their investigation on their findings of the ability of ethyl alcohol to induce vaso-dilatation. In a series of normal cases they demonstrated that ethyl alcohol given orally in doses of .5 cc. per kilogram body weight produced a rise in skin temperature of the fingers of approximately eight degrees centigrade. The final average skin temperature reading was 33.1°C. They regarded this as a good result in view of the findings of Scott and Morton who recorded a final skin temperature of 34.5°C., using spinal anaesthesia to abolish vasomotor tone.

With the above dosage the effect on a series of thirty-nine cases of obstructive vascular disease was investigated.

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Number of Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thrombo-angiitis obliterans</td>
<td>28</td>
</tr>
<tr>
<td>Arteriosclerosis obliterans</td>
<td>11</td>
</tr>
</tbody>
</table>

Results
Results.

1. 70% relief of the pain of trophic lesions in arteriosclerosis obliterans.

2. 50% relief of pain of trophic lesions in thrombo-angiitis obliterans.

3. No definite effect on healing of trophic lesions in arteriosclerosis or thrombo-angiitis obliterans.

4. No effect on pain of claudication.
111. EFFECT OF THEOBROMINE ON
PERIPHERAL VASCULAR DISEASE.

For a number of years the purine-base group of
drugs has been widely used in the treatment of
angina pectoris. The fact that the symptoms of this
disorder can often be relieved for long periods of
time by these drugs seemed to indicate that they
might be useful in the treatment of peripheral
arterial disease.

Dock had noted that the pain of intermittent
claudication was sometimes relieved by theobromine,
and in the reports of the Council of Pharmacy and
Chemistry of the American Medical Association it is
stated that claims for the occasional relief of pain
by theobromine and theophylline preparations in
angina and similar lancinating pains may be permitted.

Scurham realised that diseases of the peripheral
arteries also offered the opportunity of estimating
to some extent, at least, objective evidence of
improvement as well as subjective relief of symptoms
and in 1934 investigated six patients with this end
in view. The objective criteria employed were the
simple ones usually used in diagnosis and consisted
of/
of the appearance of the affected limb, such as the change in colour at a constant level and with a change in position, the presence of swelling and the degree of integrity of the tissues. Other objective measures used were demonstration of the condition of the superficial vessels by palpation and inspection and the measurement of the surface temperature.

The last-mentioned criterion was thought to be fairly reliable and to furnish the opportunity for some quantitative estimation. For this purpose, determinations of cutaneous temperature were made in all of the cases by means of a thermo-electric couple of the common type. The results of observations were then compared and correlated with the subjective symptoms.

Observations were made under uniform conditions of room temperature, posture of the patient, and rest. The locations at which temperature readings were taken were always the same. Readings were recorded only after the patient had been in the room for a minimum period of one-half hour or until the temperature readings became constant. Air-currents were/
were eliminated as much as possible. No attempt was made to control humidity, but it is believed that the conditions for dispersion of heat were uniform.

The apparatus was demonstrated to be accurate to 0.1 degrees C. (0.18 degree F.), but no attention was paid to changes less than 0.5 degree C. (0.9 degree F.), which allows a reasonable limit for error.

Early in the course of this work by Soupham, several drugs were used, including caffeine, theophylline, and others, but the best results seemed to be obtained with theobromine or theobromine sodium acetate, and it is only the results with these preparations which are being reported.

**Technique:** Theobromine sodium acetate was administered by mouth, three grammes daily in three divided doses for 21 days.
### Cases.

1. Arteriosclerosis with ulcer.
2. Arteriosclerosis with intermittent Claud.
3. Arteriosclerosis with varicose veins.
4. Thrombo-angiitis obliterans.
5. Thrombo-angiitis obliterans.
6. Thrombo-angiitis obliterans.

### Results.

<table>
<thead>
<tr>
<th>Cases</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Arteriosclerosis with ulcer.</td>
<td>Skin temperature up 2°C; colour improved; ulcer healed.</td>
</tr>
<tr>
<td>2. Arteriosclerosis with intermittent Claud.</td>
<td>Skin temp. up 1.8°C.; intermittent claudication improved.</td>
</tr>
<tr>
<td>3. Arteriosclerosis with varicose veins.</td>
<td>Skin temp. - no rise; colour and pain of intermittent claudication improved.</td>
</tr>
<tr>
<td>4. Thrombo-angiitis obliterans.</td>
<td>Skin temp. up 2.6°C.; intermittent claudication improved; general improvement.</td>
</tr>
<tr>
<td>5. Thrombo-angiitis obliterans.</td>
<td>Skin temp. up 2°C.; intermittent claudication improvement.</td>
</tr>
<tr>
<td>6. Thrombo-angiitis obliterans.</td>
<td>No effect.</td>
</tr>
</tbody>
</table>

### Conclusions.

1. Theobromine and its salts, particularly theobromine sodium-acetate, act as peripheral vaso-dilators.
2. They are useful in the treatment of peripheral arterio-sclerosis and early cases of thrombo-angiitis obliterans in which there is a large element of angiospasm. Their results in subjective improvement in intermittent claudication, and repair of loss of tissue integrity has been noted.
3. They are not effective in all cases, but the results obtained with them are sufficiently good to make them a valuable adjunct in the treatment of peripheral vascular disease.
References.


Reports of the Council on Pharmacy and Chemistry,

IV. ACETYL B METHYL CHOLIN CHLORIDE.

The drug, acetyl B methyl cholin chloride was synthesised by Starr, Reisinger, Richards and Elsom and its action first investigated by Starr in 1933. Simonart had demonstrated in the same laboratory, Lab. of Pharmacology Pennsylvania the action of acetyl choline on the intact human. Given intravenously this produced effects similar to stimulation of the para-sympathetic nervous system with the addition of vaso-dilatation of peripheral vessels. The effects were: - Fall in blood pressure; rise in pulse rate with subsequent fall; flushing; sweating; salivation; increased intestinal activity.

The use of such a preparation was therefore suggested to Starr and his fellow workers. Acetyl choline undergoes rapid hydrolysis to cholin and even its action intravenously is evanescent. Some other preparation was sought, so acetyl B methyl cholin chloride was synthesised.

A thorough investigation of the effects of this drug was carried out by Starr in 1933. His investigation included - (1) Action on normal individuals/
individuals. (ii) Action on cases of paroxysmal tachycardia and peripheral vascular disease.

Technique Adopted.

47 normal subjects were investigated.

2.5 - 25 mgms. Acetyl B. Methyl Choline Chloride by subcutaneous injection.

The results were exactly those attained by acetyl cholin but were sustained over a much longer period.

Similar results were attained with oral administration, and the findings corresponded in human and animal investigations.

Tachycardia was relieved in a large percentage of sufferers.

In view of the peripheral vascular dilatation attained, Starr decided to try the efficiency of the drug in relieving the syndrome of peripheral vascular disease. He pointed out that the phenomena suggestive of spasm could be demonstrated in many cases of obstructive vascular disease of organic nature.

He investigated seven patients.

Classification/
Classification.

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>No.</th>
<th>Pain</th>
<th>Healing</th>
<th>Skin Temp.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thrombo-angiit. obl.</td>
<td>3</td>
<td>Relieved</td>
<td>Increased</td>
<td>Raised</td>
</tr>
<tr>
<td>Diabetic arterio-scler.</td>
<td>3</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Obstruct. vasc. disease</td>
<td>1</td>
<td>indefinite</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

In discussing clinical utility he points out that there is no attempt at final evaluation from the above results, but points out that it is suggestive that it repeatedly gave a rise in skin temperature in cases of thrombo-angiitis obliterans and relieved pain in certain cases of gangrene from that cause.

Goldsmith, in 1934, carried out an investigation into the effects of oral administration of acetyl B methyl cholin (mecholin) on skin temperature, pulse rate and blood pressure of 29 subjects who had peripheral vascular disease.

The table of results is appended.

Dosage: 50 - 1,500 mgs.

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>No.</th>
<th>Degrees Centigrade</th>
<th>Skin Temperature</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td>4</td>
<td>6.6</td>
<td>33-36</td>
</tr>
<tr>
<td>Raynaud's disease</td>
<td>8</td>
<td>7.45</td>
<td>27-35</td>
</tr>
<tr>
<td>and Scleroderma</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thrombo-angiit. Oblit.</td>
<td>7</td>
<td>3.6</td>
<td>29-35</td>
</tr>
<tr>
<td>Arteriosclerosis</td>
<td>5</td>
<td>4.7</td>
<td>27-35</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>5</td>
<td>6.6</td>
<td>21-36</td>
</tr>
</tbody>
</table>
Those results relative to typhoid vaccine as a means of vaso-dilatation gave 75% efficiency. There were no toxic effects, so it was concluded that this was a most valuable drug in inducing vaso-dilatation and clinically in obstructive vascular disease with a spastic element superadded.

Page, in 1935, was unable to corroborate the above. He found that mecholin produced flushing of the face and thorax but none in the hands or feet.

Kovacs administered the drug by iontophoresis, using 10% acetyl B methyl cholin chloride (1 gm. - 100 ccs.).

The positive pole for induction, a current of 20-30 milliamps for 20-30 minutes. Length of course not specified.

The physiological effects:

Local.
1. Goose flesh.
2. Sweating.
3. Increase in skin temperature.
4. Increased rate of capillary flow, but no capillary dilatation.
5. Slight redness of skin lasting 5 hours (arteriole dilatation?).
6. Warmth in the part.
7. Oscillometry increase in some patients.
8. Relief of pain.

General. When large areas treated.
1. Flushing and sweating.
2. Salivation.
3. Pulse rate up, then down.
5. Intestinal movements increase.

Conclusion/
Conclusion.

The same as that of Starr, viz. -

Acetyl B methyl cholin chloride acts as para-sympathetic stimulant and vaso-dilator.

Kovacs, on the basis of physiological results, investigated the effect of a few cases of obstructive vascular disease. He does not specify the type or the number, but states that he found -

1. Rise in temperature of the skin.
2. Unusually rapid healing of ulcers.
References.


B. BY NON-SPECIFIC PROTEIN THERAPY.

The application of protein intravenously in the treatment of peripheral vascular disease was suggested by Goodman and Gottesman. They noted relief of pain and improvement in general appearance of the extremities. Brown, Allen and Mahorner employed this method of treatment from 1923 to 1928 and in 1928 published a monogram stating therein their opinion that intravenous protein therapy was the most effective medical measure. The rationale of the treatment is based on two considerations.

1. The relief of pain; this is not specific for the pain of vascular disease, since the treatment has long been used in other painful disorders such as chronic arthritis. The explanation of the relief is not entirely clear.

2. The increase of the blood supply to the affected part. Undoubtedly the relief of pain obtained depends to a great extent on the increased volume flow of blood which occurs with fever. It is also true that the relief is at times out of proportion to the amount of demonstrable vaso-dilatation and is also prolonged for longer periods than fever of vaso-
vaso-dilatation can be demonstrated. There is apparently another factor of pain relief from protein treatment of which little is known. Brown, Allen and Mahorner carried out studies on the physiological effects on the circulation following the induction of fever by non-specific protein. Calorimetric studies on the greater heat elimination showed sharp decided increases in the rate of heat loss in the extremities during fever. This loss is an indirect measurement of the rate of volume flow of blood in the limb. The surface temperature is sharply increased, the mechanisms of which is concerned with the adjustments of the vaso-motor system on the surface vessels to increase the amount of heat loss and thus maintain the normal body temperature. The increased surface temperature represents the actual increase in the blood temperature, and those changes due to shifting an abnormal amount of blood to the surface, or, in other words, vasomotor effects.

The technic, carried out in their work, was the use of the triple typhoid vaccine consisting of typhoid bacteria and paratyphoid A. and B. An initial dose of from 20,000,000 to 50,000,000 was given.
given intravenously. This can be increased by 50,000,000 at a time up to 250,000,000 or 300,000,000. Such doses were usually given every fourth or fifth day or, when occasion demanded, every second or third day for a short period. A satisfactory reaction was manifested by a mild chill and a maximal period of fever; an increase in temperature of 2° or 3°F. was desirable. The systemic symptoms were usually those of headache, mild nausea, and malaise, which usually disappeared in twenty-four hours. They gave many hundred injections of the typhoid vaccine in the treatment of vascular disease and many thousands were given in cases of chronic arthritis, without harmful effects. Their usual plan was to give from four to six injections in a course, then allow a period of three or four weeks, and repeat the course if indicated.

Allen and Smithwick, in 1928, published their experience of the treatment of 25 cases of chronic vascular disease by the method of Allen, Brown and Mahorner. They believe that the method hastens the development of collateral circulation.

The technic of Barker, 1931, differed from that of/
of Allen, Brown and Mahorner. He was of the opinion that sulphur in oil, as discussed by Waller, produced satisfactory fever reactions when given intramuscularly, but that local reactions were occasionally severe. Bacterial vaccines given intravenously, particularly those of the typhoid group, were the most successful. The most satisfactory preparations were the ordinary T.A.B. (bacillus typhosus, bacillus paratyphosus A and B.) and the typhoid H. antigen, those preparations being used by Barker in treatment. The initial dose was from 15 to 30 million organisms. The number of injections depended on the response in relief of pain and in healing. Injections were given as often as every other day and as many as eighteen to a course. Sometimes they were given once a week for a prolonged period. The dose, if necessary, was increased to keep up the reactions, for patients varied considerably in their tolerance; usually the dose had to be increased by 25 million organisms each time. As much as five hundred million was given in a single dose towards the end of a course. If prolonged treatment was necessary it was considered advisable/
It is advisable to give a period of rest of a month or so after 12 injections.

Brown, writing in 1934, confirmed his own early experience and the experience of Barker in that the most satisfactory method of induction of fever was the intravenous injection of vaccine, and that the most satisfactory vaccine was either (i) triple typhoid, or (ii) typhoid antigen H.

The Results of Allen, Brown and Mahorner.

<table>
<thead>
<tr>
<th>Cases</th>
<th>No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thrombo-angiitis obliterans</td>
<td>43</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Classification</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Relief of Rest pain.</td>
<td>Trophic changes.</td>
</tr>
<tr>
<td>Complete</td>
<td>Partial</td>
</tr>
<tr>
<td>Complete</td>
<td>25</td>
</tr>
</tbody>
</table>

There is no mention of intermittent claudication.
The Results of Allen and Smithwick.

<table>
<thead>
<tr>
<th>Classification</th>
<th>No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vaso-motor</td>
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</tr>
<tr>
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<td>6</td>
</tr>
<tr>
<td>Thrombo-angiitis obliterans</td>
<td>13</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>4</td>
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</table>

<table>
<thead>
<tr>
<th>Disablement.</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Partial</td>
<td>Total</td>
</tr>
<tr>
<td>19</td>
<td>6</td>
</tr>
</tbody>
</table>

These results appear to refer chiefly to ulcer and gangrene.
The Results of Barker.

<table>
<thead>
<tr>
<th>Classification</th>
<th>No. of cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Claudication - nil else - no rest pain - no gangrene</td>
<td>17</td>
</tr>
<tr>
<td>Rest pain - no ulcer - no gangrene</td>
<td>28</td>
</tr>
<tr>
<td>Ulcers and rest pain.</td>
<td>55</td>
</tr>
<tr>
<td>Ulcers: 26 quick healing 21 slow healing 8 no healing</td>
<td></td>
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<tr>
<td>Rest pain and gangrene limited to digits</td>
<td>46</td>
</tr>
<tr>
<td>Gangrene: 30 Complete healing 16 no healing</td>
<td></td>
</tr>
<tr>
<td>Massive gangrene of digits</td>
<td>4</td>
</tr>
<tr>
<td>1 healing 3 no healing.</td>
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**Results.**

<table>
<thead>
<tr>
<th>Complete Relief</th>
<th>Partial Relief</th>
<th>Nil</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>7</td>
<td>8</td>
</tr>
<tr>
<td>24</td>
<td>3</td>
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<td>40</td>
<td>7</td>
<td>8</td>
</tr>
<tr>
<td>21</td>
<td>14</td>
<td>11</td>
</tr>
</tbody>
</table>

**Summary.**

There was marked improvement in 73 cases, slight or slow improvement in 41 cases, and no improvement on 36 cases.
References.


11. SPECIFIC MEASURES.

(a) By Local Action.

1. BALNEO THERAPY.

The origination of bath treatment of obstructive vascular disease was probably derived from the introduction by Beneke of Marburg about 1860 of the carbon dioxide bath in the treatment of cardiac and circulatory disorders. Baths used in obstructive vascular disease may be classed as follows:

1. Carbon dioxide baths.
2. Hyperpyrexic baths.
3. Contrast baths.
4. Paraffin baths.
5. Whirlpool baths.

The rationale is the local effect, heat locally produces hyperaemia by local vaso-dilatation of arterioles. Contrast baths are thought to exercise the arterioles by causing alternate relaxation and contraction. CO₂ and movement of the water is thought to enhance the effect of heat.

Mehrtens and Pouppirt report good results in cases of intermittent claudication treated by hyperpyrexic baths; the water temperature was 110°F.

Sedwitz reported greater clinical and subjective results/
results when the paraffin bath was utilised as an adjunct to other forms of treatment chiefly Pavaex and intermittent venous occlusion.

Samuel does not recommend the use of contrast baths, stating that they have proved dangerous, in his experience, in obstructive vascular disease.

There are no records of the actual value of balneo therapy in obstructive vascular disease.

11. DIATHERMY.

In 1924 Buerger described the treatment of obstructive vascular disease by conservative methods. Included in these measures was treatment by diathermy. Buerger was of the opinion that much greater benefit was derived from his postural exercises.

Livingstone, in 1931, was of the opinion that diathermy was of considerable value in improving the circulation in peripheral vascular disease. The therapy may be applied locally or to induce artificial increase in temperature. The local action is to increase blood flow by local vaso-dilatation by direct action or by axon reflex.

Coulter, in a review of results of diathermy, is of the opinion that it is a valuable form of therapy wherever there is an insufficient blood supply.

Chevalin and Chezet in Paris reported good results in cases of diabetic gangrene.

Barbash reported successful results in a series of cases of diabetic gangrene. He believed that the effect of diathermy was lasting and appeared/
appeared to be permanent and sufficient to maintain a good blood supply to the affected parts.

According to Samuels, diathermy should not be used in the presence of ulceration or gangrene in the extremity because of the possibility of increasing pain and of encouraging secondary infection. Diathermy treatment should be given for a period of twenty minutes or at longer intervals depending on the individual and attending circumstances. A recent innovation has been the employment of short wave diathermy. No results of this therapy are published. Diathermy in general should be used as an adjunct to other forms of treatment. As in the case of postural exercises, diathermy has been superseded by more modern methods of increasing blood flow.
References.


Postural exercises were first advocated by Buerger. They were based on his observations on "induced rubor" or "induced hyperaemia" and comprised an attempt to use this knowledge therapeutically.

The procedure is as follows:— The affected limb is elevated with the patient lying in bed, to from 60° or 90° above the horizontal, being allowed to rest upon a support for from 30 seconds to 3 minutes, the period of time being the minimum amount of time necessary to produce blanching or ischaemia. As soon as blanching is established, the patient allows the foot to hang down over the edge of the bed for from two to five minutes, until reactionary hyperaemia or rubor sets in, the total period of time being about one minute longer than that necessary to establish a good red colour. The limb is then placed in the horizontal position for about 3 to 5 minutes, during which time an electric heating pad or hot water bag is applied, care being taken to prevent the occurrence of a burn. The placing of the limb in these three successive positions constitutes/
constitutes a cycle, the duration of which is usually from 6 to 10 minutes. These cycles are repeated over a period of about one hour, some six to seven cycles constituting a seance.

The number of seances cannot be categorically stated but should vary with the case.

Samuel's modified Buenger's original technique. The technique of Samuels is as follows:- The patient is instructed to lie flat on his back and elevate both legs to an angle about 45°. The physician then notes the number of minutes necessary to produce, blanching of the feet while in this position. This is then used as the standard time for elevation of the extremities for that particular patient. Two minutes of elevation is usually sufficient for the average case. The patient now changes his position so that he is sitting on the side of the bed with his feet in a pendant position. The time necessary for the appearance of rubor is then noted. In most cases this is about three minutes. The next position is one of recumbency with the extremities horizontal, which should be maintained for about 2 minutes.

The cycle of elevation, pendency and rest is repeated/
repeated four or five times in succession, according to the patient's ability to endure the slight exertion entailed.

Each session of four or five cycles should be repeated from two to four times during the day, according to the physician's judgment.

The introduction of intermittent venous occlusion by Collens and Wilensky in 1936 has largely replaced postural exercises.
References.


11. PAVAEX THERAPY.

1. Historical and Physiological Basis.

In 1924 Herrmann and Reid published a review of the treatment of 75 patients suffering from obstructive vascular disease by a method termed Paevex—a word coined by them to denote passive vascular exercise. This method consisted of the rhythmic alternation of negative and positive pressures about the affected extremity or extremities. The physiological effect of diminished atmospheric pressure upon the body or extremity and the marked increase in the arterial circulation which could be brought about in this way was described in detail over 100 years ago and has, at intervals, been rediscovered and redescribed since that time—most recently by Landis and Gibbon, and by Herrmann and Reid. Sir James Murray of Dublin was perhaps the first to apply this principle to the treatment of disease. As early as 1612 he subjected animals as well as patients to various degrees of rarefied and compressed air. It was not until 1832, however, that he
he began to publish the results of his experimental and practical studies. In 1835 he described the effects of diminished atmospheric pressure upon man in the following words:— "The effects of a rare atmosphere are pointed out by those who have ascended very elevated situations, but in such cases the air inhaled was as light as that around the body. On the contrary, it is natural to expect different results if you place a man in a rarefied atmosphere, who is at the same time breathing air of the usual density and pressure. Abstraction of a ton and half—a ton of weight from the surface of the body permits the cutaneous vessels easily to fill, and favours their distension as it were by suction while, at the same time, the lungs receive a column of the usual expansive force supporting the interior trunk and organs, pressing and propelling blood out from the centre to the circumference. In this consists the novelty and value (if any) of the principle I propose."

Since that time there have been many variations in the methods of applying negative or positive environmental pressure to modify the circulation of blood in the various parts of the human body. In 1833/
1833, Victor Junod published his thesis for doctorate from the University of Paris in which he described the use of negative pressure in the treatment of various diseases under the title of "Haemospasia and Aerotherapeia". In 1835, W. Reid Clanny, of Sunderland, England, working independently of Murray and Junod, published a description of the apparatus which he had devised for removing the pressure of the atmosphere from the body or limbs. It was not until 1887, however, that negative and positive pressures were used alternately to modify the arterial circulation in the extremities. It was Edgar Bluck, of South Hampstead, England, who first applied the rhythmic alternation of these pressures as he described it - "to bring about an influx and efflux of the blood in the part or parts affected".

The first record of the application of diminished atmospheric pressure as a treatment for organic peripheral arterial disease was published in 1917 by Sinkowitz and Gottlieb. They applied the Bier's suction hyperaemia treatment to four patients with thrombo-angeitis obliterans with very good results. In 1930, Braeucker applied the same method of/
of treatment to nineteen patients with true Raynaud's disease with equally good results.

In 1932, Herrmann designed and built an apparatus which would automatically bring about the rhythmic alternation of the environment pressure of an extremity from any desired amount of negative pressure to any desired amount of positive pressure and at any selected rate of alternation. Because of the fact that this apparatus was essentially causing passive exercise of the vascular system, he called the method of treatment Pavaex.

The physiological basis for the treatment of intermittent suction and pressure was investigated by Landis and Gibbon in 1933.

According to Poiseuille's law, the amount of fluid flowing through a rigid tube depends upon the fall in pressure along that tube. If other factors remain constant doubling the peripheral fall in blood pressure should approximately double the amount of blood flowing through the rigid arterial vessels. The total fall in pressure in the peripheral vascular system may be increased in two ways - (a) by elevating systemic blood pressure, or (b) by diminishing capillary and venous pressures.
The first method is impracticable for numerous reasons. It seemed possible, however, that capillary and venous blood pressures might be reduced temporarily to negative values, i.e. below atmospheric pressure, by applying suction to the skin of the extremity.

The full effect of externally applied negative pressure can only be obtained if there be a reservoir capable of accommodating blood which has flowed through the narrowed arteries. The capillaries and veins when not constricted offer such a reservoir - of limited capacity.

Landis and Gibbon(1) observed that inflating a pneumatic cuff on the upper arm to a pressure of 30 cm. water for 5 minutes increased the volume of a segment of forearm by 25 cc., of which 3 cc. consisted of extra-vascular fluid, while 22 cc. consisted of blood trapped in the congested peripheral vessels. Similarly, a venous pressure of 60 cm. water during 6 minutes increased the volume by 38 cc., of which 7 cc. was extra-vascular fluid and 31 cc. was blood in the congested vessels.
The total volume of the segment of forearm was 720 cc. so that at pressures of 30 and 60 cm. water the reservoir available was 3 and 4 cc. per 100 cc. of arm respectively. Average blood flow in the normal forearm amounts usually to less than 5 cc. per minute per 100 cc. of tissue (Lewis and Grant). Hence with a slight rise of pressure the veins and capillaries can accommodate the blood flowing through normal vessels during a period of approximately one minute.

From these observations it seemed possible that the periodic application of negative pressure to the surface of the lower extremity might be expected to increase blood flow, even though the arterioles had been changed into rigid tubes by reason of structural disease. Moreover, if the suction were applied for relatively short periods of time the efficiency of the method would be greater since the available reservoir would not be filled to capacity during any one suction period. The accumulation of blood in the capillaries and veins must lead to stretching of their walls, the resistance to further distension increasing as the amount of trapped blood becomes greater. This resistance would, of course, lessen the effect of external/
external suction on the peripheral drop in blood pressure, particularly if suction were prolonged. It seemed essential, therefore, not only to use relatively brief periods of suction, but also to empty the capillary and venous beds of their contained blood after each brief suction period, so that space might be available for the accommodation of fresh arterial blood to be drawn in during the succeeding suction period. Therefore, suction and pressure were applied alternately.

Landis studied the effects of alternate suction and pressure on flow in a circulatory schema, and in the lower extremities of normal subjects and of patients with peripheral vascular disease. His conclusions were as follows:

1. In a circulation schema it was found that alternate suction and pressure increased by 45 to 78 per cent., the rate at which fluid flowed past an obstruction.

2. In normal subjects alternate suction and pressure (a) diminished the rate of cooling of an extremity originally warm, and (b) in the majority of instances caused an originally cold extremity/
extremity to become conspicuously warmer. Suction and pressure sometimes failed to affect blood flow in the cold extremity but, as soon as vasoconstrictor tone was diminished slightly, blood flow was conspicuously and preferentially increased in the extremity exposed to external pressure variations.

3. The vasodilator response to warming one forearm was studied in normal subjects with and without the use of external pressure changes. Alternate suction and pressure caused vasodilator response to appear earlier and the final skin temperatures reached were definitely higher in the extremity exposed to external pressure change.

4. In patients with peripheral vascular disease alternate suction and pressure increased blood flow even though organic obstruction had advanced to such a stage that no rise in skin temperature was obtained when vasoconstrictor tone was completely abolished by immersing both forearms in warm water or by anaesthetizing the posterior tibial nerve.

5. To obtain maximal effects on blood flow it is apparently advisable to have (1) relatively brief/
brief periods of suction; (2) intermittent, brief periods of pressure, and (3) diminished vasoconstrictor tone.

Herrmann and Reid's original Pavaex unit was so constructed that the change of pressure was brought about slowly. This was in order to conform to the generally accepted principle of dilating and stretching muscular tissue slowly rather than suddenly. The complete cycle of the variation from atmospheric pressure to seventy millimetres of mercury negative pressure, then to seventy millimetres of mercury positive pressure, and finally back again to atmospheric pressure took about thirty seconds. After much experimentation they came to the conclusion that four complete cycles of alternating pressure from about eighty millimetres of mercury negative pressure to twenty-to-forty millimetres of mercury positive pressure will bring about the greatest increase in the arterial circulation with the least damage to the tissues of the extremity. In one complete cycle of fifteen seconds about five seconds are used for the positive pressure phase and about ten seconds are used for the negative/
negative pressure phase. There seems to be no limit to the length of time the treatment can be carried out without discomfort or untoward effects. The frequency or length of the treatments should depend entirely upon the urgency of the condition to be treated, as, for instance, acute arterial occlusion either by operation, trauma thrombosis, or embolism must be considered as surgical emergencies and treated intensively until adequate circulation has been permanently established. For patients who are hospitalized the number of hours of actual treatment vary from four to eight each day, while the less urgent and ambulatory patients receive from three to seven hours treatment each week.

In the method advocated by Landis and Gibbon considerably greater degrees of positive and negative pressure were used and the alternation so arranged that only five seconds were allowed for the eighty millimetres of mercury positive pressure to act upon the extremity and twenty-five seconds for the negative pressure of 120 millimetres of mercury to be maintained about the extremity which was being treated. In the opinion of Herrmann and Reid the elevation/
elevation of the extremity several inches above the 
level of the heart has been found to be more 
satisfactory than the use of large amounts of 
positive pressure to free the extremity from venous 
blood.

II. CLINICAL EXPERIENCE.

Passive vascular exercise as a method of 
treatment for obstructive arterial disease has been 
investigated by the following:-

Herrmann and Reid, 1934.
Landis, 1934.
De Takats, 1934.
Allen and Brown, 1935.
Landis and Hitzrot, 1935.
Wilson and Roome, 1936.
O'Neil, 1937.

The results of their experiences are tabulated 
below.
Author: Herrmann and Reid

Date: 1934

Cases examined and treated:


Number: Total 75

Criteria and Results:

Amputation necessary 11%
Improved 45%
Major symptoms relieved 44%

Affecting:

Major arteries 10 100%
Secondary arteries 46 7% 48% 43%
Arterioles 19 42.1% 42.1% 15.8%

Total 75

Conclusions:

1. The addition of passive vascular exercises (Pavaex therapy) to all those measures of general care advocated by Allen, Buerger, Reid and others will materially aid in bringing comfort to the patient and preventing serious sequelae from making their appearance in patients with arteriosclerosis peripheral vascular disturbance.

2. The benefits of the Pavaex treatments have been least obvious in those patients with extensive obliteration of the arteriolar bed of the feet and most striking when the pathological changes were primarily limited to the major or secondary arterial pathways, especially when there was a rapid occlusion of the artery by embolism, trauma, surgery, or thrombosis.

3. The active treatment of the obliterative arterial disease of the extremities is, as a result of recent work, rapidly becoming a truly non-surgical procedure and may soon rightfully become the function of the department of internal medicine.
Observations.

1. Four cases with definite gangrene, in which gangrene was limited by treatment by Pavaex.

2. Major symptoms referred to include intermittent claudication and rest pain.

<table>
<thead>
<tr>
<th>Author</th>
<th>Date</th>
<th>Cases examined and treated.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Classification. Number.</td>
</tr>
<tr>
<td>De Takats</td>
<td>1934</td>
<td>Art. Sclerosis Ob. 10</td>
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<td></td>
<td>Thrombo-angeitis Ob. 2</td>
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<td>End. Obliterans. 4</td>
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<td></td>
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<td>Acute Vas. Occlusion 4</td>
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<tr>
<td></td>
<td></td>
<td>Total 20</td>
</tr>
</tbody>
</table>

Criteria and Results.

- Rest pain - 100% relieved.
- In. Claud. - some improvement.
- Colour - improved.
- Oscillomet. - no change.
- Trophic changes - some improvement
- Gangrene - no change.

Conclusions.

1. The therapy is a valuable adjunct to other methods already in use.

2. Most favourable results attained in cases presenting involvement of smaller vessels.
### Cases examined and treated.

<table>
<thead>
<tr>
<th>Author</th>
<th>Date</th>
<th>Classification.</th>
<th>Number</th>
</tr>
</thead>
</table>

#### Criterions and Results.

<table>
<thead>
<tr>
<th>Criterion</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rest pain</td>
<td>relieved during treatment</td>
</tr>
<tr>
<td>Skin temp.</td>
<td>rose during treatment</td>
</tr>
<tr>
<td>Trophic changes</td>
<td>improvement</td>
</tr>
<tr>
<td>Cyanosis</td>
<td>some improvement</td>
</tr>
</tbody>
</table>

#### Conclusions.

1. **Alternate suction and pressure increase blood flow temporarily.**

2. **This procedure elevates skin temperature conspicuously, tends to relieve cyanosis, diminishes rest pain, and favours, at least temporarily, the healing of superficial, indolent ulcerations.**

The practical importance of suction and pressure in the treatment of peripheral vascular disease will necessarily depend to a great extent on the degree to which collateral vessels take over the function of those arteries which are closed by disease.
## Cases examined and treated.

<table>
<thead>
<tr>
<th>Author</th>
<th>Date</th>
<th>Classification</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allen and Brown</td>
<td>1935</td>
<td>Arteriosclerosis</td>
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</tr>
<tr>
<td></td>
<td></td>
<td>Thrombo-angeitis Ob.</td>
<td>16</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Sudden occlusion</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Total</strong></td>
<td><strong>32</strong></td>
</tr>
</tbody>
</table>

## Criteria and Results.

- Rest pain - improved.
- Inter. Claud. - improved.
- Trophic changes - improved.
- Skin Temp. - temperature rise.
- Gangrene - indefinite.
- Pain of occlusion - worse.

## Conclusions.

The intermittent suction and pressure treatment of chronic occlusive arterial disease increases the skin temperature temporarily, may relieve the pain of ischaemic neuritis and trophic changes, and may induce healing of ulcers. It is not clear that these results are superior to those following other methods of treatment. However, the impression is formed that the pain of ischaemic neuritis is relieved to a greater degree than is ordinarily observed. As a result of the experience gained it is believed that passive vascular exercises constitutes some, but as yet poorly defined, contribution to the treatment of vascular disease.
Author: Landis and Hitzrot
Date: 1935

Cases examined and treated.

<table>
<thead>
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<tr>
<td>Arteriosclerosis</td>
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<tr>
<td>Thrombo-angeitis</td>
<td>11</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>29</strong></td>
</tr>
</tbody>
</table>

Criteria and Results.

- Cyanosis - improved
- Rest pain - improved
- Trophic changes - improved
- Intermit. claudic. - improved
- Gangrene - no effect

Conclusions.

Suction and pressure therapy, if carefully applied, appears to be worthy of clinical trial in the treatment of peripheral vascular disease even when organic obstruction has advanced to the point where arterial blood flow can no longer be increased by vaso-dilatation. The method may be of service by increasing local blood flow temporarily during episodes of pain or ulceration so that time is gained for the development of adequate collateral blood flow.
Author: Wilson and Rome
Date: 1936
Cases examined and treated:

<table>
<thead>
<tr>
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<th>Number</th>
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<tbody>
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<td>Thrombo-angeitis ob.</td>
<td>8</td>
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<tr>
<td>Embolism</td>
<td>3</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>23</strong></td>
</tr>
</tbody>
</table>

Criteria and Results:

- Rest pain: no definite effect.
- Intermittent claudication: no definite effect.
- Trophic changes: no definite effect.
- Colour: no definite effect.

Conclusions:

Many of the patients felt improved during the course of the treatment but reported no permanent beneficial results when questioned two or three months later. This is evidence of the lack of permanent benefit from the treatment and may indicate a considerable psychologic factor.

In this series of cases, passive vascular exercise treatment did little good, and it was difficult to say whether the beneficial results were to be attributed to it or to the other measures that were concurrently employed.
Author    Date    Cases examined and treated.

Classification    Number.

O'Neil    1937    Arteriosclerosis    33
           Diabetic arterioscler.    14
           Periph. embolism    7
           Frozen feet    6
           Thrombo-angeitis Ob.    20
           Total    80

Criterions and Results.

Gangrene    - nil.
Intermittent Claud.:    - improved.
Trophic changes    - nil.
Skin temp.    - temporary rise.
Ischaemic pain    - improved.

Conclusions.

It must be obvious that while suction pressure
therapy is not a panacea for all circulatory ailments
of the extremities, it is nevertheless a distinct
addition to the various therapeutic measures already
at our disposal, and should be evaluated in relation
to the demands of the individual case.
References.


CLANNY, W.R.: Quoted by Herrmann and Reid.


BIER: "Reactive Hypeaemia", 1928.


HERRMANN, L.G.: Quoted by Herrmann and Reid.


LEWIS, T., GRANT, R.: Heart, vol. 12, p. 73, 1925.


111 INTERMITTENT VENOUS OCCLUSION.

Physiological Basis and History.

The physiological basis of treatment by intermittent venous occlusion rests on Lewis and Grant's observations on reactive hyperaemia.

Reactive hyperaemia was first described in man and is familiar to all surgeons who have used a tourniquet or Escherich's bandage to control haemorrhage. Conheim and Lister give early descriptions of the phenomenon. Clinically, it is seen as a bright flush of the skin, together with an increased volume pulse on releasing the obstruction to the circulation. Before the investigations of Bier (1897) the reaction was thought to result from vaso-motor paralysis produced by pressure on the nerves. Bier showed that it occurred equally well when all connection with the limb had been severed, save the artery itself. Lewis and Grant (1926) further demonstrated that the reaction is a local one, being independent of central nervous system and local reflexes. They are of the opinion that though deficient blood supply is the obvious primary cause/
cause, it is highly improbable that the reaction is due to any one blood constituent. It is thought to result from an accumulation of slowly diffusible substances in the extra-vascular tissues, the products of metabolism during the period of circulatory arrest.

Lewis and Grant further showed that reactive hyperaemia followed occlusion from pressures ranging from arterial to venous at 30 mm. Hg., and demonstrated the relationship of time of occlusion and pressure of occlusion to reactive hyperaemia. The greatest increase in flow occurred with arterial occlusion, the least after venous occlusion. Arterial occlusion of five seconds or more produced reactive hyperaemia. The reactive hyperaemia lasted from half to three quarters of the time of claudication. At the release of arterial occlusion increased blood flow of the nature of 600% took place. This rapidly declined depending on the duration of occlusion. With venous occlusion the blood flow increase was much less.

The reactive hyperaemia is greatest in a limb, the temperature of which has been raised.
Collens and Wilensky, familiar with the work on venous ligation and impressed by Lewis and Grant's paper decided that the benefit derived from venous occlusion comes, not from the obstruction, but from the release of the obstruction. They utilised an apparatus designed to produce alternating periods of venous congestion and release.

The apparatus utilised by Collens and Wilensky.

The apparatus consists of a motor-driven pump which supplies air to a pneumatic cuff. The pressure/
pressure is regulated by means of a pressure-measuring indicator. The required venous pressure is imposed on the proximal position of the diseased extremity and results in restriction of returning venous blood.

A suitable mechanism is incorporated in the device which maintains the pressure for 2 minutes after which a release valve is actuated electrically to cause an automatic deflation on the cuff. A diagram illustration of the instrument is given above.

**Technique:** Consisted in applying venous compression at mid-thigh alternating with release in periods of two minutes for as long as 12 hours continuously each day. The pressure used was 30 - 60 mm. Hg.

**Criteria Employed:**

1. **Walking test.**
   
   The patient was required to walk at 11 paces per 5 seconds. The total distance and the time the patient was able to walk and the time of claudication development were recorded.

2. **Vaso-dilatation - i.e. skin temperature readings after abolition of vasomotor tone by the method of Landis and Gibbon.**

3./
3. Oscillometric readings.
4. Relief of pain.
5. Healing of ulcers.
6. Effect of treatment on skin temperature.


**CLINICAL EXPERIENCE**

### SERIES I

<table>
<thead>
<tr>
<th>Cases Examined and Treated</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arteriosclerosis with diabetes</td>
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<tr>
<td>Arteriosclerosis without diabetes</td>
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</tr>
<tr>
<td>Thrombo-angeitis obliterans</td>
<td>1</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Type</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oscillometry</td>
<td></td>
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<tr>
<td>Skin temperature resting</td>
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</tr>
<tr>
<td>Skin temperature vaso-dilated</td>
<td></td>
</tr>
<tr>
<td>Trophic pain</td>
<td></td>
</tr>
<tr>
<td>Healing</td>
<td></td>
</tr>
</tbody>
</table>

**Results**

- Oscillometry: Readings increased. One case.
- Skin temperature resting: " " Two cases, 2.25°C.
- Skin temperature vaso-dilated: " " One case, 2.3°C.
- Trophic pain: " " All cases.
- Healing: " " All cases.

**CONCLUSION OF COLLINS AND WILENSKY:**

Intermittent venous occlusion appears to have the following effects:

1. Relief of pain.
2. Increase in skin temperature.
3. Increase in walking efficiency.
4. Increase in vascularity.
5. Healing of chronic indolent ulcers.
### Series 2

**Cases Examined and Treated**

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Diagnosis</th>
<th>No.</th>
<th>Ulceration and Gangrene</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Thrombo-angiitis obliterans</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>2.</td>
<td>Arterio-sclerosis (Diabetic)</td>
<td>13</td>
<td>12</td>
</tr>
<tr>
<td>3.</td>
<td>Arteriosclerosis (non-diabetic)</td>
<td>10</td>
<td>1</td>
</tr>
<tr>
<td>4.</td>
<td>Frost bite with gangrene</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td></td>
<td>29</td>
<td>18</td>
</tr>
</tbody>
</table>

**Results**

<table>
<thead>
<tr>
<th>Relief of Pain</th>
<th>Healing of ulcers and gangrene</th>
<th>Walking</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Healed</td>
<td>Improved</td>
</tr>
<tr>
<td>1.</td>
<td>5</td>
<td>4</td>
</tr>
<tr>
<td>2.</td>
<td>12</td>
<td>4</td>
</tr>
<tr>
<td>3.</td>
<td>9</td>
<td>0</td>
</tr>
<tr>
<td>4.</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>27</td>
<td>8</td>
</tr>
</tbody>
</table>

Intermittent claudication decreased in one-third of the cases. A full report is not available. Oscillometry increased in one-third of the cases, but again a full report is not available.

Skin temperature: Collens and Wilensky note that they have seen a rise of as much as 1.65°C. in experimental studies in the normal. In one case of arterio-sclerosis obliterans a rise of 2.2°C. was observed.

**Conclusions:**
CONCLUSIONS:-

This method in twenty-nine cases gave:

(1) Relief of pain (resting and claudication).
(2) Healing of ulcers.
(3) Increased walking capacity.
# Series 3

## Cases Examined and Treated

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Diagnosis</th>
<th>No.</th>
<th>Ulceration and Gangrene</th>
<th>Rest Pain</th>
<th>Oscillometry</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Thrombo-angeitis Obliterans</td>
<td>27</td>
<td>17</td>
<td>27</td>
<td>+</td>
</tr>
<tr>
<td>2.</td>
<td>Arterio-sclerosis Obliterans</td>
<td>33</td>
<td>8</td>
<td>33</td>
<td>+</td>
</tr>
<tr>
<td>3.</td>
<td>Arterio-sclerosis Obliterans (diabetic)</td>
<td>48</td>
<td>34</td>
<td>48</td>
<td>+</td>
</tr>
<tr>
<td>4.</td>
<td>Embolism</td>
<td>7</td>
<td>7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5.</td>
<td>Frost-bite gangrene</td>
<td>1</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6.</td>
<td>Varicose ulcers</td>
<td>7</td>
<td>7</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7.</td>
<td>Raynaud's disease</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total:</strong></td>
<td></td>
<td>127</td>
<td>67</td>
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<td></td>
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</table>

## Results

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Rest Pain Relief</th>
<th>No Relief</th>
<th>Ulcers or Gangrene Healed</th>
<th>Failed</th>
<th>Oscillometry</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>26</td>
<td>1</td>
<td>15</td>
<td>2</td>
<td>++</td>
</tr>
<tr>
<td>2.</td>
<td>31</td>
<td>2</td>
<td>7</td>
<td>1</td>
<td>++</td>
</tr>
<tr>
<td>3.</td>
<td>45</td>
<td>3</td>
<td>25</td>
<td>9</td>
<td>++</td>
</tr>
<tr>
<td>4.</td>
<td>7</td>
<td>0</td>
<td></td>
<td></td>
<td>-</td>
</tr>
<tr>
<td>5.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6.</td>
<td></td>
<td></td>
<td>Healed</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7.</td>
<td></td>
<td></td>
<td>No report</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

## Conclusions:

1. Relief of rest pain - marked
2. Increased walking capacity
3. Regeneration of tissues
4. Improved nutrition of nails and hair
5. Intermittent claudication improved.
Allen and McKechnie studied the effect of intermittent venous occlusion on circulation of extremities. There was no rise in skin temperature in normal and abnormal as a result of intermittent venous occlusion.

Kramer studied a series of 31 patients, utilising the method of Collens and Milensky. Over 300 treatments were given, entailing 400 hours.
### Classification of Cases

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thrombo-angeitis obliterans</td>
<td>7</td>
</tr>
<tr>
<td>Arterio-sclerosis Obliterans (diabetic)</td>
<td>12</td>
</tr>
<tr>
<td>Arterio-sclerosis Obliterans</td>
<td>6</td>
</tr>
<tr>
<td>Phlebitis</td>
<td>4</td>
</tr>
<tr>
<td>Arteritis with</td>
<td>1</td>
</tr>
<tr>
<td>Osteo-angeitis</td>
<td>1</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>31</strong></td>
</tr>
</tbody>
</table>

#### Symptoms Improved

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Cramps</td>
<td>6</td>
<td>3</td>
<td>2</td>
<td>2</td>
<td>1</td>
<td>14:77.7%</td>
</tr>
<tr>
<td>Fatigue</td>
<td>6</td>
<td>5</td>
<td>4</td>
<td>2</td>
<td>2</td>
<td>19:83.3%</td>
</tr>
<tr>
<td>Pain</td>
<td>6</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>14:56%</td>
</tr>
</tbody>
</table>

#### Symptoms not Improved

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Cramp</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>-</td>
<td>-</td>
<td>4:22.3%</td>
</tr>
<tr>
<td>Fatigue</td>
<td>4</td>
<td>3</td>
<td>3</td>
<td>1</td>
<td>-</td>
<td>11:44%</td>
</tr>
<tr>
<td>Pain</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>-</td>
<td>-</td>
<td>3:16.7%</td>
</tr>
</tbody>
</table>

#### Results:

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Good</td>
<td>6</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>-</td>
<td>12</td>
</tr>
<tr>
<td>Fair</td>
<td>2</td>
<td>3</td>
<td>2</td>
<td>-</td>
<td>2</td>
<td>8</td>
</tr>
<tr>
<td>Slight</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>-</td>
<td>5</td>
</tr>
<tr>
<td>None</td>
<td>3</td>
<td>1</td>
<td>1</td>
<td>-</td>
<td>-</td>
<td>5</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>12</strong></td>
<td><strong>7</strong></td>
<td><strong>6</strong></td>
<td><strong>4</strong></td>
<td><strong>2</strong></td>
<td><strong>31</strong></td>
</tr>
</tbody>
</table>

Kramer states that though unable to make complete studies he was in/
in a position to observe occasional skin surface
temperature and oscillometric readings. Invariably
he states there was a rise in skin surface tempera-
ture averaging 1 - 3°C, in most of the patients.
An increase in oscillometric readings was noted both
immediately after the treatment and at the
termination of the series of treatment.

Conclusions of Kramer.
1. Circulatory function tests confirmed Collens and
Wilensky's observations in rise in temperature and
increase in oscillometry.
2. Cramp, fatigue - benefitted 77.7 - 83%.
Pain not so satisfactory in response, 56%.
3. The new method of periodic reactive hyperaemia
is an advance in treatment of peripheral vascular
disease and is a desirable addition to the
accepted methods of managing this group of
diseases.

Arnott and Brown.

The above observers in 1937 instituted treatment
by intermittent venous occlusion in Edinburgh. They
introduced a simpler apparatus than that used by
Collens/
Collens and Wilensky. As the treatment of 24 patients investigated by the author was given by means of this apparatus, a short description is desirable. Three forms have been used by Brown and Arnott. Of these, the second was utilised in the series of 24 patients quoted above. In the case of both Arnott and Brown, and in our own series, pressures of from 30 to 60 mm. Hg. were utilised with a two-minute cycle.

**Description of Apparatus:** The original apparatus, which is illustrated, consists of a reciprocating air-pump driven by a constant-speed electric motor. The motor is fitted with a reducing gear driving a cam revolving once in four minutes. The cam actuates the valves connecting the pump and the cuff, so as to provide two minutes' pressure and two minutes rest. A mercury manometer indicates the air pressure, which is regulated by an adjustable valve. As the apparatus has to be in operation for long periods, a series of coloured lamps have been incorporated. These indicate (a) when the machine is in operation; (b) when there is no pressure in the cuff; and (c) the elevation of the pressure to more than 10 mm. Hg. above the predetermined pressure.
The apparatus in its second form is such that it can be used in places where electric current is not available. The required pressure is developed by the difference in level between a water reservoir and a pressure bottle. The cycle of operations can be controlled by either a clock-work or electrical timing gear. The third form is the cheapest and most compact. It consists of a small electric rotary air-pump, which also controls a cam-operated piston valve.

Safety valves are fitted to the first and third types of apparatus to prevent excessive inflation. No such device is necessary in the second type, as the pressure depends on relative levels of water.

Working diagram of the original apparatus. For the sake of clarity the electric wiring and the signal lights have been omitted.
**Results of Arnott and Brown.**

<table>
<thead>
<tr>
<th>Cases</th>
<th>Number</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thrombo-angiitis obliterans</td>
<td>12</td>
<td></td>
</tr>
<tr>
<td>Arteriosclerosis obliterans</td>
<td>35</td>
<td>47</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Chief Disability</th>
<th>No.</th>
<th>Result - Failures</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Satisfactory</td>
</tr>
<tr>
<td>Intermittent Claudic.</td>
<td>37</td>
<td>29 - 78% Were all</td>
</tr>
<tr>
<td>Nocturnal pain</td>
<td>28</td>
<td>26 - 93% cases of</td>
</tr>
<tr>
<td>Gangrene</td>
<td>19</td>
<td>14 - 73% arteriosclerosis obliterans.</td>
</tr>
</tbody>
</table>

**Conclusion.**

These results compare favourably with other methods.

**Present Investigation.**

In the present investigation of obstructive vascular disease by intermittent venous occlusion there has been assessed -

1. The results of treatment.

2. The mode of action of intermittent venous occlusion.

   1. The results of Treatment by Intermittent Venous Occlusion.

The cases studied comprised fifteen of thrombo-angiitis obliterans and nine of arteriosclerosis obliterans/
obliterans, a total of twenty-four. Treatment was by the water occluder apparatus, with a pressure of 60 mm. Hg. at a two minute cycle.

A complete table of the investigation and a summary of results is appended.

Assessment of improvement was made on purely clinical grounds, but a record of skin temperature and oscillometry was taken.

Table of Investigation /
<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age</th>
<th>Complaint</th>
<th>Duration</th>
<th>Diagnosis</th>
<th>Skin Temperature on Vaso-dilation</th>
<th>Oscillometry</th>
<th>Hours of treatment</th>
<th>Distance Walked</th>
<th>Coldness Most. Pain</th>
<th>Trophic Changes</th>
<th>Time of Improvement</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>70</td>
<td>Gangrene (R)</td>
<td>6/12</td>
<td>Art. Sel. Oblit.</td>
<td>23.1:1:38</td>
<td>34.4</td>
<td>24.4</td>
<td>0</td>
<td>400</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>2</td>
<td>54</td>
<td>L. R IC++ IC+++</td>
<td>4</td>
<td>Th. Ang. Oblit.</td>
<td>27:9:2:37</td>
<td>34.6</td>
<td>34.6</td>
<td>0</td>
<td>1000</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>3</td>
<td>55</td>
<td>IC++ IC+++</td>
<td>7</td>
<td>Art. Sel. Oblit.</td>
<td>13:6:3:38</td>
<td>32.4</td>
<td>32.4</td>
<td>0</td>
<td>3000</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>4</td>
<td>33</td>
<td>IC++ IC+++</td>
<td>10</td>
<td>Th. Ang. Oblit.</td>
<td>16:2:3:38</td>
<td>34.2</td>
<td>34.2</td>
<td>0</td>
<td>1000</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>5</td>
<td>49</td>
<td>IC++ IC+++</td>
<td>2/12</td>
<td>Th. Ang. Oblit.</td>
<td>21:9:3:38</td>
<td>34.4</td>
<td>34.4</td>
<td>0</td>
<td>500</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>6</td>
<td>60</td>
<td>IC++ IC+++</td>
<td>2</td>
<td>Th. Ang. Oblit.</td>
<td>21:1:3:38</td>
<td>33.4</td>
<td>33.4</td>
<td>0</td>
<td>300</td>
<td>++</td>
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</tr>
<tr>
<td>7</td>
<td>48</td>
<td>IC++ IC+++</td>
<td>2</td>
<td>Th. Ang. Oblit.</td>
<td>13:1:3:38</td>
<td>33.4</td>
<td>33.4</td>
<td>0</td>
<td>100</td>
<td>++</td>
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</tr>
<tr>
<td>8</td>
<td>55</td>
<td>IC++ IC++</td>
<td>1</td>
<td>Th. Ang. Oblit.</td>
<td>17:1:3:38</td>
<td>34.2</td>
<td>34.2</td>
<td>0</td>
<td>100</td>
<td>++</td>
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<td>9</td>
<td>51</td>
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<td>2/12</td>
<td>Th. Ang. Oblit.</td>
<td>8:3:3:38</td>
<td>34.4</td>
<td>34.4</td>
<td>0</td>
<td>300</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>10</td>
<td>23</td>
<td>IC+ IC+++</td>
<td>1</td>
<td>Th. Ang. Oblit.</td>
<td>31:3:3:38</td>
<td>33.4</td>
<td>33.4</td>
<td>0</td>
<td>100</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>11</td>
<td>74</td>
<td>IC+++</td>
<td>1/2/12</td>
<td>Art. Sel. Oblit.</td>
<td>3:4:3:38</td>
<td>32.4</td>
<td>32.4</td>
<td>0</td>
<td>100</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>12</td>
<td>64</td>
<td>IC++ IC+++</td>
<td>1</td>
<td>Th. Ang. Oblit.</td>
<td>21:4:3:38</td>
<td>34.4</td>
<td>34.4</td>
<td>0</td>
<td>100</td>
<td>++</td>
<td>++</td>
</tr>
<tr>
<td>13</td>
<td>60</td>
<td>IC++ IC++</td>
<td>5</td>
<td>Art. Sel. Oblit.</td>
<td>22:4:3:38</td>
<td>32.4</td>
<td>32.4</td>
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<td>++</td>
</tr>
</tbody>
</table>

151.
<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age</th>
<th>Complaint</th>
<th>Duration</th>
<th>Diagnosis</th>
<th>Skin temperature on Vaso-dilatation</th>
<th>Oscilometry</th>
<th>I.C.</th>
<th>L.R.</th>
<th>Distance Walked</th>
<th>Coldness (rest.)</th>
<th>Noct. Pain</th>
<th>Trophic Changes</th>
<th>Pain</th>
<th>Time of Improvement</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>72</td>
<td>I.C. R.L.</td>
<td>1 1/2</td>
<td>A. Sl.</td>
<td>Oblit. 21:10:36 32.2 27.4</td>
<td>.4</td>
<td>0</td>
<td>-</td>
<td>++</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>100</td>
</tr>
<tr>
<td>II</td>
<td>64</td>
<td>I.C. L.L.</td>
<td>1/2</td>
<td>T.</td>
<td>Angitis 16: 5:39 23.7 30.3</td>
<td>.3 1.6</td>
<td>0</td>
<td>0</td>
<td>++</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>140</td>
</tr>
<tr>
<td>III</td>
<td>46</td>
<td>I.C. L.L.</td>
<td>3 1/8</td>
<td>Th. Ang.</td>
<td>Oblit. 9:10:37 24.8 30.8</td>
<td>1.1</td>
<td>0</td>
<td>0</td>
<td>++</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>0</td>
</tr>
<tr>
<td>IV</td>
<td>72</td>
<td>I.C. L.L.</td>
<td>1</td>
<td>A. Sl.</td>
<td>Oblit. 23: 8:36 29.5 32.5</td>
<td>2.2</td>
<td>0</td>
<td>0</td>
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<td>-</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>100</td>
</tr>
<tr>
<td>V</td>
<td>62</td>
<td>I.C. L.L.</td>
<td>4/12</td>
<td>A. Sl.</td>
<td>Oblit. 10: 3:39 30.2 31.2</td>
<td>1.1</td>
<td>0</td>
<td>0</td>
<td>++</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>0</td>
</tr>
<tr>
<td>VI</td>
<td>67</td>
<td>I.C. L.L.</td>
<td>1 3/12</td>
<td>A. Sl.</td>
<td>Oblit. 12:12:38 26.4 34.6</td>
<td>1.2</td>
<td>0</td>
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<td>-</td>
<td>100</td>
<td>++ + +</td>
<td>+</td>
<td>0</td>
</tr>
<tr>
<td>VII</td>
<td>56</td>
<td>I.C. L.L.</td>
<td>6/12</td>
<td>Th. Ang.</td>
<td>Oblit. 29: 6:37 28.6 33.3</td>
<td>2.3</td>
<td>0</td>
<td>150</td>
<td>++</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>+</td>
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<tr>
<td>VIII</td>
<td>70</td>
<td>I.C. L.L.</td>
<td>2</td>
<td>A. Sl.</td>
<td>Oblit. 6: 9:38 26.6 25.6</td>
<td>1.2</td>
<td>0</td>
<td>0</td>
<td>++</td>
<td>-</td>
<td>150</td>
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<tr>
<td>IX</td>
<td>75</td>
<td>Gangrene R. T.</td>
<td>2/12</td>
<td>A. Sl. 8:15:37 29.2 31.2</td>
<td>2.4 2.2</td>
<td>0</td>
<td>0</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>Red-Purple</td>
<td>++</td>
<td>-</td>
</tr>
<tr>
<td>X</td>
<td>39</td>
<td>Ulcers L. Hand</td>
<td>1</td>
<td>T. 16: 6:38 25.3</td>
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<td>0</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>Red-Red</td>
<td>++</td>
<td>-</td>
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<tr>
<td>XI</td>
<td>59</td>
<td>I.C. L.L.</td>
<td>1 3/12</td>
<td>Th. Ang.</td>
<td>Oblit. 21:1:38 30.8 32.2</td>
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<td>-</td>
<td>+</td>
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152.
### SUMMARY OF RESULTS

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<td>24</td>
<td>22</td>
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<tr>
<td>Arterio-sclerosis obliterans</td>
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<td>Improved</td>
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<tr>
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<td></td>
<td>Arterio-sclerosis</td>
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<td>Not Improved</td>
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<td>2. Intermittent Claudication</td>
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<td>Thromb. Ang. Oblit.</td>
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<td></td>
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<td>5</td>
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<table>
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Total - 1540          Total - 2250
Average - 144         Average - 281
## Skin Temperature

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<tbody>
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<td>Right Toe</td>
</tr>
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<td>24.4</td>
</tr>
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<td>4</td>
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<tr>
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</tr>
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<td></td>
<td><strong>285.2</strong></td>
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</table>

Total - 584

Average - 29.2

Total - 590

Average - 29.5
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<thead>
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<th></th>
</tr>
</thead>
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<td>Left Ankle</td>
<td>Right Ankle</td>
<td>Left Ankle</td>
<td>Right Ankle</td>
</tr>
<tr>
<td>1</td>
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<td>1.4</td>
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<td>.2</td>
</tr>
<tr>
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<tr>
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<td>.7</td>
<td>1.0</td>
<td>.8</td>
<td>1.6</td>
</tr>
<tr>
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<td>1.1</td>
<td>.2</td>
<td>1.8</td>
<td>.2</td>
</tr>
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<td>6</td>
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<td>1.4</td>
<td>1.2</td>
<td>1.4</td>
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<tr>
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<td>5.2</td>
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<td><strong>Total - 30.5</strong></td>
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<td><strong>Average - 2.96</strong></td>
<td><strong>Average - 3.05</strong></td>
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COMMENTARY.

Twenty-four cases of obstructive vascular disease have been treated by intermittent venous occlusion at a pressure of 60 mm.Hg. with two minute cycles. There were fifteen diagnosed thromboangiitis obliterans and nine arteriosclerosis. The outstanding clinical manifestation was intermittent claudication, twenty-two patients being affected. Fourteen complained of coldness, ten of rest pain, three of trophic pain, five had colour changes, three had ulceration, and two had frank gangrene.

Intermittent claudication was relieved in 17 out of 22 patients.
Coldness was relieved in 8 out of 14 patients.
Rest pain was relieved in 5 out of 10 patients.
Trophic pain was relieved in three patients.
Colour was improved in 3 out of 5 patients.
Ulceration was improved in all 3 patients.
Gangrene was improved in both patients.

Of fifteen patients suffering from thromboangiitis obliterans, three only did not improve. They had adequate treatment and the reason is not obvious.
obvious. Outstanding improvement was shown in the pain of intermittent claudication (12 of the 15 were considerably relieved), resting pain was relieved in half of the cases, and coldness in two-thirds. In one case with discolouration, ulceration, and trophic pain there was improvement of colour, healing of the ulcer and relief of pain.

Of nine patients suffering from arteriosclerosis obliterans, one only did not improve. However, the improvement in two other cases was so slight as to be doubtful. Intermittent claudication was relieved in five out of seven patients, coldness in four out of seven, colour improved in two out of four, and the condition of ulcer with gangrene improved in two patients.

From a consideration of the above results it is clear that there has been a general improvement as a result of intermittent venous occlusion. This is quoted above. It is observed that intermittent claudication is relieved in 77% of cases and rest pain in 50%. This is in keeping with the results of Kramer, but entirely contradictory to those of Brown and Arnott and those of Collens and Wilensky. Again, whereas/
obvious. Outstanding improvement was shown in the pain of intermittent claudication (12 of the 15 were considerably relieved), resting pain was relieved in half of the cases, and coldness in two-thirds. In one case with discolouration, ulceration, and trophic pain there was improvement of colour, healing of the ulcer and relief of pain.

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whereas Brown and Arnott attained 100% improvement in thrombo-angiitis obliterans and very much less improvement in cases of arteriosclerosis obliterans, in our series, improvement was only very slightly greater in the cases of thrombo-angiitis obliterans. Kramer has the third alternative a greater improvement in his cases of arteriosclerosis.

With regard to the skin temperature before and after treatment, we were unable to demonstrate any difference whatsoever. In a series of ten cases, all of whom showed marked clinical improvement. This is the direct opposite of the statements of Kramer, and conflicts with the suggestions and observations of Collens and Wilensky, and Arnott and Brown. But it is in agreement with the findings of Allen and McKechnie. The uniformity of the averages of temperature before and after treatment is striking. In oscillometric observations we are again at variance with Kramer and Collens and Wilensky. Our results, as in skin temperature, of oscillometric readings before and after treatment, are strikingly similar.

Conclusions.

1./
1. Intermittent venous occlusion is a valuable method of treatment in cases of obstructive vascular disease.

2. The beneficial effect on the clinical manifestation is general, though intermittent claudication would seem to be specially relieved.

3. The prognosis with this form of treatment is better in cases of thrombo-angitis obliterans.

4. Skin temperature and oscillometry were not increased in ten cases of obstructive vascular disease showing marked clinical improvement.
III. COMMENTARY.

Two chief factors emerge from a review of treatment of peripheral vascular disease. The first is the surprising progress which has been made in the last five or six years. The second is the surprising discrepancies in results.

Samuel and Silbert are convinced that intravenous chloride and citrate is the best method of treatment. Barker is the advocate of typhoid vaccine and fever therapy. Silbert's figures of 83% improvement in 524 cases of thrombo-angiitis obliterans treated by infusion therapy, and Barker's figures of 76% improvement in cases treated by typhoid vaccine brook no contradiction. Collens and Wilensky, on the other hand, and Arnott and Brown are strong advocates of intermittent venous occlusion and their figures are equally impressive. Pavaex, which has perhaps been most fully investigated and universally used in treatment appears to give more than good results. The very fact that pavaex and intermittent venous occlusion have been more widely used than the other methods of treatment is certainly in their favour, but at the same time the fact that all/
all clinicians are not prepared to adopt any one standard treatment demonstrate the lack of any one reliable method. The complete deduction is that ideal treatment is not one form of therapy but a skilled combination of several forms. Sound therapy is based on the complete understanding of the physiological principles upset in any disease and it is particularly in this respect that treatment of peripheral vascular disease is deficient. Measures to increase, to dilute the blood, or to alter the constitution of the blood comprise most medical measures adopted. In view of the small influence exerted by the vasomotor nerves on muscle blood flow it is difficult to understand the rationale of vaso-dilator drugs in cases suffering from intermittent claudication in any circumstances. On the other hand, vaso-dilatation may have real value in trophic conditions. In both cases it is utterly valueless in purely organic obstructive vascular disease. If, as seems likely, there is reduction in blood volume and increased concentration in some cases of obstructive vascular disease, then a combination of infusion therapy and pavaex or intermittent venous occlusion/
occlusion might be useful.

Though one cannot say which is absolutely the best form of treatment or which is the best form of treatment for any one disease or sign or symptom, it seems probable that thrombo-angiitis obliterans has in general a better response to treatment and perhaps particularly to treatment by intermittent venous occlusion. In our experience and in that of Arnott and Brown, Kramer, and Collens and Wilensky, this condition was particularly benefitted.

It must be pointed out that great confusion in assessing treatment has arisen through wrong diagnosis, through various forms of treatment being given at the same time, and through the use of elastic tests such as "the walking capacity" of the patient, the skin temperature of the patient, and the oscillometry of the patient. Especially is this so when, as is often the case, such tests are not carried out in standard environmental conditions.

We have mentioned the criterion suggested by us in utilising skin temperature and oscillometry as an index of improvement or regression in blood flow. With regard to the various form of therapy we/
we do not deny the value of rest and careful prophylaxis - care of the feet, avoidance of trauma, &c. We are in entire agreement with the restriction of tobacco and consider the evidence presented sufficiently damning to justify its complete withdrawal. With Roentgen Ray therapy the results are impressive though we cannot agree with the second of the theoretical explanations offered. There may be some truth in the suggestion of Philip and Tunich of the action of roentgen rays on the prevertebral ganglia. It is possible that irradiation in this region could stimulate the vaso-dilator fibres of the posterior roof and in certain cases increase blood flow.

Fever therapy, Papaverine, Acetyl B. Methyl Choline and Ethyl Alcohol, and such forms of treatment will obviously be of value in cases of obstructive vascular disease with a considerable nervous element. In such circumstances the abolition of vaso-motor tone would give a corresponding increase in blood flow. Vein ligation as a method of treatment has been proved a doubtful one/
one, and in the light of present knowledge is unphysiological. There may well be clinical improvement in treatment by hypertonic salt solution as there is considerable evidence that there is concentration and diminished volume of the blood. The value would seem to lie in the fact that 2-500 ccs. of fluid is run into the circulation every other day. Pavaex and intermittent venous occlusion have uniformly good clinical results and have in each case a sound physiological basis. Those methods are considered to be the most promising and most rational.

It seems certain that in purely organic obstructive disease Pavaex does increase the volume flow to the part. Skin temperature readings have shown an increase in three degrees centigrade in those circumstances. Detailed oscillometric readings are not available.

With regard to the effect of intermittent venous occlusion and blood flow, however, we are in doubt. Collens and Wilensky, Kramer, Arnott and Brown, and De Takats have all quoted increased skin temperatures of 1 to 2.5 degrees centigrade and increased/
increased oscillometric readings of an unspecified amount. Allen and McKechnie have offered a direct contradiction, and we concur with their opinion. We believe that increased utilisation of existing flow, and not increased flow, is the effect of intermittent venous occlusion and the cause of its beneficial results. It is our purpose to furnish evidence for this belief.
References.

LEWIS, T., & GRANT, R.T.: Heart, vol. 13, 1926.

COHNHEIM: "Untersuchunger ueber die embolischen Processe", Berlin 1897.


BIER: Virchow's Archives, vol. 147, p. 256-293 and p. 444-474, 1897.


VI. THE INVESTIGATION OF THE MODE OF ACTION OF INTERMITTENT VENOUS OCCLUSION.

The conviction has just been stated that intermittent venous occlusion is a most valuable method of treatment of peripheral vascular disease. This conviction is based on the results obtained, and on those of others. On the findings of Lewis and Grant on reactive hyperaemia, it has been assumed by most that the great improvement is due to increased blood flow. We have pointed out in our introductory section the criterion employed in the assessment of improvement of blood flow by most authors. The clinical signs and symptoms we cannot question, though we have emphasised the question of increased utilisation of existing circulation or diminished need. We have demonstrated the fallacy of utilising skin temperature and oscillometry as indicative of blood flow rate from time to time. We concluded that a sustained rise in skin temperature of at least three degrees centigrade over a period of at least one week was probably evidence of an increased blood flow. With regard to the oscillometer, we are more doubtful. It seems probable/
probable that with carefully controlled technique in oscillometry—investigations being always made by the same individual—a sustained increased of at least two large divisions may be taken as indicative of increased blood flow. We state this, however, with considerable misgiving.

We have as evidence of (i) increased flow, or (ii) increased utilisation of existing flow, our clinical findings and those of Collens and Wilensky, De Takats, etc. To settle the issue between the two possibilities, we investigated—

1. Skin temperature before and after treatment.
2. Oscillometric readings before and after treatment.

The results are shown in the tables below.
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<tr>
<th>Case</th>
<th>Maximum skin temperature before treatment</th>
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Total   531 564   581 585

Grand total 1095 Grand total 1166

Average 28.8 Average 30.7
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<td>0.1</td>
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<tr>
<td>17.</td>
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<tr>
<td>Average</td>
<td>1.135</td>
<td>1.17</td>
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</table>
Results.

1. Skin temperature in 19 cases of obliterative vascular disease investigated before and after treatment by intermittent venous occlusion shows an average rise of 2°C.

2. Oscillometry in 17 cases of obstructive vascular disease show no change whatsoever.

Commentary.

The obvious conclusion, as judged on our own standards, is that there has been no increase in blood flow in 19 cases of obstructive vascular disease treated by intermittent venous occlusion which have improved clinically as a result of treatment. There must logically, then, as a result of treatment, have been an increased utilisation of existing flow.

Conclusion.

Intermittent venous occlusion acts in obstructive vascular disease not by increasing blood flow to the part, but by improving utilisation of existing blood flow.

It was felt, however, that this conclusion required substantiation in view of our lack of faith in skin temperature and oscillometry. We decided to investigate/
investigate the immediate effect of intermittent venous occlusion on skin temperature. It must be pointed out that, though skin temperature in identical circumstances in normal and abnormal subjects may vary over at least a three degrees centigrade range from one occasion to another, it will stabilise and remain stable for an indefinite time during one investigation, and we have observed stability over a period of two hours both in the individual with vaso-motor tone intact and in the individual after vasodilatation. It is accordingly possible to utilise skin temperature in those circumstances as a criterion of blood flow to the part. As it is more difficult to attain stability with vaso-motor nerves intact we considered it advisable to carry out this investigation after the abolition of vaso-motor tone. This, as well as abolishing all possibility of nervous reflexes, gives a greater gradient between the temperature of the part and that of the environment.

The experiments carried out were as follows:

1. Effect of intermittent venous occlusion on skin temperature of the normal individual after vasodilatation.

2. Effect of intermittent venous occlusion on skin temperature of an obstructive vascular diseased individual/
individual after vaso-dilatation, (a) with between
gradient/skin and environment, and (b) without
gradient between skin and environment.

Technique.

The apparatus as described in Section 1. was
used. The thermocouples were attached to the palmar
aspect of the forefingers. Intermittent venous
occlusion was applied by a cuff round the upper part
of the limb in the exact fashion as that in which
it is utilised in treatment. The pressure used was
60 mm.Hg, and the cycle 2 minutes. The graphs are
appended below.
Results.

1. In the normal subject and the case of obstructive vascular disease with a gradient between internal and external temperatures there is, as a result of intermittent venous occlusion, a fall in temperature.

2. In the case of obstructive vascular disease without a gradient between internal and external temperatures there is no effect whatsoever on skin temperature.

Conclusion.

Intermittent venous occlusion at a pressure of 60 mm. Hg. and two minute cycles causes a reduction in blood flow to the skin in the normal subject and in the sufferer from obstructive vascular disease.

B. The effect of intermittent venous occlusion on muscle blood flow.

Methods of Investigation.

There are three possible methods of measuring blood flow to muscle - (i) Calorimetry. (ii) Plethysmographic. (iii) By thermo-couple.

The calorimetric method, while giving an accurate index of the blood flow to the skin relatively...
relatively neglects that of deeper structures. Secondly, it is a cumbersome method, and on those grounds it is not considered suitable. The plethysmographic method is excellent though requiring skilled technique. However, because it employs intermittent venous occlusion as part of the method it is excluded from use in the investigation of the effect of venous occlusion on muscle blood flow. We therefore had recourse to the thermo-couple method.

Criterion of the Thermo-couple Method.

This method may be criticised in two ways, -

1. There is a delay in the galvanometer recording of changes in the region of thermo-couple.

2. As the gradient of temperature between blood temperature and muscle temperature is small, it requires relatively enormous changes in blood volume in the viscosity of the thermo-couple to bring about relatively small galvanometer recordings.

Apparatus.

(Only a brief outline of the apparatus devised will be given.

It was necessary for the above reasons to be able to measure very minute changes in temperature. To do so we employed a galvanometer which was capable of/
of recording to $1/150^\circ C$. As the cold junction employed was again melting ice and as the temperature of muscle is in the region of $35^\circ C$, it was necessary to use a device to balance the difference in temperature of muscle and cold junction at the start - the reason being that this sensitive galvanometer would only read $31^\circ C$ on either side of zero. A potentiometer was used. A diagrammatic representation of the device is shown below, together with one of the actual circuits employed. By alternating the ratio of the two resistances it is possible to balance the E.M.F. generated by the thermo-couple in the muscle. When this is done any change in the temperature in the region of the thermo-couple is recorded on the galvanometer, which, as has been stated, and was established as a result of calibration, is sensitive to the extent of $1/150$ degree centigrade.
THE CONTROL OF MUSCLE ARTERIOLES.

It was now necessary to investigate the control of muscle arterioles. It has been generally accepted, as has been stated, that the metabolic factor is pre-eminent, the nervous factor playing a minor part in this control. Most observers seem to be agreed that the effect of vaso-constrictor nerves on muscle vessels is slight. That there is a nervous factor was demonstrated by Kuntz, Sadler 1869, Gaskell 1876. Nevertheless Vulpian, 1875, obtained constriction by stimulating the sciatic nerve and Grutzner and Heidenhaim (1877) by stimulating the abdominal sympathetic. Grutzner, Heidenhaim and Gaskell in 1878 found there was marked vascular dilatation in the extensor muscles of the thigh when the abdominal sympathetic was cut and this has been confirmed by Spalbetta and Consiglio (1897) and plethysmographically by Bayliss and Hartmann, Blatz and Kulborn (1919). However, the whole subject of sympathetic control of muscle arterioles is still in need of clarification.

The Investigation of the Control of Muscle Arterioles.

From/
From our particular point of view it was necessary to satisfy ourselves, if possible, of the relative importance of the two factors (i) metabolic, and (ii) nervous. The following investigation was therefore carried out:

1. Estimation of change in muscle temperature in exercise of the muscle.

2. Estimation of change in muscle temperature as the result of direct faradic stimulation of the distal end of the cut sympathetic chain.

Method.

In each case we utilised the thermo-couple method outlined above. The exercise was attained by an isometric muscular contraction as it was our experience that movement of the muscle needle caused a deflection of the galvanometer and falsified results.

Direct faradic stimulation of the distal end of the cut sympathetic chain was investigated by the courtesy of Mr Norman Dott and Sir John Fraser. We had the privilege of carrying out our investigations in their theatres with their co-operation and the benefit of their skilled technique. The duration of stimulation and the duration of contraction was in each/
each case twenty seconds. The results are shown below in graphic form.

![Graph showing temperature change](image1)

**Results.**

There was a fall in temperature of 2/7 degrees centigrade.

![Graph showing temperature change](image2)
Result.

There was a rise in temperature of nearly two degrees centigrade.

Commentary.

On six occasions we carried out direct faradic stimulation of the distal end of the cut sympathetic chain, investigating on two occasions the effect on the upper limb of stimulation of the central region, and on four occasions the effect on the lower limb of stimulation on the lumbar region. On all occasions we obtained a vaso-constriction. The result shown was outstandingly the most marked response obtained. In view of the fact that the change in temperature in this case was only 1/7 of that obtained by isometric contraction sustained for the same duration as nerve stimulation, we felt satisfied that the metabolic factor had a much greater effect than the nervous in the control of the muscle arterioles. It must also be pointed out that the direct stimulation of the nerve trunk for twenty seconds (the time of stimulation) is relatively a much greater stimulus than a corresponding
tering-period of isometric muscle contraction.

**Conclusion.**

Though muscle arterioles are affected by both nervous and metabolic factors, the control is chiefly metabolic, i.e. muscle blood flow is largely dependent on the metabolic factor.

**THE EXPERIMENTS CARRIED OUT.**

**Introduction:** In view of the fact that muscle arterioles are supplied by vaso-motor nerves it was considered essential to abolish vaso-motor tone. This was done, as in the case of the skin vessels, by the method of Landis and Gibbon. The actual technique adopted was to introduce the muscle thermo-couple, and attach a skin thermo-couple to the digit of the limb, the muscle of which was to be investigated. The skin thermo-couple gave an index of the time of vaso-dilatation. A rise in muscle temperature accompanying the rise in skin temperature was anticipated. Having observed this, it was our intention to wait for stability of muscle temperature and then apply intermittent venous occlusion and ascertain the effect. As will be presently demonstrated, we were not to attain this as/
as easily as had been anticipated.

The photographs demonstrate (i) the muscle thermo-couple; (ii) the experimental technique.
Section 1.

The Record of Change in Muscle Temperature during Vasodilatation induced by the method of Landis and Gibbon.

A record was taken - 1. In forearm muscle.
2. In pectoral muscle.

during vasodilatation induced by the method of Landis and Gibbon.
Results.

1. A marked rise of 1.3° C. in forearm muscle.
2. No rise in pectoral muscle.

Conclusion.

As we have no reason to assume that there should be a different nerve supply to the pectoral muscle arterioles from that of the forearm muscle arterioles, we concluded that some other factor must come into play to account for the great discrepancy in the muscle readings in vaso-dilatation.

Section II.

The Effect of a Tourniquet applied at the Wrist on the Muscle Temperature of the Forearm.

We had noted that the change in muscle temperature occurred after warming of the skin of the finger during vaso-dilatation. This fact, allied with the above discovery led us to apply arterial occlusion distal to the level at which the muscle temperature was being recorded and then to induce vaso-dilatation. The progress of dilatation was followed by a thermo-couple on the digit of the limb under investigation and on the digit of the corresponding/
The corresponding limb of the other side. The graph
demonstrates the result.

Results.

1. No rise in muscle temperature when
tourniquet is applied to the wrist.

II. Release of tourniquet gives a fall in
muscle temperature and followed by a
marked rise.

Conclusions.

1. The rise in muscle temperature in the forearm
muscle which we had first thought to be due to
release of vaso-constrictor tonus is actually
due to return of warm blood from the hand.

II./
II. The cooling effect of cold blood from the hand on the muscle is also seen.

III. We were not able to demonstrate any rise in temperature either in forearm or pectoral muscle which might be attributed to release of vaso-motor tone.

IV. This is support for our contention that the control exerted by vaso-motor nerves on muscle arterioles is slight.

Section III.

The Effect of Intermittent Venous Occlusion on Muscle Temperature

Technique: Being aware, therefore, of the above facts we were now in a position to investigate the effect of intermittent venous occlusion on muscle blood flow.

It was not necessary to apply a tourniquet to the wrist during the investigation as after considerable experience in technique we were able to attain and keep complete stability of muscle temperature. In those circumstances then we applied intermittent venous occlusion at a pressure of 60 mm.Hg. and using a two minute cycle, the cuff being applied proximally/
proximally to the muscle which was being investigated. This was done in normal subjects and in cases of obstructive vascular disease. The results are shown graphically.
Results.

1. In the normal subject and in the case of obstructive vascular disease there is, as a result of intermittent venous occlusion at a pressure of 60 mm. Hg. in two minute cycle, a fall in muscle temperature.

II. It is seen that at release there is a reactive hyperaemia.

III. This reactive hyperaemia is not sufficient to bring the temperature back to the level at which it was at the time of onset of occlusion.

Conclusion.

The effect of intermittent venous occlusion at a pressure of 60 mm. Hg. and at two minute cycles is to produce a fall in muscle temperature, i.e. there is a reduction in the total blood flow through muscle in unit time during intermittent venous occlusion relative to the total blood flow through muscle in normal circumstances.

Section IV:

The question of Arterial Reactive Hyperaemia.

A further possibility was envisaged, viz. that
in the sufferer from obstructive vascular disease a pressure of 60 mm. Hg. might induce not a venous but an arterial reactive hyperaemia.

It seemed possible that arterial reactive hyperaemia might give an increased blood flow to the muscle, and though in our investigation of six cases of obstructive vascular disease with a pressure of 60 mm. Hg. there had been a fall in muscle temperature in all six, still it might have been that in those six a pressure of 60 mm. Hg. did not give an arterial reactive hyperaemia.

The effect of intermittent arterial occlusion on the muscle temperature of the normal individual was investigated, it being considered inadvisable to apply arterial occlusion to a known case of arterial vascular disease.

The Effect of Intermittent Arterial Reactive Hyperaemia.

Technique: Stability of muscle temperature was attained as has been described above. The blood pressure of the subject being known, intermittent arterial occlusion was applied to the limb under observation, proximal to the site of the thermocouple.
couple. The result is shown graphically.

Results:

1. Intermittent arterial occlusion in the normal subject has produced a fall in muscle temperature.

II. Reactive hyperaemia is much more marked than venous reactive hyperaemia.

Conclusions:

1. Intermittent arterial occlusion in the normal individual though producing a marked reactive hyperaemia, has the effect of causing a fall in muscle temperature, i.e. there is a reduction in the total blood flow through the muscle in unit time/
time during intermittent arterial occlusion relative to the total blood flow through muscle in normal circumstances.

II. Even if an intermittent occluding pressure of 60 mm. Hg. should give rise to an arterial reactive hyperaemia in cases of obstructive vascular disease, the effect will still be to produce a reduction in blood flow through the part.
References.


VII. Commentary on above Results: It has been established as a result of our investigation that intermittent venous occlusion reduced the blood flow through skin and muscle in unit time and the normal and abnormal subjects. We have further stated, in view of our experience and that of others, that intermittent venous occlusion is beneficial in cases of obstructive vascular disease.

We are desirous of offering some suggestions as to how this benefit is attained. Collens and Wilensky observed that maximum clinical results were attained with an occluding pressure of 30 - 60. In view of the findings of Lewis and Grant on reactive hyperaemia this seemed illogical. Lewis and Grant demonstrated that the higher the occluding pressure the greater the resulting hyperaemia. Surely then greater clinical improvement is to be expected with an occluding pressure of 90, than that attained with a pressure of 60. Lewis and Grant further observed that at pressures at or below 30 mm.Hg. there was no reactive hyperaemia.

The explanation of reactive hyperaemia suggested by Landis and Gibbon was that the accumulation of/
of tissue metabolites during occlusion of circulation brought about a direct vaso-dilatation of the arterioles in the vicinity and with the release of obstruction there was, therefore, a greatly increased blood flow to the part.

It is known that the pressure at the arteriolar end of the capillary is approximately 30 mm. Hg. and that at the venous end 6-10 mm. Hg. The osmotic pressure of the blood is 12 mm. Hg. Further, it is generally accepted that the fluid and ionic interchange through the capillary wall, though not following the physical and chemical laws of a semi-permeable membrane absolutely, does so to a large extent. Fluid and ionic interchange then is dependent on the balance between capillary pressure and osmotic pressure. A fall in capillary arteriolar pressure will reduce the volume of fluid passing out and a rise in venous capillary pressure will increase the volume of fluid passing out. Increased osmotic pressure of the tissue spaces and of the cells or decreased blood osmotic pressure will increase the fluid passage from blood to exterior and increased osmotic pressure of blood or reduced osmotic pressure of the tissues will increase the fluid passage from tissues.
and cells to blood.

Any upset then of osmotic pressure and capillary pressure will necessarily cause upset in interchange of vital ions, organic and inorganic, between blood and tissues.

During activity it has been shown that the water content of frog’s muscle rises from 0.74 to 1.4, i.e. it is approximately doubled. The increased water content is the result of metabolic needs of that muscle. During activity there is the breakdown in muscle of large molecules to smaller molecules. That is, there is a greatly increased osmotic pressure developed and more water is taken up. The extraordinary requirement is shown by the fact that water content is almost doubled after average activity in normal muscle.

We would suggest then that reactive hyperaemia can well be explained as a process of repayment of osmotic pressure debt. During occlusion of the circulation the tissue cells continue to live and follow normal katabolic processes. There is therefore an increased osmotic pressure in the tissues.
tissues and the requirement of water and possibly other essential ions may be met only by the supply in the blood confined distal to the occlusion. This supply is limited and in the circumstances is bound to be deficient. The whole part, therefore, develops an osmotic pressure debt. With the release of the obstruction not only will the blood be impelled by the force behind, but it will be actively sucked in by this osmotic pressure.

In obstructive vascular disease then is it not probable that there is all the time a potential osmotic debt to the tissues distal to the obstruction? If this theory should be correct, it would explain the numerous observations on concentration of blood and diminution in blood volume in thromboangiitis obliterans and obstructive vascular disease. It would probably account for the invincible belief of Silbert and Samuels in the efficacy of their treatment of obstructive vascular disease by intravenous salt solution. They gave 500 cc. of fluid every alternate day till improvement was attained.

Approaching the subject from the angle of capillary pressure a reduction in arteriolar capillary/
Capillary pressure would automatically increase the osmotic pressure of the blood and therefore reduce fluid extracted by the tissues. This therefore would increase the osmotic pressure debt of the tissues. The raising of venous pressure would, however, increase filtration pressure and increase the supply of fluid to the tissues.

If we accept the above explanation of reactive hyperaemia then any pressure applied proximally which will slow the circulation will give rise to a certain degree of osmotic pressure debt and therefore to a certain degree of reactive hyperaemia with its release. As the pressure at the arteriolar end of the capillaries is 30, the presumption is that any pressure above 30 mm. Hg. will slow the circulation and at its release reactive hyperaemia will ensue.

This is the exact findings of Landis and Gibbon. Furthermore, and obviously, the higher the occluding pressure the greater the slowing and the greater the debt.

Therefore better clinical results would be attained by lower pressure and this is the very finding of Collens and Wilensky.
In obstructive vascular disease the probability is that arteriolar capillary pressure is reduced as a result of the obstruction and therefore filtration pressure reduced, and not only is there diminished supply but also there is an increased difficulty in attaining existing supply.

The solution, therefore, is to apply an occluding pressure which will raise the filtration pressure to its maximum without diminishing the total blood flow through the part in that unit time. This pressure is on the basis of Lewis and Grant's work not more than 30 mm Hg. It is equally obvious that a continuous pressure will be more beneficial than an intermittent pressure.

We have shown now by studies on (1) skin temperature and oscillometry and (2) on skin blood flow and muscle blood flow that intermittent venous occlusion acts by promoting greater utilisation of existing blood flow and by so doing gives clinical improvement. On the basis of the work by Landis already referred to, whereby he showed that in a rigid tube, by negative pressure applied distally the flow through the tube could be increased at least one and a half times, and in the human subject, skin temperature raised more than three degrees centigrade by negative pressure, and on the clinical results of/
of Pavaex therapy we believe that Pavaex therapy acts by increasing blood flow to the part.

A combination of increased utilisation and increased flow will give better results than either alone.

An increased volume would still further enhance the tissue nutrition.

Clinically, therefore, -

1. Continuous venous occlusion at not more than 30 mm.Hg.

2. Negative pressure environment, and

3. Intravenous saline would be expected to give the best response in obstructive vascular disease.
VIII. CLINICAL APPLICATION OF RESULTS.

Outline of Treatment Suggested for Cases of Obstructive Vascular Disease.

On the basis of what we have said we suggest the following treatment in cases of obstructive vascular disease.

1. By plethysmographic or thermo-couple method establish the occluding pressure, which will not give a slowing of the circulation.

2. With this occluding pressure as a standard, apply a cycle as follows:
   
   (a) 2 minutes negative pressure environment, using pavaex technique to the limb.

   (b) With atmospheric pressure apply occlusion of above standard for two minutes.

   (c) Limbs in normal circumstances, two minutes.

It is suggested that this be carried out for two-four hours daily; allied to this occasional intravenous normal saline might be beneficial.

This treatment would be combined with exclusion of tobacco and general prophylactic measures.

IX. Final Conclusions.

1. A review has been given of the historical development/
development of the medical treatment of obstructive vascular disease.

2. An evaluation of different forms of therapy has been considered.

3. In an investigation on the most recent form of treatment it has been established that though the basis on which this treatment rests is sound the explanation of the mode of action is not sound.

4. An explanation of the mode of action is offered.

5. Suggestions for a better method of treatment of obstructive vascular disease have been advanced.