No explanation is given as to why the 14% with no predisposition should break down with only a mild aggravation, but the reason is probably either that there was an undetected, perhaps constitutional, predisposition, or that there were contributory factors, such as worries at home, which sapped the vitality. It would be interesting to investigate how far contemporary worries of this type contribute to the so-called "war neuroses." Our experience is that it is considerable, particularly in the way of "separation anxiety," men being worried about their families being bombed, their wives and other men, financial matters, or illness at home.

A further investigation into the amount of aggravation as related to (i) constitutional and (ii) psychological predisposition is of interest. In a group of 62 patients of both types who broke down with only a mild aggravation the proportion of constitutional to psychological was 3 to 1—that is to say, the constitutional patient as a whole breaks down sooner with a milder degree of aggravation than the psychological, who appears to stand up to it better, presumably because he has more courage. It takes less aggravation to affect a constitutional case than an acquired one, and the former subject cracks up more easily.

Previous Adaptation to Life

A further investigation was made into the important question of the patient's adaptation to life before he entered the Army. So many patients—for instance, persons of *limited adaptation*—got on perfectly well in their routine civilian life, but broke down when removed into strange surroundings of Army life, while others had always been misfits. How far could one anticipate a breakdown by reference to the individual's earlier objective history, which is so often accepted as significant of a neurotic tendency?

The following were the forms of adaptation for the first 100 patients:

TABLE III

	Ill Adapted (I.A.)	Limited Adaptation (L.A.)	Well Adapted (W.A.)
Physical (e.g., habitus, endocrine, etc.) ..	17	25	58
Mental (e.g., introversion, cycloid, etc.) ..	38	37	25
School	15	26	59
Work	8	31	61
Social	15	46	39
Army	31	28	41
Total	124	193	283

The following points may be noted:

1. Not by any means all of these psychoneurotics got on badly in the Army: 41% were well adapted to Army life, and many wished to remain in the Service; only 31% were ill adapted.

2. As regards civilian life, it was surprising to find how many were well adapted to school life and to work. 59% were well adapted to school life, and only 15% were ill adapted; while as many as 61% were well adapted and only 13% ill adapted to their work. School life and work together averaged 60% W.A., 28.5% L.A., and only 11.5% I.A.

3. On the other hand, the largest group of those ill adapted in civilian life were those *mentally* ill adapted (38% I.A., with 37% L.A. and only 25% W.A.), usually with constitutional peculiarities, such as the inferiors or schizoid.

4. In social life only 39% were well adapted; 46% were limited in their adaptation and 15% ill adapted. Mental and social together average only 32% W.A., with 41.5% L.A. and 26.5% I.A.

The conclusion to be drawn seems to be that in his *objective* adaptation to life and work the psychoneurotic

patient shows up better (60%) than in his more subjective relations, such as mental and social adaptation (32%). Objective adaptation is therefore not a good criterion by which to judge whether a man is psychoneurotic (although it is of course of the greatest importance in judging mental deficiency), whereas mental and social adaptation are more dependable. A man may be a good and efficient worker while suffering from severe neurosis. A neurosis is not a failure in biological adaptation: the neurotic is one who cannot adapt himself to himself, and therefore to others.

As regards *physical* adaptation, 58% were well adapted and only 17% ill adapted, 25% being of limited adaptation. So far as it goes, this refutes the Adlerian view that organ inferiority is the exclusive origin of the neuroses.

(This paper will be concluded in our next issue.)

INTRAVENOUS SERUM IN THE TREATMENT OF PERIPHERAL VASCULAR DISEASE

BY

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One of the chief aims in the treatment of peripheral vascular disease is to aid the development of an adequate collateral circulation in the affected limbs. Good results have been obtained with passive vascular exercises by the Buerger method, alternating suction and compression by the pavaex boot, or intermittent venous occlusion, and it has been shown (Herrman, 1936) that an adequate collateral circulation can be re-established after all the major arterial pathways to a limb have been obliterated.

It has also been claimed that procedures which increase the blood volume stimulate the formation of a collateral circulation. Koga (1913) and Silbert *et al.* (1930) observed that the blood volume in patients with thrombo-angiitis obliterans was decreased. Koga (1913) gave saline or Ringer's solution intravenously, and reported striking improvement in 13 patients, with an increase in the peripheral circulation and diminution in both rest pain and pain on exercise. Silbert (1926, 1930) and Samuels (1936) have recorded good results following the intravenous injection of 300 c.cm. of 2 to 5% saline; the oscillometric readings in the legs increased, the legs became warmer, and trophic changes tended to clear up. The injections were given quickly—300 c.cm. in ten minutes—three times a week at first, and later at weekly intervals. The beneficial results of saline therapy have been confirmed repeatedly (Samuels, 1936).

The effects of intravenous saline on the peripheral circulation are presumably mechanical, produced by the immediate increase in blood volume. This increase is a transient one, lasting several hours only (Gilligan *et al.*, 1938), and it seemed probable, therefore, that if the blood volume could be increased for a longer period of time the effect on the peripheral circulation would be greater. For this reason the effects of increasing the blood volume by giving human serum intravenously were studied.

The serum used was pooled liquid serum, obtained from the North-East London Blood Supply Depot. It has a protein content of 7% and can be safely given to patients of any blood group without cross-matching. The amount

transfused each time was 800 c.cm. (two bottles), and the rate varied between 5 and 15 c.cm. a minute. Most of the transfusions were given without any untoward reactions, although several patients complained of transient lumbar pain during the early part of the procedure. Rigors were encountered in 15 out of 50 transfusions. The possible influence of these reactions in the interpretation of the results is discussed later.

Effects on the Circulation

The effects of the serum transfusion on the circulation have been studied in several ways.

1. *Changes in Blood Volume.*—These have been followed by means of frequent determinations of the haemoglobin and packed cell volume (haematocrit). The changes in blood volume following serum transfusion in normal patients as well as in those with peripheral vascular disease will be described more fully in a subsequent communication by Jordan and myself: the results in the patients reported here are given in Table I. After an initial increase, equal to the amount of

TABLE I.—*Changes in Haemoglobin (Hb) and Haematocrit (Hc) following Intravenous Serum*

Case		On Day of Transfusion		Days following Transfusion			
		Before	Immediately After	1	2	3	4
1	Hb	104	79	93	100	100	
	Hc	50	42	—	48.5	—	
2	Hb	97	90	90	99		
	Hc	48	43.5	42.5	44.5		
4	Hb	107	94	96	92	95	107
	Hc	51	45	44.5	44.5	44	47
5	Hb	98	84	91	90	93	94
	Hc	49.5	39.5	41.5	41.5	43.5	43.5
6	Hb	112	101	101	104	112	
	Hc	55	46	46	50	53	
8	Hb	114	102	93	95	103	110
	Hc	50	43.5	40	44	46	45.5
9	Hb	96	72	83	93		
	Hc	91	87	87	95		

800 c.cm. of serum given in all cases except Case 1, which received 1,200 c.cm. All estimations on venous blood: Hb in % Haldane, Hc in %.

serum injected, the blood volume gradually returns to normal over a period of from two to three days, although some patients appear to remove the added serum in twenty-four hours and in others it is retained for five days. The fate of the transfused protein is discussed later.

2. *Changes in the General Circulation.*—If the transfusion is given slowly there is usually no change in blood pressure, the

FIG. 1.—A: Case 16. Normal blood vessels, showing increased oscillometric readings after 800 c.cm. serum, returning to normal after 24 hours. B: Case 9. Arteriosclerosis. Initial oscillometric readings abnormally low; increased after serum, and have not returned to normal after twenty-four hours. ●—● Before serum. ○—○ After serum. ○---○ 24 hours after serum.

pulse rate shows a transient increase of from 8 to 16 a minute, and there is no increase in venous pressure as judged by the degree of filling of the neck veins. These results agree with the findings of Altschule and Gilligan (1938).

3. *Oscillometric Readings.*—Measurement of the amplitude of the arterial pulsations in a limb is possible with the Pachon oscillometer, and measurements have been made before and at intervals after the transfusion. In patients with the distal type of obliterative arteritis, and with normal pulsations in the dorsalis pedis and posterior tibial vessels, increased oscillometric readings have been obtained at the calf and ankle immediately after the transfusion. This increase disappears after a period of from six to thirty-six hours. Patients with obliteration of the larger arteries and with small or absent initial oscillometric readings have shown only a slight increase after transfusion (Fig. 1).

4. *Changes in Skin Temperature.*—It has been difficult to measure changes in skin temperature occurring from day to day, owing to the many variable factors which it has been impossible to control, but most of the patients with peripheral vascular disease and cold limbs have shown clinical increase in warmth lasting for several days. The immediate changes in skin temperature following transfusion have been studied by means of a thermo-electric thermometer. If the legs are exposed in a cool room until equilibrium has been reached the injection of serum produces no significant change in skin temperature. When, however, the legs are warm the injection of serum produces a gradual rise in temperature of from 1° to 7° C. in one to two hours (see Table II).

TABLE II

Case	Maximum Oscillometric Readings			Temperature of Warm Limb (°C.)		Reflex Vasodilatation Maximum Temperature (°C.)	
	Before Serum	After Serum	24 hrs. After	Before Serum	After Serum	Before	After
1	1.75	2.5	1.5	—	—	31.6	33.2
3	3.25	6	4	34	36.8	34.9	36.4
4	2	4.5	—	—	—	(a) 33	36.4 (a) Rt. 1st toe
						(b) 24.7	34.4 (b) Lt. 1st toe
5	(a) 0	0	0	26.8	31	19	20 (a) Calf
	(b) 6.5	8.5	7	—	—	—	(b) Thigh
6	0	0	0	—	—	—	—
7	0	0	0	—	—	—	—
8	0	0	0	31.8	36	—	—
9	(a) 3	10	7	—	—	—	(a) Rt. calf
	(b) 2.5	4	5	—	—	—	(b) Rt. ankle
10	0.25	0.25	0.25	31.6	33.6	22	22
11	(a) 0	0	0	26	33	19.2	20 (a) Ankle
	(b) 2	4.5	2.5	—	—	—	(b) Thigh
12	0.25	1.75	0.75	27.4	33.8	—	—
13	7.5	9	7	—	—	28.8	31.2
14	—	—	—	—	—	(a) 33.2	34.8 (a) Rt. 1st toe
						(b) 19.4	30.6 (b) Lt. 1st toe
15	—	—	—	—	—	17	31.9
16	4.5	7.5	5	31	32	—	—

5. *Response to Reflex Vasodilatation.*—It has been claimed that a more accurate impression of the state of the peripheral circulation in a limb may be gained by measuring the maximum degree of vasodilatation of which the limb vessels are capable. This may be produced by removing vasomotor tone by spinal anaesthesia, by local nerve block, or, reflexly, by heating the arms or trunk. This reflex method of producing vasodilatation in the legs by warming the arms and trunk has been used in the present investigation; the degree of vasodilatation has been estimated by measuring the changes in skin temperature with the thermo-electric thermometer. The response to reflex vasodilatation has been measured before and at intervals after the transfusion of serum (Table II), and the results in typical cases are shown in Figs. 2 and 3. In limbs giving a normal response (rise to at least 32° C.) before serum, the rise in skin temperature immediately after serum has been consistently greater by 1.5° to 3.4° C. (Table II). Failure to produce reflex vasodilatation in the vessels of the legs may be due either to a high degree of vasomotor tone or to organic arterial disease. Two patients with a high degree of vasomotor tone, with cold feet and intermittent claudication, were encountered. In one (Case 15) there was no rise in temperature of any of the toes before serum, even with prolonged heating of the trunk, whereas after serum a prompt normal rise in temperature was obtained. In the other (Case 14) the response of the right foot before serum was normal (rise to 32.4° C.), but the left foot remained cold throughout. After serum, the right foot gave a greater response (rise to 34.8° C.), and the left foot after a longer period of time showed a rise in temperature to 30.6° C. (Fig. 3). In

Case 4 the maximum vasodilatation which could be produced before serum was only enough to raise the temperature of the skin of the left toe to 24.7°C . There was a progressive increase in the response after each transfusion, and after two transfusions

FIG. 2.—Case 4. Skin temperature after reflex vasodilatation, showing greater response immediately after serum transfusion. ●—● Before serum. ○—○ After serum.

FIG. 3.—Case 14. Skin temperatures after reflex vasodilatation. Right first toe (R.I.) shows normal initial response, with greater response after serum. Left first toe (L.I.) shows poor initial response, with greater response after serum.

FIG. 4.—Case 4. Initial response of left first toe to reflex vasodilatation (19/9/41) characteristic of moderate arterial disease. Progressive increase in response after two transfusions of 800 c.cm. serum on 21/9/41 and 28/9/41.

Clinical Results

Effect on the Warmth of the Skin.—An increase in warmth of those limbs with impaired blood supply has been a striking result of serum transfusion, and this has been associated with a diminution of postural changes in skin colour. The change was most pronounced in Case 9, and was associated with rapid healing of the ulcer of the foot. Cases 1 and 2, with a distal type of obliterative arteritis and gangrene of fingers, also showed striking improvement. In both of these patients the hands at room temperature were cold and cyanosed before transfusion. After transfusion the hands remained warm and red, and there was rapid separation of the blackened tips of the fingers. Two patients (Cases 5 and 11) with arteriosclerosis and absent pulsations in the dorsalis pedis and posterior tibial vessels and no oscillometric pulsations below the knee showed a similar improvement. In all, 7 out of 10 patients with cold limbs had improvement in the warmth of the limb; in the remaining 3 there was very little increase in warmth.

Rest Pain.—Eight patients had pain in the feet, which persisted during rest in bed. All were relieved of pain; in 6 it was complete after the first transfusion, and in the remaining 2 entire relief of pain was obtained after three transfusions.

Intermittent Claudication.—This was a prominent symptom in 6 patients (Cases 6, 8, 10, 12, 14, and 15). No. 8 lost his pain completely after the first transfusion; No. 12, who had failed to improve after two months of intermittent venous occlusion, more than doubled the distance he could walk before the onset of pain; and Cases 14 and 15 were considerably improved. Cases 6 and 10 showed no improvement after serum transfusions.

Raynaud's Syndrome.—Three cases were treated. Cases 1 and 2 were greatly improved, although Case 1 relapsed three weeks after transfusions were discontinued. Case 3 responded well to reflex vasodilatation immediately after transfusion but did not improve, the hands and feet on the following day still being cold and blue.

Ulcers Associated with Gangrene.—Pre-gangrenous colour changes in the skin were observed in 4 cases (Cases 4, 5, 8, and 10). All were definitely improved after two transfusions. Actual gangrene was present in 7 cases (Cases 1, 2, 6, 7, 9, 11, and 13), two in the hands and five in the toes or feet. The most striking improvement occurred in Cases 1 and 2, and was associated with a considerable increase in the temperature of the hands, the gangrenous tips separating rapidly and the fingers healing. Case 9, with a non-healing ulcer of the foot following amputation of the fifth right toe for gangrene, also improved rapidly. After the first transfusion the ulcer stopped discharging, and it subsequently became satisfactorily epithelized. Case 11, with gangrene of the toe, rest pain, and severe hyperaesthesia of the feet, lost both pain and hyperaesthesia after the first transfusion, and after one month of treatment the feet were warm and the gangrenous tip had separated. Case 13, with a perforating ulcer of the sole of the foot and diabetes, also improved, but here the effect of rest in bed and removal of the thick skin around the ulcer was probably the more important factor in healing. All of the 6 patients with ulcers of the limbs associated with chronic arterial disease recovered after from one to three transfusions. Another patient (Case 16), who had a deep non-healing ulcer of the leg of ten months' duration following a crush injury, was given weekly transfusions of serum. There was a pronounced increase in the oscillometric readings immediately after each transfusion (Fig. 1); the ulcer became cleaner and shallower, but after one month of treatment it was still not quite healed.

Discussion

In assessing the results of serum therapy reported in this paper it is important to determine how long the transfused serum remains in the circulation. In the absence of direct measurements of blood volume in man, indirect observations on changes in blood volume, and animal experiments where direct measurements are made, may be helpful. Freeman and Wallace (1938) measured the blood volume in dogs before, directly after, and twenty-four hours after transfusion of serum. They found that there was an immediate increase in blood volume corresponding to the amount

a normal response was obtained (rise to 34.4°C) (Fig. 4). In those patients whose blood vessels are incapable of dilating because of organic disease, the administration of serum could not be expected to produce any change, and none was observed. Cases 5, 10, and 11 belong to this group.

injected, but that twenty-four hours later the blood volume was almost back to normal, whether serum or saline was used. Similar results in the rabbit were reported by Scimone (1940). In animals, therefore, some mechanism exists whereby transfused serum, both protein and fluid, is removed very rapidly from the circulation. Observations on the present series and on normal subjects—which will be reported in greater detail in the further communication already mentioned—using the haemoglobin and haematocrit as a gauge of changes in blood volume, show that in most cases restoration of blood volume after transfusion of 800 c.cm. of serum takes place in from two to three days, although occasionally, as in animals, it may be complete in twenty-four hours. Similar results have been obtained by Hill, McMichael, and Sharpey-Schafer (1940) and by Harper *et al.* (1941).

The fate of the injected protein is interesting. None escapes as protein in the urine, and concentration of the blood to its original volume produces no increase in the plasma protein percentage, so that the added protein must be removed from the circulation. The ultimate fate of the transfused protein is still uncertain, but there is evidence from animal experiment that it may be utilized in body metabolism (Holman, Mahoney, and Whipple, 1934) or stored as unchanged protein or in the form of large aggregates of amino-acids (Howland and Hawkins, 1938).

If the serum is administered slowly the cardiovascular system adjusts itself to the increased blood volume readily. There is no increase of venous pressure, and in most cases the blood pressure shows no significant change. The extra fluid is presumably accommodated in the peripheral vascular bed by opening up new vascular channels. This mechanism should encourage the formation of a collateral circulation when the arteries are occluded, and would account for the promising results obtained in some of the cases here reported. The studies on skin temperature support this view. The greater rise in temperature with reflex vasodilatation after serum transfusion means an increased blood flow through the skin vessels, produced by the opening up of new vessels.

The oscillometric studies made on these patients have shown that in some of those with the distal type of obliterative arteritis an increased amplitude of arterial pulsation is produced by serum transfusion, and this alone suggests increased blood flow. Clinical improvement, however, was often observed when there was little or no change in oscillometric readings.

This work was started with the assumption that the action of serum would be largely a mechanical one, and the experimental evidence supports this view. Some of the transfusions caused rigors or a rise in temperature to 100–101° F. without rigor, and so it seemed possible that the beneficial results might have been due to the injection of small amounts of a foreign protein produced by the denaturing of serum proteins on storing. Injection of T.A.B. and other foreign protein has been used in the treatment of obliterative arterial disease with good results (Barker, 1931), but in the present series there has been no direct correlation between reactions and clinical improvement. When a rigor did occur, however, the additional vasodilatation may have been helpful in aiding the healing of ulcers or the separation of gangrenous areas.

The clinical results in this small group of patients with chronic obliterative arterial disease have been encouraging. Following the transfusion of serum the peripheral circulation in the affected limbs has been improved, as shown by the disappearance of rest pain, increased warmth of the foot, and rapid healing of ulcers and gangrenous areas. The use of intravenous serum would therefore seem worthy

of extended trial in patients with incipient or developed gangrene of the extremities due to chronic arterial disease. The results in patients with intermittent claudication have been variable, some having been considerably improved and others showing no change. On the whole, the results are no better than have been obtained with hypertonic saline or intermittent venous occlusion, but when these fail it seems that in some cases serum is successful. For simple ulcers and non-healing wounds in normal limbs, it seems likely that the increased peripheral circulation following serum is of value. If the injected protein is stored or incorporated in the tissues, as is probable, this may be another factor in promoting healing (Ravdin, 1940).

Throughout this investigation serum has been used because it has a higher protein content than the plasma available. Liquid plasma may be more readily obtainable owing to the presence of numerous blood banks throughout the country, and, although it has a lower protein content and would therefore not produce the same increase in blood volume, it could be used.

The danger of drawing conclusions from clinical improvement in such a small series of cases is fully appreciated, and no claim is made that these results are necessarily better than those which might have been obtained by other methods. They are encouraging, however, and the experimental part of this paper shows that transfusion of serum increases the circulation in the affected limbs, so that some benefit might be expected.

Summary

Intravenous injections of serum have been used in the treatment of patients with chronic arterial disease. Those cases with incipient or actual gangrene have been improved, as shown by increased warmth in the limbs, disappearance of rest pain, and healing of any ulcerated areas. Gangrenous areas separated rapidly. Some patients with intermittent claudication had partial or complete relief of pain.

The action of intravenous injections of serum in stimulating the formation of a collateral circulation is probably a mechanical one, produced by the increase of blood volume which follows the transfusion. Oscillometric and skin temperature studies on the action of serum on the peripheral circulation are reported and these support this hypothesis.

Case Reports

Case 1.—Man aged 44. Raynaud's syndrome, obliterative arteritis, gangrene of finger. Cold fingers since 1935. March, 1941: blackening of both index fingers, healing slowly. July, 1941: gangrene of right middle finger. On admission, hands cold, going white on exposure to cold. Gangrenous tip to right middle finger. Radial artery thickened. B.P. 180/110. W.R. negative. Smoked 20 cigarettes a day. Given four weekly transfusions of 800 c.cm. of serum. Hands became warm and red after the first; the gangrenous tips soon separated and the finger was healed in two weeks after the first transfusion. Hands remained warm for three weeks after transfusions were stopped, and then relapsed.

Case 2.—Woman aged 56. Raynaud's syndrome, obliterative arteritis, gangrene of fingers. In 1940 for the first time hands became abnormally sensitive to cold, and were white and painful. Condition progressed until she was unable to hold anything in her hands because of pain. On examination the hands were cold and blue, with the tips of the left fourth and right third fingers ulcerated and the skin blackened. Thickening of both radial arteries. Legs normal. W.R. negative. Given 800 c.cm. of serum, and one week later 400 c.cm. Hands became warm and red after the first transfusion and the ulcers healed. Flexion became full and painless, and hands have remained in this condition for eight weeks without further transfusion.

Case 3.—Woman aged 37. Raynaud's syndrome. In 1928 chronic purpuric eruption on legs and non-healing ulcers on right calf. Raynaud phenomenon in hands and feet since 1931. On admission hands and toes blue and cold, with early trophic changes in the skin over the tips. B.P. 106/64. Tourniquet test negative. W.R. negative. Peripheral pulses present and equal. Ulcer on right calf practically healed. Blood count and platelets normal. Given three transfusions of 800 c.cm. of serum with immediate increase in temperature of hands and feet, lasting several hours each time, but

within twenty-four hours the hands were as cold as before transfusion. The ulcer healed rapidly in fourteen days.

Case 4.—Man aged 38. Thrombo-angiitis obliterans, gangrene of toes. Intermittent claudication both legs for 1½ years. One month before admission left third toe became painful and blue. General examination normal. B.P. 120/80. Hands normal. Feet warm; gangrene of left third toe. All peripheral pulses present and equal. Marked postural colour changes in foot, and reflex vasodilatation test showed moderate arterial disease in the toes with some vasospasm. W.R. negative. Gangrenous tip separated with rest in bed, but toes were still blue. Given 800 c.cm. of serum twice—greatly improved response to vasodilatation test (Fig. 4). Colour of foot improved but only slight increase in temperature of feet.

Case 5.—Man aged 58. Arteriosclerosis, gangrene of foot. August, 1940: pain and redness of right big toe, worse on exercise and present at rest. December, 1940: gangrene of right fourth and fifth toes. Periarterial sympathectomy gave temporary relief, but in February, 1941, mid-thigh amputation of the right leg was performed. August, 1941: numbness and pain in left foot, with discoloration on outer side. Popliteal, dorsalis pedis, and posterior tibial pulses absent. B.P. 130/80. W.R. negative. Pain persisted with rest in bed. Given five transfusions of 800 c.cm. of serum. Rest pain disappeared after first, and foot became warm, with disappearance of the discoloured areas. Patient has remained well for two months after the last transfusion.

Case 6.—Man aged 37. Thrombo-angiitis obliterans, ulceration of foot. In 1935 intermittent claudication, gradually getting worse. Several attacks of phlebitis of legs. June, 1941: ulceration just below right medial malleolus. On examination toes of both sides bright red and warm, and sharply demarcated from rest of foot, which was pale. Small ulcer of right ankle. Femoral pulses present; all others absent in both legs. W.R. negative. Given three injections of serum. Feet became warmer, and ulcer healed; little change in the distance walked before the onset of pain in the right leg, but no pain in the left.

Case 7.—Man aged 49. Arteriosclerosis, ulceration of foot. In 1936 intermittent claudication. In 1938 bilateral lumbar sympathectomy—slight improvement. February, 1941: ulceration of left second and fourth toes, with rest pain. Ulcers remained unhealed for eight months. On examination brownish discoloration of lower part of left leg, with two small ulcers on second and fourth toes. Feet fairly warm. Arterial pulsations below popliteal absent on both sides, with no oscillometric readings. W.R. negative. Given 800 c.cm. of serum: immediate disappearance of rest pain, and ulcers were healed in ten days.

Case 8.—Man aged 59. Arteriosclerosis, intermittent claudication. In 1939 pain in right foot, followed by gangrene of toes. March, 1940: mid-thigh amputation of right leg. Femoral artery found to be occluded by grey organized thrombus. September, 1940: pain in left leg, present at rest and made worse by exercise—able to walk only twenty yards. Treated by diathermy and intermittent venous occlusion without improvement. General examination normal. B.P. 160/90. W.R. negative. Right stump healthy. Left leg warm but slightly discoloured on the dorsum and in tips of toes. Marked postural colour changes. All arterial pulses below femoral absent. Given 800 c.cm. of serum: able to walk over 200 yards afterwards without pain, and rest pain disappeared. Foot good colour. Slight recurrence of rest pain after three weeks, relieved by a further transfusion.

Case 9.—Man aged 62. Arteriosclerosis, gangrene of foot. July, 1940: gangrene of right fifth toe. February, 1941: admitted to hospital. Generalized arteriosclerosis. B.P. 136/80. Cyanosis and coldness of right foot, with gangrenous fifth toe. Left foot appeared normal. Arterial pulsations below the popliteal absent on both sides. Treated with perandren (testosterone propionate) 25 mg. twice weekly without improvement. June, 1941: amputation of right fifth toe and metatarsal. Healing fairly good at first, but small area 1½ in. by 1 in. on outer side remained ulcerated and discharging for six weeks. Given 800 c.cm. of serum; foot became warm and rest pain disappeared; two days later discharge ceased. Four further transfusions given; ulcer epithelized after second, and foot has remained warm and free from pain for two months.

Case 10.—Man aged 53. Hypertension, arteriosclerosis, intermittent claudication. July, 1941: intermittent claudication after walking 300 yards. Coldness and numbness of left leg when resting, and slight rest pain. On examination generalized arteriosclerosis. B.P. 160/100. Pallor of left first toe and bluish discoloration on outer side of this foot. Femoral pulses present; other pulses absent in both legs. Radiograph shows calcification of calf vessels. W.R. negative. Given two transfusions of 800 c.cm. of serum. Rest pain disappeared, both feet became warm and red, and the patient stated that walking was much easier, but no definite increase in claudication distance could be demonstrated.

Case 11.—Man aged 65. Arteriosclerotic heart disease, auricular fibrillation, gangrene of foot. April, 1941: intermittent claudication in right calf. Feet cold; pain in toes when resting. On examination

generalized arteriosclerosis. Heart slightly enlarged; auricular fibrillation. B.P. 180/80. Both feet cold and blue, with severe hyperaesthesia. Early gangrene of tip of right first toe. Right popliteal pulse absent; dorsalis pedis and posterior tibial pulses absent on both sides. W.R. negative. Treated with intermittent venous occlusion for two months without improvement. Given 800 c.cm. of serum. Rest pain disappeared within three hours, bluish line of discoloration on dorsum disappeared and foot became warmer. Hyperaesthesia less. Two further transfusions given. Hyperaesthesia disappeared. No rest pain, and gangrenous tip of toe separated. Feet have remained warm and free from pain for six weeks after the last transfusion.

Case 12.—Man aged 52. Arteriosclerosis, intermittent claudication. In 1918 phlebitis both legs following pneumonia. In 1922 ulcers on legs, constantly healing and breaking down until 1934, when varicose veins were injected and ulcers healed. In 1935 intermittent claudication after walking thirty to fifty yards. General examination negative. Healing ulcers on both anterior tibial regions. No pulsations in main vessels of either leg. Legs warm and good colour. W.R. negative. Treated by Buerger exercises and intermittent venous occlusion for two months, with healing of ulcers but without improvement in the claudication. Given six weekly transfusions: able to walk 220 yards before onset of pain.

Case 13.—Man aged 75. Arteriosclerosis, diabetes, perforating ulcer of foot. Diabetes for twenty years, treated with insulin for past nine years. In 1933 right third toe amputated for gangrene. January, 1941: perforating ulcer sole of left foot. On examination generalized arteriosclerosis. B.P. 180/105. Left leg definitely warmer than right, slightly swollen, and deep perforating ulcer present on sole of foot. Right foot cold and blue, but no gangrene present. Right dorsalis pedis present; other pulses at the ankle absent on both sides. Given 800 c.cm. of serum twice. Temperature of both feet was increased and the ulcer started healing, but no more quickly than would have been expected with conservative treatment and rest in bed.

Case 14.—Man aged 64. Arteriosclerosis, intermittent claudication. July, 1941: onset of intermittent claudication, gradually getting worse. Recent rest pain. General examination negative. B.P. 180/95. Radial and brachial arteries thickened. Both feet cold and blue, but no gangrene. Popliteal pulses present; left posterior tibial pulse present; other pulses at ankle absent. Response to reflex vasodilatation showed a normal rise of temperature in the right leg and no rise in left. After serum both gave good response, greater in the right (Fig. 3). Claudication distance increased from 400 to 1,200 yards after three transfusions.

Case 15.—Man aged 57. Obliterative arteritis, intermittent claudication. March, 1941: attacks of numbness in right first toe. September, 1941: intermittent claudication. History of syphilis in 1904. W.R. negative now. Smoked forty cigarettes a day. General examination negative. B.P. 130/90. Legs: feet cold, no gangrene or ulceration. Peripheral pulses all present and equal. No response to reflex vasodilatation before serum, but normal response after serum. Walking improved. Claudication distance increased three times.

Case 16.—Man aged 34. Crush syndrome, non-healing ulcer of right leg. November, 1940: buried as result of bomb explosion, and had severe crush injuries of both legs, followed by renal failure (crush syndrome). Deep non-healing ulcer on anterior tibial surface of right leg. September, 1941: ulcer in same condition. Wasting of calf muscles, anaesthesia of right foot, but arterial pulsations good. Given five weekly transfusions of serum. Slow but definite progressive healing of the ulcer.

No other treatment apart from rest in bed was given to these patients while they were receiving serum transfusions, and no attempt was made to stop them smoking.

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