A Study of

THROMBO-ANGIITIS OBLITERANS.

or

Pre-senile Gangrene of the extremities in Russian and Polish Hebrews, based on an investigation of five cases.

by

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I am indebted to Dr G. Duncan Whyte for allowing me to append these photos.

THROMBO-ANGIITIS OBLITERANS.
INTRODUCTION.

My interest in pre-senile non-syphilitic gangrene occurring among Jews from Eastern Europe was aroused about eighteen months ago when I saw in London Mr H. K., an old friend of mine from South Africa. He was suffering from gangrene of the great toe of his right foot. He had already lost the corresponding toe of the opposite foot.

CLINICAL STUDY.

The clinical picture of the disease which is in our mind after a study of the five cases is very clear cut.

It is a condition occurring in anaemic, thin male Jews who came from Russia or Poland. The disease is insidious and hardly ever manifests itself before the fourth decade although it may have been developing for a long period prior to this.

It/
It occurs among middle-aged men whose ancestors have shewn no similar trouble. Syphilis is certainly not a cause, as in none of the cases was a positive Wassermann found. The patient may come from the upper or lower classes.

Sometimes the disease starts as a migrating thrombosis in the form of cutaneous nodosities of the veins of the lower limbs. In others, the first symptom is **intermittent claudication** or angina cruris causing a feeling of cramp in the muscles of one or both legs after walking for a few minutes, relieved by resting for a short while.

After a longer or shorter period the patient develops Cyanosis or redness with some oedema in one or both feet. This is succeeded by ulcers leading to gangrene of a toe or the whole foot. The toe if left alone will be amputated by nature at the metatarso phalangeal joint. Very frequently the nail of the big toe becomes painful and cyanotic. After the lapse of a short period a tiny swelling makes its appearance under the inner side of the nail. The case is then diagnosed as an ingrowing toe nail, and treatment is carried out in accordance with this conclusion. The disease now becomes extremely painful. Not only is the patient troubled when he walks, but/
but also when he rests in bed. Sleepless nights have to be met with morphia, as this pain which is of an ischaemic nature and lasts for days on end without any remissions is enough to drive the sufferers to thoughts of suicide.

The small surgical operation which may have been performed by the family doctor who is under the impression he is dealing with a very simple malady, often leads to disasters. The condition which has so far only affected, say, the big toe, begins to spread rapidly. The whole foot as well as the leg becomes greatly engorged; the pain is even worse than before, and gangrene is imminent. A specialist is called in, and an operation of a more heroic type is recommended. The patient is lucky if he escapes with the loss of a big toe. Very often amputation through the thigh is advised. The surgeon is surprised to find clotted cords in place of bleeding vessels on removing the tourniquet. He wonders whether a Gritti-Stokes amputation was sufficiently high. Even after this drastic performance, the flaps may slough, the patient may have pain in the stump, and may even have to run the gauntlet of a cerebral thrombosis leading to amnesia and monoplegia.

On physical examination of the patient, usually nothing abnormal is found in the viscera. The muscles of/
of the limb may be extremely atrophied as a result of the disease. **Pulseless vessels are found.** The dorsalis pedis and posterior tibial where it passes behind the internal malleolus are always occluded. Very often the popliteal even on careful palpation by flexing the knee and sometimes the femoral in Scarpa's triangle are discovered to be pulseless. The apparently sound limb may also show signs of obstructed vessels. The dorsalis pedis may already be blocked. Furthermore the radial arteries are sometimes occluded. The affected limb in a horizontal position is cyanotic or pinkish in colour, the dorsal aspect of the foot a little congested and running under the skin are seen thin bluish vessels. On raising the limb a few inches above the level of the bed the congestion rapidly disappears and the member becomes blanched and lifeless, and the patient may complain of increased pain as a result of this manoeuvre. This pain, however, is at once relieved if the limb is lowered to below the horizontal level, and the foot and ankle become almost instantly cyanosed and oedematous. This characteristic symptom-complex has been called by Dr Parkes Weber "erythromelalgia", a term used by Weir Mitchell for painful swelling of the upper limbs, found in females as well as in males, and not associated with thrombo-angiitis obliterans. To avoid confusion/
confusion Buerger's term "elythro-melia"\(^1\) is preferable.

This syndrome is frequently absent in arteriosclerotic and diabetic conditions.

It is evidently nature's effort to improve the circulation. It points to a blood supply which is under no sympathetic control. Gravity alone seems to cause this hyperaemia, and as we shall see later, treatment by Bier's congestion is an imitation of nature's attempt to re-establish the blood supply.\(^2\)

**Oehler's sign:**

This sign is not so useful as the others, because it cannot always be applied, owing to the pain which accompanies its demonstration. It is often found in the unaffected as well as in the diseased limb. Rapid flexion and extension at the ankle joint produce great temporary anaemia of the foot.

**Intermittent Claudication:**

With regard to intermittent claudication which forms such a constant and early symptom of thromboangiitis obliterans, many references are found in the literature. According to Dr Parkes Weber\(^3\) the term "Claudication intermittente" was first employed by G.H. Bouley (Jr.) in 1831, in regard to a rare arterial affection in horses usually affecting one or both of the animal's hinder extremities.
Mr Greig says "It comes on after muscular exertion . . . . increases with the continued effort to use the affected muscle, and is characterised by a hopeless lameness and stiffness in the limbs."

It may be associated with organic disease of the arteries or with angiospasm. (H. Oppenheim.)

Mr Greig in his paper describes a case where intermittent claudication occurred in a man of 72. He thinks it was due in this case to "venous, not arterial affection".

Dr Byrom Bramwell read a paper before the Medical Chirurgical Society of Edinburgh, July 1, 1908, on Intermittent Claudication, and shewed a case of a Jew aged 42 with obliterated femoral. A bloodless amputation through the knee joint had been performed. He says there are three factors which have to be considered in connection with this syndrome - Vascular obstruction, Vaso-motor spasm and increased demand on the circulation of the part which muscular activity entails.

Sir Clifford Allbutt disapproves of "Potain's notion of intermittent claudication of the heart, the current explanation of angina pectoris." He further says "Arterio-sclerosis of vessels distributed to muscular organs is common, yet intermittent claudication is something of a rarity. It is true/
true we cannot say that the heart in angina never claudicates, but when it does there is an end of the case. The halt is the halt of death".

I remember the late Prof. Wyllie used to describe angina pectoris as the "cry of the heart for more blood". In this connection it is interesting to note that swimmer's cramp or the cramp sometimes noticed in debilitated patients brought on by sudden movement of the leg in bed is quickly relieved by massage of the affected muscles, and in that way improving the blood supply.

The interesting point about intermittent claudication in so far as it bears on thrombo-angitis obliterans, is that it tends to disappear after a time. Is this due to the establishment of an adequate collateral circulation? If so, it is to be found in the canalisation of the thrombus and increased subcutaneous vascularity. The erythromelia symptom-complex never disappears even after the acute symptoms have subsided.

Castellani and Chalmers⁷ give a description of this complication occurring in unusual types of subtropical malarial fevers. They talk of an "intermittent claudication" type, an "Erythromelalgia" type and a "pseudo-endarteritis" type. During the "intermittent claudication there is an absence of pulse in the dorsalis pedis artery or in the posterior tibial". It is evidently due to a blocking of the vessels by the parasites and is speedily relieved by quinine.
In making a diagnosis of thrombo-angiitis obliterans it is worth remembering that male Jews from Eastern Europe are prone to this disease. Dr Buerger has seen a large number of cases in New York. While in this country Dr Parkes Weber has reported a number of cases occurring among the Jews in the East End of London. Dr Duncan Whyte of Swatow, China, has seen a large number of cases of spontaneous gangrene occurring in Chinese which he claims to be of a similar nature. In his articles on Thrombo-Angiitis obliterans he describes a case where the patient himself hacked through his leg with a meat chopper in order to stop the agony of his toes. But he gives no pathological report of any of his cases.

The age of the patient is important. It rarely or never occurs in the young. The fourth decade is the period when this disease usually manifests itself.
DIFFERENTIAL DIAGNOSIS.

The allied conditions, frost bite, Raynaud's disease, trench foot, endarteritis obliterans, senile gangrene due to arterio-sclerosis, erythromelalgia of Weir Mitchell and malarial conditions have to be remembered. Dr Farquhar Buzzard puts "intermittent claudication" in a class by itself. As this occurs in many diseases I think it is a mistake to look upon this symptom complex as a disease or a clinical entity.

Frost bite and trench foot will cause no trouble, as the names tell us when to look for the conditions.

Raynaud's Disease: This occurs more often in females whereas thrombo-angiitis obliterans attacks men only. Raynaud's disease is usually symmetrical, the hands being more often attacked than the feet. It is of a spasmodic and intermittent nature, and is aggravated by cold. The causation is said to be a spasm of the vessels. Obliterating thrombo-angiitis differs entirely from this. Usually one toe is affected first. It gets progressively worse, is not influenced very much by cold weather and is not of an angio-spastic nature. The pathological picture is quite different.
Erythromelalgia. This condition Dr Farquhar Buzzard\textsuperscript{9} says occurs between 20 and 60 years, males are more often affected than females. It is symmetrical in the feet and rarely bilateral. It is associated with functional and organic disease of the central nervous system. It is \textbf{aggravated by the dependent position of the limb as well as by warm application.} Thrombo-angiitis, as we have seen, is \textbf{ameliorated by putting the foot in a dependent position; this is made use of in the treatment of cases.} (See Case I.)

\textbf{Endarteritis obliterans:—} In conditions due to \textit{endarteritis obliterans}, a history of syphilis or tubercle will be obtained. It has no predilection for the male sex.

\textbf{Senile gangrene} — associated with intermittent claudication. To exclude this condition look for pipe stem arteries which will cast a shadow on the X-Ray plate. It is usually found in people in advanced age, or in people who are suffering from some condition which causes disease of vessels like Interstitial nephritis and gout.
Malarial conditions - giving rise to intermittent claudication have already been discussed. They yield to quinine.

One final word in connection with the diagnosis of limb conditions generally. In our routine examination of symptoms referable to the feet and legs, it is as important to palpate the dorsalis pedis and posterior tibial as is the examination of the radial pulse for diseases generally.
THROMBO-ANGIITIS OBLITERANS.

First Case.

Condition of feet 7 years after onset of disease.
Result of conservative treatment.
FIRST CASE.

H. K., born in Cape Town, 1880.

Male, of Russian Hebrew parents - a solicitor by profession.

Marital: Married 7 years: wife alive and well.
No children and no miscarriages.

Complaint: Severe pain in and sloughing of right great toe.

History of Present Case.

About April 1912 he noticed that his foot was occasionally swollen and felt abnormally hot.
The symptoms would come and go, growing gradually worse at each recurrence, until about four months later walking became impossible, and the swelling permanent.

Throughout this period walking became gradually worse and was always accompanied by a peculiar grip-like sensation. This sensation forced him to stop walking and to rest the foot by lifting it off the ground. He could then walk another fifty yards or so. He had to rest the foot for one to three or four minutes, seldom more. Wet, stormy or windy weather would aggravate the trouble.

This symptom complex is well recognised and known as intermittent claudication; it is found both in human beings and horses and is associated with a disturbance in the vascular supply to the limbs.

In August 1912 he first called in medical aid, and/
and was told he was suffering from gout, rheumatism, diabetes, arterio-sclerosis, syphilis and ingrowing toe-nail. He received treatment in accordance with each new diagnosis, but to no avail. He derived great benefit from a month's stay at the Montague National Hot Water Baths. These are thermal springs certified to possess water with a radio-active property. He drank and bathed in the waters. The swelling of the foot was reduced to normal.

Here for the first time he noticed an abrasion of the skin, at the joint of the 2nd phalanx of the little toe. This grew into a deep ulcer. He next tried electrical treatment and had applied to him "high-fluency". The foot got very much worse. The wound grew larger and more fiery, the swelling increased and the pain became more intense and occurred more frequently.

"Hot and cold water" treatment was next tried. This consisted in alternate applications of hot and cold water to the foot. He also tried electric baths, but could not bear them for longer than a few minutes. Bathing became difficult because the foot could not tolerate being in the same level as the rest of the body, and it was always more comfortable in a position lower than the thigh.

At/
At night he had to bolster up his bed so as to ensure having the foot at a lower level than the rest of the body. His most comfortable position would be to lie on his "stomach" with the sore foot just hanging out of bed. Unless the relative position of the foot to the rest of the body was maintained, the pain would become intense enough to wake him from the soundest sleep. He was extremely susceptible to draughts however slight. Throughout all this time he learned that when his bowels were loaded, the pain in the foot was much worse. He could actually feel distinct easing of the pain in the foot when he had quite finished at the stool.

As the foot did not improve, he was advised to have the wound scraped. This was carried out under an anaesthetic on New Year's day 1913. The leg began to swell; the swelling soon reached to somewhere near the knee, and the foot itself was swollen more than ever and very badly inflamed. Amputation was next advised, but to this he did not consent and came to London for further advice. Here he had a second Wassermann test of his blood, the first was in Cape Town. Both examinations shewed no trace of syphilitic infection. He denied having ever contracted venereal disease. During the last eight years he has had the Wassermann test applied at least six or seven times;
times; all these tests have proved negative.

In London he saw Dr M. D., who treated him by ionisation. He was also given considerable doses of Potassium Iodide. This treatment he received daily for about three months. The wound in the little toe healed, but the joint remained stiff up to the present. He returned to South Africa in July 1914 and got married the same year. His wife has had no children and no miscarriages. She has remained quite well. His health by this time had greatly improved, and he thought he would never be troubled again with this most agonising malady.

But in April 1915 he felt a small pimple was forcing its way up underneath the nail of the big toe of the left foot. It was very painful. The toe shewed some redness and some swelling. Mortification made its appearance in the big toe. The arresting feeling in his walk reappeared, and gradually became more marked. The only relief he got was by keeping the foot in a basin of cold water day and night. The foot got much swollen. Eventually the toe rotted away, first the top phalanx and then the next, and by the time he reached London a second time in July 1916, the 2nd phalanx of the left big toe was practically all gangrened away. The foot was X-Rayed and it was found that the head of the metatarsal of the/
the big toe was projecting. About \( \frac{1}{2} \) inch of the bone was clipped away under an anaesthetic. The wound was "bipped" and sewn together and a dressing applied. When the dressing was removed ten days later the wound gaped. About the end of 1917, the wound was practically closed and showed a scaly growth issuing and growing from the centre of the wound.

In December 1918 he developed an attack of phlebitis of the internal saphenous vein of the left leg from which he recovered after lying in bed for five weeks in hospital. Before being discharged, he was carefully examined, and declared to be free from arterial trouble. He had a slight relapse of the phlebitis and went to bed for another week or so.

The foot progressed well after that, and stood him in very good stead, when later trouble occurred in the right foot. He is greatly inclined to believe that the arch of the left foot dropped whilst the big toe was gangrenous. But gradually when this foot was called upon to be his only medium of walking with crutches, it seemed gradually to acquire a more normal tread with a certain amount of elasticity in its movement. This is the state in which it is at the present day. (March 1920).

About Aug. 1919 the big toe of the right foot became swollen and red. This toe underwent the same changes/
changes as the big toe of the left foot.
The intermittent claudication returned. The pimple under the nail grew in the other foot into an open wound. The pain in the toe became agonising, sometimes the pain would lessen of its own accord, and keep away for a few hours. Then for no reason it would start, sometimes in the manner of shooting pains, or at other times just one continuous burning pain, as if seared with a hot iron.

His stools now became blood stained. He lost a fair amount of blood this way, and he became quite anaemic. An iron tonic and some good burgundy diluted with boiling water worked wonders. The bleeding practically stopped, the pain appeared less keen and his system felt generally strengthened.

During this period he obtained an ointment which silenced the pain as if miraculously. This he applied to the wound with a piece of matchwood and then covered the wound with a piece of plain lint and cotton wool. The portion of the toe round the wound is now somewhat inflamed, and cannot tolerate any of the ointment being bandaged on it. The ointment has to be re-applied three or four times a day. He discovered that a loaded bowel dissolved the ointment, and caused it to run on the skin round the wound. He therefore had to dress the wound after each/
each motion, which was about three or four times a day.

His diet was never restricted, but by experience he found that beans, peas, vinegar, alcohol, unless taken very hot, were unsuitable. Beef did not suit him, but mutton never seemed to cause any trouble. He found it inadvisable to eat between meals. Strict adherence to 3 meals a day at regular hours gave him the greatest comfort. It ensured regular evacuations and regular times for treating the foot.

Constipation he greatly dreaded as it always made the pain worse. He always found relief in a small piece of rhubarb root.

Gradually the big toe of the right foot came away. A line of demarcation formed a little proximal to the web. The toe dropped off in December 1920.

He can confidently say the ointment has been the making of him. His chief concern was to keep down as much as possible the irritation and pain in the wound.

Prescription of the Ointment:-

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<tr>
<th>Ingredient</th>
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<tr>
<td>Zinc. oxidi</td>
<td>4 drm.</td>
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<tr>
<td>Cocain. HCl.</td>
<td>3 1/2 gr.</td>
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<tr>
<td>Liq. Hamamel.</td>
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<td>Acid. Carbol.</td>
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<td>Ol. olivae.</td>
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Previous illnesses.

When about six years of age he had a very bad attack of sore eyes, which kept him in bed for some weeks and out of school for about six months. When about 9 years old he got his left foot very badly scalded by dipping it into a bath of boiling or very hot water. It took some weeks before he was allowed to get it into a boot again. In 1902 he had a slight attack of malaria in Rhodesia, but it only kept him in bed three or four days and he never had a repetition of it.

(Quinine has no effect on present illness.)

Neither his parents nor his two brothers and five sisters were ever troubled with phlebitis or arterial trouble. His father died at 65 from cancer of the bowel (?); mother is still alive and hale at 60. There are in the family eight children living; four died in infancy. One of his brothers, about a year younger than himself, suffers from severe bleeding from the nose and is paralysed in the left arm and left leg.

He used to smoke about ten cigarettes a day. He takes little alcohol.

Physical Examination - March 1920.

Heart and lungs normal. Alimentary system - teeth very good, tongue clean; stomach not enlarged; spleen/
THROMBO-ANGIITIS OBLITERANS.

First Case.
Condition of feet 7 years after onset of disease.
Result of conservative treatment.
spleen not palpable; kidneys not palpable; urine—no albumen or sugar; Sp. g. 1020; reaction slightly acid.

No pulsation felt in either arteria dorsalis pedis or popliteal arteries. Slight pulsation in femoral arteries.

Blood pressure 120.

Blood—R.B.C. 4500,000; Whites 8000; G.I. 90; no abnormal cells.

The left foot, when I first examined the patient, had the appearance shown in the (opposite) photograph.

The left great toe is completely absent. There is a small cornified structure protruding from the stump. The left small toe has a scar on the outer aspect at the metatarso phalangeal junction—the site of a healed ulcer. The phalangeal and metatarsal phalangeal joints are ankylosed. The foot is somewhat atrophied, and there are a few varicose veins on the anterior aspect of the leg.

The right foot is swollen and red and tender. The erythromelilia symptom-complex is present.

The terminal phalanx of the great toe had sloughed off when I first saw the patient; (a few months after my first examination the second phalanx of this toe came away too, and a healthy wound was left.) When the foot is moved rapidly at the ankle joint, it/
it (the foot) becomes blanched and oedema disappears. The redness and congestion return when the foot is allowed to hang over the bed, and quickly assumes its ordinary appearance (Oehler's sign).

There were no signs of disease in the nervous system, or any other part of his body.
SUMMARY OF FIRST CASE.

The first symptom to appear was intermittent claudication. This was followed by another kind of pain which was of ischaemic origin and was relieved by the induction of hyperaemia produced by placing the affected foot at a lower level than the rest of the body.

It shows the advantage of waiting for nature to do the amputation. The patient refused to have any major operation performed, with the result that after seven years he had lost only the two big toes. He was thus left with impaired but quite useful feet.

Aqueous solutions irritated the wounds and should not be applied. He found an ointment containing cocain and carbolic acid very useful.

Attention to the bowels was very important.
I could find no cause to explain the disease.
SECOND CASE.

This case I first saw in the London Hospital in January 1921, and I traced him to his home in the East End in March 1921.

M. R., born in Russia in 1881.

Male, of Russian Hebrew parents and a double-bass player in a Restaurant in London.

Marital - Married 22 years ago.

9 children. 8 well and living; 1 died at 14 months, from pneumonia.

Wife well and living; had 1 miscarriage.

Complaint - severe pain and burning in the left big toe - otherwise healthy.

History of present illness: - About two years ago patient developed pain in the left calf after walking a short distance. The pain would disappear after resting for a few minutes, but only to return on resuming his walking. He also noticed that during these attacks the foot would go dead. Nothing that he tried had any effect on permanently preventing the attack of pain which gradually became worse, lasting longer and recurring at shorter intervals.

In/
In September 1920, i.e. about 18 months after the onset of pain in the left calf, he developed severe pain in the left big toe. The toe was slightly swollen and bluish. He noticed a black spot under the nail. This gradually spread until it affected the whole nail-bed. By this time the nail had become of a brownish, almost black, colour.

The nail was removed on the 25th April 1920 in the O.P.D. London Hospital. Three months later he developed severe pain and burning in the left great toe. He was admitted into the London Hospital on Dec. 15th, 1920. The condition did not improve, and he left the Hospital on February 2nd, 1921, after refusing an operation.

As the condition did not improve he went to the Metropolitan Hospital two weeks later where the toe was removed. After this operation the left knee had to be kept flexed to relieve the pain. He has not been able to fully extend the knee since.

Previous history:— Had measles as a child.

He never had syphilis. His blood test done recently gave a negative Wassermann reaction.

He has been rather constipated since his arrival in England about 25 years ago. The eating of meat always made/
made him worse. He never passed blood by the bowel. His bowels have been regular, moving daily since the toe was removed.

Ten years ago he had what appeared to be an attack of acute lymphangitis of the right foot and leg. Fomentations cured this in a few weeks. He used to get headaches as a young man. This he put down to indigestion.

Habits:— Commenced smoking when he was 12 years of age, and has smoked from ten to fourteen cigarettes a day ever since. He was a great walker when he was in his teens. He could easily walk thirty-five miles a day or even more. He takes little alcohol.

When he was 21 years of age he returned to Poland to be examined for the Russian Army. To avoid service he tried to develop varicose veins.

For about six weeks in succession he put a tight elastic bandage round the left thigh for the greater part of the day. This caused the leg to swell very much and the veins to stand out. But at the end of the time he failed to find any varicose veins, and so gave up the idea. He is a double bass player. This entails a good deal of standing. He was fourteen years of age when he commenced playing in public.

He belongs to a stock of people noted for longevity.
He has three brothers all living and well.

Father died at 73 from hemiplegia.

Mother still alive and well at 75.

Mother's father died 110 and his brother died 115.

Mother's mother died at 70.

Father's mother died at 80.

Father's father died at 60.

Physical examination: He is a thin well-developed man. His cardiac, respiratory, alimentary and nervous systems were normal.

Urinary system - nothing abnormal found.

Urine analysis - no sugar or albumen. Sp. gr. 1015. Slightly acid reaction.

Vascular system. Blood pressure (Systolic) 100.

Pulse in both radials was palpable. There was no thickening of the walls of the arteries. The blood shews slight secondary anaemia. Both fundi were normal.

Right leg. Well developed. Calf muscles very sensitive to deep pressure. Some pes planus in right foot. Metatarsal phalangeal joint of right big toe has little movement.

Right femoral pulse palpable but small. No pulsation in dorsalis pedis or posterior tibial.

No ulceration or scarring.
Left Leg: Knee cannot be straightened beyond 120°. (He has not been able to straighten the leg since amputation of great toe.)


The erythromelalgia symptom-complex was present. When the limbs are elevated to slightly above the horizontal, the feet rapidly become blanched, only to become red and swollen again when allowed to hang over the bed. Oehler's sign was positive. Feet become blanched when rapid movement is performed at the ankles, especially the left. Both knee jerks were rather brisk.

P.S. Through the courtesy of the Medical Registrar of the London Hospital, I was able to trace M.R. to his home in the East End of London, where I again examined him after seeing him in the Hospital.
SUMMARY OF SECOND CASE.

In this case were present all the cardinal signs and symptoms, viz., intermittent-claudication, erythromelia, ischaemic pain, and Oehler's sign, and gangrene.

The patient started smoking while he was still young, but whether this had any connection with the condition cannot be said.

The importance of interfering with thromboangiitis obliterans as little as possible is well borne out in this case. He was unable to fully straighten the knee after a toe had been removed from the corresponding foot.

These cases stand any form of trauma very badly.

There was no sign of any hereditary disease as his parents and grandparents lived to a ripe old age.

There was no inherent weakness in the blood vessels. This is borne out by the patient's failure to develop varicosity of the veins.
THIRD CASE.

W. S., male, born in Lithuania, of Russian Hebrew patents. 36 years of age; single, three sisters and one brother. All well. Father and mother alive and well. Bachelor.

Complaint: - Ulcers and agonising pain in left foot and loss of toes.

History of present illness: - In 1900 while in Cape Town he was subject to "lumps" in the veins of both lower extremities (? Phlebitis migrans). These lumps were sensitive to touch and of a purplish colour. They never ruptured. These attacks lasted for six months, and never kept him off his work. In 1903 he had slight attacks of pain in both legs. These were not affected by walking. He then remained well till 1906 when he developed ingrowing toe nails (?) in both big toes, for which the nails were removed. The toes healed.

In 1910 he next developed soft white corns in the adjacent sides of the small toes of both feet. Corns then appeared on the balls of these toes. These toes turned red and painful.

Between/
Between 1910 and 1915 he lost the 2nd toe of the right foot, and all the toes of the left, owing to painful corns and gangrene. He remained well till Feb. 1921 when he developed pain in the calf muscles on walking a short distance. This would make him stop for a few minutes when the pain would go, only to return after walking another hundred yards or so.

The worst symptom of all then made its appearance. This took the form of throbbing pain, as though somebody was scraping his bones with a knife, in the distal part of the left foot. This became unbearable and he went to England for advice. He developed a few sores in the stumps of the 4th and 5th toes of the left foot. He was admitted to Guy's Hospital. His faeces were examined and vaccines made for him, and injections given in the buttock, without any improvement.

While in bed a black spot, followed by a blister developed on the back of the left heel. An ulcer then formed where the blister had been and another one a little higher up.

Previous history:- He always enjoyed good health and never had syphilis.

He lost his left eye as a child, but does not remember how. The Wassermann test on his blood was negative.
The patient has been a very hard worker. He has been a stone-breaker, kitchen boy, waiter, shop-keeper, produce merchant, butcher, tea-room keeper, and bottle store-keeper, and he always made a point of doing most of the work himself.

He has always enjoyed good health, and has never been liable to chilblains.

Physical Examination: The patient is well developed and shows no signs of visceral disease. Urine analysis – nothing abnormal. (Guy's Hospital report). Blood had not been examined. He did not look anaemic. His blood pressure was about 150. The right fundus was normal.

Nervous system – mentally bright.

Knee jerks – both exaggerated.
No Babinski. Slight ankle clonus of right foot. This test could not be performed in the left foot owing to the ulcers.

Extremities – ears pale and cold.

Arms – well developed. Both radial pulses normal, but the arteries feel thick though not calcified. The left median nerve is closely adherent to the brachial artery and cannot be separated from it.

Right leg. Muscles well developed. Femoral, popliteal and internal plantar felt pulsating.

Dorsalis pedis pulse not palpable.

2nd toe missing. No signs of ulceration or discoloration.
Left Leg:— Femoral pulse felt without difficulty. There are some enlarged glands in Scarpa's triangle probably due to the sepsis in the foot. Popliteal, dorsalis pedis and posterior tibial pulsations not felt. Muscles of calf were extremely atrophied. I could feel the posterior surface of the tibia and fibula quite easily as there was hardly any muscle left. The left heel has two punched-out ulcers one above the other, about the size of a five shilling piece. The Tendo Achillis can be seen glistening in the hollow of the upper ulcer. These ulcers are probably due to pressure. The left foot is somewhat pinkish in colour, oedematous, and shews a large number of thin bluish vessels on the dorsum. There are no toes present. In the place where the fifth toe was, there is a deep crateriform ulcer in the hollow of which is seen the cancellous bone of the shaft of the fifth metatarsal. This ulcer is frightfully tender. The skin around it is very painful to touch and oedematous and red.

Owing to the ulcers on the left heel I could not try Oehler's test. But this was present in the right foot.

The erythromelia symptom-complex was present in both feet, especially in the left foot, which would become almost instantly blanched or congested according as to whether the foot was placed above or below the horizontal/
horizontal position.

Pulse ranged from 80 to 100.

Temp. 100. Bowels regular. No blood in the stools.

The resident surgical officer in charge of the case, through whose kind courtesy I was able to examine this patient, told me that the patient had to be given Morphia every night as the pain was unbearable.

Injections of sodium citrate solutions into the veins had been tried, but the results had not been encouraging. This patient refused amputation of the left leg. Owing to the almost complete absence of any muscle tissue in the calf, I doubt if the left leg will ever be of any use.
SUMMARY OF THIRD CASE.

The trouble began with a migrating phlebitis of the veins of the lower extremities. The chief signs and symptoms were positive.

The characteristic feature of this case is the loss of all the toes of the left foot, and the severe ischaemic pain. The ulcers on the left heel were due to pressure, and came on rapidly. This teaches us the importance of avoiding pressure in these cases.

Injections of sodium citrate solutions intravenously - as recommended by some observers - proved a failure in this case.

The ischaemic pain in this case will probably force the Surgeon to amputate the leg. The patient is running the risk of becoming a morpho-maniac.
FOURTH CASE.

S. K., male, born in Russia, of Russian Hebrew patents: 46 years of age.
Married 16 years ago; wife well and living; 4 children; 1 died in infancy from pneumonia and measles.

This patient had an amputation for gangrene of the left foot performed in the London Hospital in 1920. The Resident Medical Officer of the London Hospital allowed me to see the case sheet and make use of the notes. He further told me that Professor H.M. Turnbull of the Pathological Institute of the London Hospital had cut sections of the diseased vessels. Through the kindness of Prof. Turnbull I have been able to study the sections, and thus give a report on the pathology of the case.

I further traced the patient to the Bancroft Road Infirmary, London E., where he had been admitted after the amputation, as the patient had almost complete loss of speech, which had come on before the operation.

Present complaint: - Loss of speech and weakness of right hand.

I/
I interrogated his wife who gave me the following history.

**History of present illness:** About 1915 it was noticed that he was getting thinner. In 1916 he complained of numbness in the left leg and foot, left arm and left side of face. There was no twitching. He always had cold feet, but never had chilblains or painful corns.

In June 1919 he lost his speech for an hour. On the following day the same thing happened, but there was no unconsciousness with the loss of speech. About the same time he developed pains in the legs after walking a short distance. He got relief only by stopping for a few minutes. These pains were always worse in the left leg.

In July 1919 a bicycle went over his left foot. His thigh was badly cut and the wound bled a good deal. Shortly before the accident he began to complain of pain in the big toe of the left foot. The bicycle accident aggravated the pain. Three weeks later a small black nodule was noticed on the painful toe. The nail was removed. He got slight relief from the pain after this operation.

The pain in the big toe, however, returned with greater severity. He could neither eat nor sleep for the pain. He was admitted into the London Hospital where he got great relief from electric bath/
bath treatment. But three months later the toe began to fester, an ulcer developed on the inner side of nail area, with surrounding inflammation. (He was treated with peroxide of hydrogen and potassium iodide). He was readmitted to the London Hospital.

I here append a report of the case while the patient was in the Hospital, which I obtained from the registrar's office.

X-Ray shews necrosis of both phalanges of the great toe.

21.7.20. Foot very dirty and stinks.
28.7.20. Left leg amputated above the knee. (Stokes-Gritti).
6.8.21. Wound healing well.

History after leaving the London Hospital.

He remained well till Jan. 1921, when he developed pain in the right little toe. He was told he would have to have his right leg off. This upset him very much. He gradually lost his power of speech, and on admission to the Bancroft Road Infirmary he hardly spoke at all.

The little toe was removed, and the wound slowly granulated over.
Previous history: - He had typhus or typhoid as a child. He liked a little whisky over the week-end, but never came home drunk.

He had been a hearty eater. He smoked a fair amount, but his wife does not think he smoked more than 8 or 10 cigarettes a day, as he could not smoke while working in a tailor's shop.

Physical examination (which I made in the Bancroft Road Infirmary) is as follows: -

Heart and lungs and abdominal organs normal.

Blood pressure 115 mm. of mercury.

Nervous system: -

Expression dull and stupid.

Speech - slurring almost completely lost. All he could mumble was "wha i' i" (meaning "What is it").

No difficulty in swallowing.

Hearing - good. He more or less heard and understood what was said to him.

Facial nerve was intact.

Eyes - movements of eye balls normal.

Fundus - both central arteries looked markedly small. The veins/
Dorsalis Pedis Artery.  (V. G. Stain)  X 80.

1. Tunica Adventitia.
2. Tunica media.
3. Tunica intima - greatly crenated, with distinct elastic lamella - degenerated in places, separated from indistinct boundary stripe by thin musculo-elastic, and hyperplastic thickened especially at 3(a).
4. Foci of calcification in lamella just internal to media.
5. Organised red thrombus replaced by connective tissue and shows round celled infiltration.
6. Haemosiderin pigment in organised red thrombus.
7. New blood vessel with well marked intima and media in organised thrombus.
8. New blood channel with intima only. Cut longitudinally as it passes through intima into occluded lumen.
veins stood out well but were tortuous.

Vision was not affected. The eye reflexes were normal to light; convergence was unaffected.

There was some weakness in the right hand although there was no actual paralysis. The interosseous muscles of his hand were atrophied. Was this weakness, together with his loss of speech, due to a middle cerebral thrombosis?

Tendon and muscle reflexes of right arm were slightly increased.

Stump of left leg - Scar healthy - no loss of power.

Right leg - no loss of power.

Tendon reflexes normal. No Babinski.

On raising foot above the horizontal it rapidly becomes blanched and on allowing it to hang over the bed, it becomes congested, assuming a bright pink colour.

Examination of Microscopic Sections.

Dorsalis Pedis artery ($\frac{1}{8}$) .

Adventitia gummed to surrounding structures.

Media - rather thin. Muscle cells and nuclei stain well.

The layers of muscle fibres are being replaced by a round celled infiltration. The new tissue has separated the fibres and so caused spaces which are filled with small deeply stained nuclei.

Intima -/
Intima - The crenated lamella is thick in some places and replaced in others by several areas of focal calcification.

The musculo elastic layer is not well marked and is degenerated.

The hyperelastic layer is well seen and contains several layers of elastic fibres.

Lumen. The lumen is completely occluded by organised tissues which have become canalised by several channels which have only one coat. One large vessel, however, and a number of small ones have a well formed media also. In the organised tissue are found groups of haemosiderin granules, probably remains of the old red thrombus. There is also a round cell infiltration throughout the organised tissue. The larger channels contain red blood corpuscles.

Interpretation - A vessel somewhat collapsed, which becomes occluded by a red thrombus. This has been organised and canalised.

Some active change going on in the media which is gradually being replaced by granulation tissue.

Venae Comites. Three large veins with patent lumina, but with no change in their coats.

(2)
(2) Posterior tibial Artery shows large foci of medial calcification and fibrosis. There is a recently formed white thrombus in the lumen.

There is probably here a combination of degenerative arterio-sclerosis of the ordinary type plus the changes which are peculiar to the disease from which the patient suffers.

NOTE:— In connection with his aphasia and slight loss of power in the right arm, it is interesting to note that Mott in his article on Syphilitic arteritis in Allbutt and Rolleston's System of Medicine basing his statement on Oppenheim's work says "the transitory character of the early phenomena of syphilitic arteritis before thrombosis has occurred, is a very important feature. The narrowing of the lumen may be well marked, but still some blood can get through ................

There is time for collateral circulation to be established. There may be a hemiparesis lasting perhaps a few minutes, a few hours, or a few days. Then it disappears again to return and eventually ends in permanent hemiplegia ...... often associated with aphasia." In this way my patient's phenomena may be explained, though in his case the vascular condition is of non-syphilitic origin.
SUMMARY OF FOURTH CASE.

This case had most of the cardinal symptoms of the disease.

We learn from it that in all probability other vessels besides those of the extremities are affected in thrombo-angiitis obliterans.

The section of the dorsalis pedis is typical of thrombo-angiitis obliterans, viz., degeneration of media, some hypertrophy of intima and an organised red thrombus which has become canalised.
FIFTH CASE.

Although I never had the opportunity of examining this patient as the man died in February 1918, I am giving a description of this case, because I have been able to study carefully the histo-pathology. He was shewn by Dr Parkes Weber at the Royal Society of Medicine in Wimpole Street, London, in October 1917, as a case of thrombo-angiitis obliterans. A full report is found in the Proceedings of the Royal Society of Medicine Clinical Section 1917, Vol.X, p.18. He was later admitted to the London Hospital where he died after an amputation of the right leg.

The clinical history of the case is based on Dr Weber's report and also on notes from the London Hospital. I am indebted to Dr P. Weber and the Medical Registrar of the London Hospital for giving me permission to use their notes.

Prof. Turnbull of the Pathological Institute of the London Hospital kindly put his private notes at my service and allowed me to make a careful study of the sections of the vessels which he made after the leg was amputated. I am greatly indebted to him for the valuable help he gave me in the elucidation of some of the more obscure points in the microscopic anatomy.
anatomy. But I must take all responsibility for the opinions expressed in the following description and interpretation of the microscopic changes.

He referred me to an article which he published in the Quarterly Journal of Medicine in 1914 on alterations in arterial structure. I found this extremely useful for the purpose of grasping the anatomy of the various layers of the vessel wall, especially those of the intima.

J. G., male Polish Jew, born 1872 in Poland. Died 1918 in London. (No P.M. examination of the body was made.)

History:—In August 1916 he noticed a small black spot on the inner side of the right big toe. There was no pain with it, and after receiving treatment at the German Hospital the foot got quite well. But a few months after this he developed a painful stiffness in the calf muscle whenever he walked for any distance. This obliged him to rest for a few minutes. (Intermittent Claudication).

In July 1917 he developed pain of another kind, the so-called ischaemic pain, in the distal part of the right foot, which for about the same period has been red or cyanosed when in a dependent position. This pain is worse at night and prevents him from sleeping.\/
sleeping. His blood serum gave a negative Wassermann reaction. Dr Weber treated him by passive hyperaemia according to Bier's method, and gave him moderate doses of KI., and opiates for insomnia. He improved and remained well till January 1918 when the distal half of the right foot became swollen and a blackish patch appeared on the dorsum of the foot. The discoloration spread and an ulcer formed.

**Physical examination on admission to the London Hospital on 12th January, 1918.**

Right great toe is shrunken and black as far as the metatarso-phalangeal joint. There is a swollen red area 1\(\frac{1}{2}\)" wide round the black area. R. Femoral artery pulsating well. But no pulse in right popliteal or dorsalis pedis artery. Movements at ankle joint normal. He smokes ten cigarettes a day.

Wassermann reaction negative.

**14.1.18. Urine.**

Straw colour. Sp. gr. 1030.

alb. nil.
sugar nil.
reaction acid.

Pulse 96. Resp. 32.

**31.1.18. Arterio-venous anastomosis.**

R. Femoral artery and vein exposed in Scarpa's triangle when it was found that the whole of the superficial/
superficial femoral artery was shrunken and thrombosed, showing no pulsation. The common femoral was normal, the line of demarcation between pulsating and non-pulsating portion being sharply defined and situated immediately below the commencement of the Profunda Femoris artery.

Lateral arterio-venous anastomosis was performed immediately above this point. The common femoral vein above this and the left saphenous vein were ligated. The artery below was ligated and a portion removed for pathological examination. The wound was closed.

Progress after operation:-

1.2.18. Leg warmer and of better colour. Patient complains of pain in the left foot.

5.2.18. Moist gangrene setting in in right foot and great toe.

7.2.18. Leg amputated through the middle of the thigh.

12.2.18. Rigor. T. 103.5°C.

15.2.18. Rigor. T. 106°C.

18.2.18. Death.

Macroscopic Report of Femoral artery removed by the surgeon.

At one end the lumen is filled by shrunken reddish brown glistening tissue; at the other end there is white tissue obliterating the lumen.

Macroscopic/
Macroscopic report of amputated leg and vessels.

The leg was removed 23 c.m. above the knee joint. The femoral, popliteal, anterior and posterior tibial and peroneal vessels were dissected out and placed in formalin.

Arteries and veins were matted to surrounding tissue throughout.

The femoral and popliteal arteries were filled by gritty firm elastic tissue of a whitish colour. Anterior tibial artery - lumen a slit placed more at one side. This patent lumen is continued to dorsalis pedis peroneal and posterior tibial; lumina greatly reduced in size. At some places only of pinhole size. Femoral popliteal anterior and posterior tibial veins were filled by reddish clots.

Microscopic findings:-

1. Femoral artery upper portion 23 c.m. from knee.
   
   Adventitia - No abnormality visible.
   Media:
   
   Muscle fibres show marked degeneration, especially towards inner two thirds where the nuclei are very scanty and where the muscle fibres are largely replaced by delicate elastic fibres stained blue with Weigert's stain. No inflammatory tissue found. A few globules of fat can be noticed here and there which are stained by Sudan III.
Femoral Artery. 2.5 c.m. from termination of lower end of Popliteal A. (Weigert's elastic stain) X 45.

1. Adventitia.
2. Media, muscular fibres distinct.
3. Media (inner 2/3) largely replaced by elastic fibres. Muscular fibres degenerated or absent.
4. Elastic lamella (outer lamina) and boundary stripe inner (lamina) with thin musculo-elastic between them.

5. Thickened hyperplastic consisting entirely of elastic tissue.
6. Organised thrombus consisting mainly of connective tissue.
7. (?) An elastic lamina limiting thrombus.
8. Lumen reduced to about half original size.
Lamella - The elastic lamella is sinuous and deficient in several places.

Intima - The elastic stripe is separated from the lamella for a variable distance and is fragmented and stains badly in some places.

Between the two lie some longitudinally directed muscle fibres and a large amount of elastic tissue, which stains blue with Weigert's. This zone is evidently the musculo-elastic zone of Thoma. Fat globules are seen here and there stained yellow by Sudan III. The stripe and portions of the stout elastic fibres internal to it are stained by Sudan. This zone evidently corresponds to the Hyperplastic layer of Jores.

Lumen. The lumen internal to the hyperplastic layer is filled completely by vascularised tissue. This is largely made up of callagenous material and some elastic fibres; globules of fat are seen here and there. A number of arterioles with well formed walls, muscular and elastic lamellae are seen.

Foci of black pigment are visible.

2. Femoral Artery - 20 c.m. above termination of Popliteal.

This section differs from the previous as follows: - Only half of the lumen is occupied by tissue, which is poorly vascularised.
Femoral Artery. 1 1/2 c.m. from term. of Popliteal A. (V. G. Stain) X 30.

1. Elastica externa.
2. Media.
3. Internal elastic lamina. Separated into two layers of elastic tissue at (4) & (5) with musculo-elastic between them.
4. Greatly hypertrophied and degenerated hyperplastic layer of Joros in which are seen masses of elastic fibres (showing up dark in the photo.)
5. Organised thrombus consisting of connective tissue and containing one large blood channel (10) and many small capillaries.
6. Media of branch of Femoral cut tangentially and terminating at (9) where thickening of the intima is seen.

(8 (a) and 9 (a) ) same as (8) and (9).

10. Large blood vessel. 11. Small blood vessels.
The obstructing mass is of looser structure and contains only a few new blood vessels. The hyperplastic layer contrasts well with the vascularised substance in that it stains with Weigert's, whereas the tissue in the lumen contains hardly any elastic tissue. The organised tissue contains a large amount of intracellular fat globules and much blood pigment, much more so than in the previous section.

We are here evidently dealing with a younger vascularised tissue.

3. In the section a centimetre or so lower down the patent part of the lumen is much smaller than in (2). There is a recently formed red thrombus adherent to the hyperplastic layer, which bounds the patent part of the lumen.

4. Femoral artery lower end 17 cms. above termination of popliteal.

The inner two-thirds of the media shows an absence of muscle fibres and an increase of stroma and resembles that of the sections higher up. The tissue inside the boundary stripe blocks the lumen and may be divided into two parts as they vary greatly in structure. The one part consists of organised tissue, traversed by badly formed channels, and containing pigment, very little elastic tissue and very dense collagen fibres. This is bounded on one side by a somewhat/
somewhat thickened hyperplastic layer, while on the other side it abuts against a zone which contains very dense masses of elastic tissue, continuous with the elastic stripe. This forms the second part. The elastic fibres here are very abundant and cannot be distinguished from the hyperplastic layer of the intima. This area is traversed by two large branches of the femoral which can be traced outside the femoral artery as they are here cut tangentially. It looks as though these masses of elastic tissue which take up half of what must once have been the lumen are developed from the hyperplastic layer and not from any preceding thrombus.

Interpretation:- It is very difficult to say which end of the femoral was occluded first, though the enormous hypertrophy of the hyperplastic layer together with the large size of the vessels in the lower end suggests that there was in the distal part of the femoral artery a great narrowing of the lumen before the vessel was finally occluded by a thrombus. The thickening of the intima must therefore be blamed for the final occlusion of the vessel.

The femoral vein is filled by a red thrombus. The walls appear normal. Some of the smaller veins are patent.
Popliteal Artery (6 c.m. from term.)

Weigert's Elastic Stain. X 30.

1. Elastica externa.
2. Media containing many elastic fibres in places which are dark.
3. Elastic lamella.
4. Boundary stripe.
5. Thin degenerated musculo-elastic between (3) & (4).
7. Organised thrombus occluding greatly reduced lumen.
8. Masses of elastic tissue in hyperplastic layer.
9. Masses of connective tissue in hyperplastic layer.
10. Small canalising vessel in organised thrombus.
11. New elastic lamina separating hyperplastic layer from organised thrombus.
12. Fault in staining section.
5. Popliteal Artery - 6 cms. from bifurcation.

Media. As in the femoral the media in its inner two thirds shows very few muscle fibres and few nuclei. In their stead are found numerous elastic fibres and a fibrillar stroma.

Intima - The musculo-elastic coat varies in thickness. In one place it is nearly one half the width of the media. Internal to the musculo-elastic coat is a layer which varies enormously in size. Were it not for the fact that at one place it is only slightly thickened, it would be difficult to say that it is the hyperplastic layer (of Jores) of the intima.

In two places especially is this great increase noticeable. One of these has a width four times that of the media, and takes up more than half of the space inside the elastic lamella. It consists of elastic and fibrous tissue bounded internally by a stout elastic lamella which can be traced to where it joins the boundary stripe and the intima. This mass forms a crescent, and contains a few capillaries in its outer part, but no blood pigment.

The other thickening has a width of a little more than that of the adjacent media.

These two crescentic thickenings reduce the lumen by more than three quarters.
The lumen is filled by organised tissue as in the femoral, containing numerous well formed arterioles, blood pigment and some elastic fibres, and appears to be of the same date as in femoral (1).

The Popliteal Vein. The intima of the popliteal vein is somewhat hypertrophied and surrounds an organised thrombus containing in parts masses of round cells.

Interpretation - It is evident that before the organised tissue appeared in the lumen, and so finally destroyed the irrigating properties of the popliteal artery, the lumen of this vessel had been greatly reduced in size by the two crescentic swellings of the intima. It is clear from a close study of the topography of the vessel that the layer from which the hypertrophied masses spring is the hyperplastic layer of the intima. There has been much degeneration in the larger swelling, some of the elastic tissue being replaced by fibrous tissue.

The changes in this vessel will be again referred to when the pathology of the disease is discussed. It will there be shewn that in all probability the failure of the blood supply to the vessels of the foot was dependent on the degeneration of the hypertrophied intima of the popliteal artery. Moreover that we need not fall back on a primary thrombosis,
1. Elastica externa.
2. Media inner 2/3 degenerated.
3. Elastic interna (2 lamina seen). Here are seen areas of fat having the degenerated internal elastic lamina yellow with sudan III.
4. Hyperplastic layer of Jores showing areas of fat as in (3).
5. New layer of elastic tissue in hyperplastic layer which is healthy.
6. Organised thrombus.
7. A new layer of elastic tissue in hyperplastic with areas of fat in it as in (3).
thrombosis, when we search for an explanation of the phenomena which are so characteristic of the disease, namely, Intermittent claudication, ischaemic ulcers and ischaemic pain, and gangrene.

6. Popliteal Artery - 3 cm. from bifurcation.

The media shews more muscular tissue in its inner two-thirds than the previous section. The intima has several large thickenings, one of which is equal to the width of the adjacent media. They are evidently enlargements of the hyperplastic layer.

The lumen is occluded by organised tissue of a similar nature to that in the previous sections.

The Veins. There are two venae comites. One contains a red thrombus. The other is occluded by vascularised fibrous tissue. The segment lying next to the artery is devoid of muscular coat or intima and the breach in the wall is replaced by fibrous tissue, which is permeated by large arterioles. The rest of the wall shews little change, except that it is invaded by newly formed arterioles and capillaries.

Interpretation - The lumen is occupied by granulation tissue which is of much later date than the focal area of the enlarged hyperplastic layer of the intima of the artery. There are far more capillaries and the tissue formation/
Posterior Tibial Artery.
(Weigert's Stain) X 140.

1. Matting of peri-adventitia.
2. Adventitia.
4. Greatly crenated intima. Elastic lamella (outer and boundary stripe (inner) with musculo elastic layer easily seen.
5. Fibrous tissue ocluding lumen.
6. Haemosiderin pigment in fibrosed thrombus.
formation is not so dense.

The erosion of a segment of the wall is difficult to explain. The extreme vascularity of the thrombus and the invasion of this segment by several large vessels point to secondary recent infection. Moreover two small veins, probably branches of the occluded veins just discussed, are invaded by a round celled infiltratia. All this points to a phlebitis of recent origin.

7. Posterior Tibial Artery:-

The vessel is collapsed, and the elastic lamella is greatly crenated, and the lumen is completely filled by vascularised thrombus which contains much blood pigment, and newly formed blood vessels. There is some irregular thickening of the intima in places. It is difficult to estimate the relative thickness of intima owing to collapse of the vessel.

Veins. The artery is accompanied by three veins, two of which show great thickening of the intima. One of these veins is occluded by organised tissue similar to that in the veins. Another also contains granulation tissue with pigment, but differs from the other veins in that it has a large eccentric newly formed channel which contains a thrombus. The third vein shows thickenings in the intima. The veins are not collapsed.

Interpretation:-/
Interpretation:— The occlusion of the artery and one vein has apparently taken place at the same time, but much later than in the popliteal or femoral artery. The large amount of pigment and marked cellularity indicate a more recent formation. The collapse of the artery indicated by the marked tortuosity of the elastic lamella is a strong proof that the collapse was probably due to the failure of the blood supply from the parent vessel, viz:— popliteal. This is a further proof that the changes in the posterior tibial took place after the organisation of the popliteal.

8. **External Plantar Artery:**—

There is extensive necrosis of artery and tissues around. The coats of the vessel can hardly be distinguished. A few streptococci and diplococci and scattered leucocytes can be noticed. The lumen of the vessel is filled by tissue which has a very loose structure and indicates necrosis. No pigment granules visible.

The veins are occluded by loose tissue which contains some pigment.

Interpretation:— Owing to the necrotic change in the tissues, resulting from the acute streptococcal infection, it/
Anterior Tibial A. & V. (V. G. Stain) X 90.

**Artery**
1. Media healthy - relatively thick owing to collapse of vessel (?)
2. Intima thickened in places.
3. White thrombus adherent to intima.
4. White thrombus free in lumen.
5. Matting of peri-adventitia.

**Vein**
6. Media of vein.
7. Red thrombus and
8. Adherent white thrombus.
9. Invasion of red thrombus by endothelium from intima.
it is impossible to say when the vessels were occluded. But the scarcity of the elastic and collagen fibres which would resist necrotic change for some time, indicates a formation of more recent date than that in the posterior tibial.

Anterior tibial artery - The appearances vary but little throughout the length of the vessel. It is collapsed and the irregular narrow slit-like lumen, contains a small white thrombus which, however, does not completely occlude it. About half way down, the thrombus is glued to the vessel wall and is being invaded by cells from the intima.

The media is thick but not degenerated. The layers of the intima are easily distinguished and the well-marked hyperplastic layer has several thickenings. The elastic lamella is crenated and broken in several places, and has several calcified foci.

There are three venae comites, two of which contain red thrombi which are being invaded by spindle cells from the somewhat irregularly thickened intima.

Interpretation: - The artery shews signs of degenerative changes. The collapse is of recent origin, as there is only very early organisation in the white thrombosis. The veins have a somewhat thickened intima.
Dorsalis Pedis Artery (V. G. Stain) X 250.

1. Media.
2. Elastic lamella - greatly crenated (fine and coarse crenations.)
3. Musculo-elastic of Thoma very thick - some nuclei seen.
4. Boundary stripe of intima.
5. Thickening in hyperplastic layer of intima.
6. White thrombus (containing many leucocytes).
7. Spaces between the occluding thrombus and hyperplastic layer of intima. Some of these spaces are beginning to be lined by endothelium from intima, others may be due to mounting.
8. Endothelium lined channel in thrombus.
9. Large endothelium lined channels in thrombus containing red blood corpuscles.
10. A space being formed into a capillary by being lined by endothelium.
10. **Dorsalis Pedis Artery.**

The lumen of the artery is narrow, very irregularly crenated and occluded by vascularised tissue. The media is well formed, and shews no changes. It is traversed by numerous large capillaries, some running parallel to the muscular layers; others at right angles evidently making for the lumen. The elastic lamella is stout, but very much collapsed, having both normal and very coarse crenations, the latter evidently due to arterial collapse. The musculo-elastic shews very few cells, and varies in width. It has one very marked thickening opposite a corresponding thickening in the hyperplastic layer of the intima, each of which being about a quarter of the lumen in width.

The boundary stripe of the intima is fragmented. The hyperplastic layer is irregularly hypertrophied and of rather loose cellular structure. It has a thickening which has already been described. The lumen is occluded by loose fibrous tissue, which has little elastic material. There are very few cells here, and these are mainly spindles. There are no pigment granules. The occluding mass is permeated by many capillaries, some of which are still in the process of formation.

Veins./
Veins. There are three venae comites, the lumina of which are occluded with dense fibrous tissue. Each of these masses is traversed by a channel. In two cases these new channels have well formed muscular walls, and in the intimae there are many rings of elastic tissue.

Interpretation: There are old degenerative changes in the intima of the artery. The collapse is probably due to the lack of blood which ordinarily keeps the vessel distended, and the elastic lamella more or less taut.

The primary nature of the occluding tissue is doubtful. It may have been a white thrombus, not sufficient to block the lumen completely. The lumen collapsed on to it and the empty spaces left were filled in by proliferation from the intima which helped to form the blood channels.

This will account for the absence of blood pigment.

The origin of the fibrous tissue in the lumen is probably of much later date than that in the posterior tibial. The young capillaries are indicative of this.

The granulation tissue in the veins seems to be older than the similar tissue in the posterior tibial. The large amount of elastic tissue around the newly formed channels inside the lumina of the veins signifies that the organisation is old.
Peroneal Artery (Upper end.)
Weigert’s Stain X 90.

1. Elastica externa.
2. Media.
3. Elastic lamella.
4. Musculo elastic between (3) & (5)
5. Boundary stripe.
6. Areas of great hypertrophy of hyperplastic layer.
7. Organised thrombus containing many.
8. Canalising vessels lined by endothelium only.
11. Peroneal artery.

Vessel somewhat contracted. The inner third of the media has few nuclei, but contains many elastic fibres. A few foci of calcification are present in the region of the elastic lamella.

The intima is thickened throughout and in several places is equal to about half the width of the media.

The lumen is filled by loose fibrous tissue which is traversed by very large channels which are lined by endothelium only, but a few small vessels have a muscular coat as well.

Veins. The two venae comites are filled by mixed thrombi; in one of these veins the thrombus is being invaded by cells from a somewhat thickened intima.

Interpretation:— The granulation tissue in lumen of the artery is of more recent date than that in the posterior tibial.

The marked looseness of the granulation tissue, and the irregular empty spaces near the intima which have not yet been lined by endothelium suggest that the thrombus was not large enough to fill the lumen after the blood supply from the parent trunk had been cut off. This might explain the large size of the endothelium lined channels helping to avoid a vacuum as it were.
Peroneal Artery (Middle) (Weigert's Elastic Stain) X 90.

1. Adventitia.
2. Media.
3. Irregularly thickened intima.
4. Lumen almost empty and collapsed.
5. Small white thrombus in lumen.
The absence of pigment suggests a white thrombus. It is likely that some of the tissue in the lumen has been poured out from the intima so as to help in the filling of the space. The almost complete absence of blood in the large channels suggests a recent origin and also that these channels were formed locally and have as yet no connection with similar channels higher up.

The questions now to be answered are:-

1. Where did the thrombus commence?

2. Was the thrombus due to a primary clotting owing to some change in the blood or was it secondary to disease in the blood vessels?

To answer these questions an investigation into the age of the thrombus in the various vessels is essential.

The relative age of thrombus formation can be arrived at with some accuracy by studying the occluding masses from the point of view of:-

1. Amount of collagen fibres and lack of cellularity.

2. Amount of elastic fibres.

3. Number of pigment granules (haemosiderin) found to give the Prussian blue reaction.

4./
4. Collapse of lumen and crenation of lamella of intima - the assumption being that these phenomena are due to deficient blood which normally distends the vessels.

The age of a thrombus varies in accordance with the number of collagen fibres and lack of cellularity, the older thrombi having more fibres and fewer cells. Applying this to our case the conclusion is that the age of the thrombus increases from the peripheral vessels upwards to the popliteal and femoral.

The thrombi in the popliteal and femoral have the greatest number of elastic fibres, and this number diminishes as we descend. The popliteal and femoral therefore have the oldest thrombi.

With regard to the pigment it is somewhat difficult to arrive at the age with any great certainty because the proportion of red blood corpuscles to whites in the thrombi probably varied a good deal. This is especially seen on a close study of the recently formed thrombi in the veins. Here some thrombi are white, some red and others mixed. The same may have been the case with the arteries. For instance the recent thrombus in the anterior tibial is white. One would here not expect to find any blood pigment after the organisation of the thrombus.

This may explain the absence of pigment granules in the dorsalis pedis.
Dorsalis Pedis Artery and Venae Comites.
Weigert's Elastic Stain X 45.

Artery
1. Adventitia and elastica externa.
2. Media - containing many channels.
3. Thickening in intima.
4. Vein within a vein with many layers of elastic of elastic tissue round lumen.
5. Like (4) but not so marked.
The number of granules increases as we follow the main trunk to its distribution in the foot with the exception of the already mentioned dorsalis pedis and anterior tibial arteries. Assuming that the proportion of pigment was originally the same, i.e. before absorption took place, the conclusion is that the age of the thrombus increases as we ascend, the age varying inversely to the number of pigment granules owing to their constant removal.

If the coarse crenation in the lamella of the dorsalis pedis and peroneal are due to the collapse of the vessel walls following failure of the blood stream, then the assumption is that the thrombi in these vessels is of comparatively recent origin. This is certainly in keeping with the other points about the age of the thrombus.

**SUMMARY OF FINDINGS IN THE VEINS.**

A. Organisation of thrombus in lumen is found in some of the venae comites of upper peroneal, upper posterior tibial, etc.

B. Organisation together with some elastic round canalising veins is found in some of the venae comites of dorsalis pedis, posterior tibial, external plantar.
Popliteal Artery. 6 c.m.s. from Termination (V.G. Stain) X 250

1. Healthy muscle fibres in media.
2. Vessel which is passing through media and running to lumen where it will anastomose with vessels canalising the occluding tissue.
3. Degenerated media inner 2/3 - few nuclei, some elastic fibres and connective tissue almost complete absence of muscle fibres in places.
4. Elastic lamella.
5. Musculo elastic layer of Thoma, degenerated, an absence of longitudinal elastic fibres. Only a few nuclei left.
6. Boundary strips staining badly.
7. Hypertrophied hyperplastic layer of intima.
C. Organising polyp is found in the upper and anterior tibial.

D. Thrombus only is seen in some venae comites of the popliteal, femoral and peroneal arteries.

E. Lumen free is seen in some of the venae comites of the lower end of the peroneal.

The tendency here is for the smaller peripheral veins to have the older thrombi, as judged by the amount of elastic tissue in the canalising vessels. Owing to superadded phlebitis, however, it is difficult to estimate the age of the thrombi.

SUMMARY OF CHANGES IN THE ARTERIES.

Periarteritis - Some periarteritis which firmly gums the vessels to the surrounding tissue is to be seen in many vessels.

Medial fibres degenerated in inner 2/3 of femoral and popliteal. Degeneration also seen in peroneal, anterior tibial, posterior tibial and external plantar.

Intimal hypertrophy and degeneration seen in most vessels.

The first question - in which vessel did the thrombus start - can now be answered.
The answer to this is the popliteal, and for two reasons. Not only is the organised tissue of the canalised thrombus the oldest for reasons already given, but the degeneration of the vessel wall especially of the intima also shews the most advanced stages.

The second question - was the thrombus due to a primary clotting owing to some change in the blood, e.g. to some toxic condition or to increased viscosity of the blood, or was it secondary to degenerative changes in the vessel itself - can now be answered.

The extensive disease especially the popliteal femoral and some of the smaller vessels which in some cases had reduced the lumen to a quarter the original size, must have been sufficient to slow the bloodstream and cause thrombosis. Moreover, the degeneration in some parts seems to have altered the intima to such an extent that desquamation was inevitable. Another point must be taken into consideration. The hypertrophy and subsequent degeneration of the hyperplastic layer of the intima is not uniform for any great distance even in the same vessel, let alone in the different vessels. In one place the lumen is a quarter while a few centimetres away it is one half the original size. The lumen varies from place to/
1. Elastica externa.
2. Media containing many elastic fibres in places which are dark.
3. Elastic lamella.
4. Boundary stripe.
5. Thin degenerated musculo-elastic between (3) & (4).
7. Organised thrombus occluding greatly reduced lumen.
8. Masses of elastic tissue in hyperplastic layer.
9. Masses of connective tissue in hyperplastic layer.
10. Small canalising vessel in organised thrombus.
11. New elastic lamina separating hyperplastic layer from organised thrombus.
12. Fault in staining section.
to place. This must have tended towards the formation of eddies and backwaters as it were, where the blood would be under very slight influence of the momentum from a greatly diminished stream.

This would necessarily lead to stagnation and eventual clotting.

Our answer to the second question is that the thrombosis was secondary to changes in the vessel walls.

The conclusion based on a study of the pathology of the case just discussed amplifies Leo Buerger's view. He says that the condition is due to a thrombotic process in the arteries and veins followed by organisation and coanalisation, and not to an obliterating endarteritis.

Leo Buerger in his original article on Thrombo-Angiitis Obliterans says that the "popliteal frequently shows no change." Our case shows very extensive change in the popliteal artery.

He bases his views on a study of 19 cases, and "suggests the names endarteritis obliterans and arterio-sclerotic gangrene should be abandoned in favour of thrombo-angiitis obliterans."

Von Winiwarter and Friedlander described the obliteration as due to proliferation of soft tissue from the intima coat.
The larger vessels in our case, viz:- the popliteal and femoral seem to show that there was a primary hypertrophy followed by degeneration which greatly reduced the size of the lumen. The reduced lumen was then finally occluded by a thrombus.

Unfortunately no post-mortem examination has so far been made on a case dead from thrombo-angiitis obliterans.

"The majority of anatomo-pathological conditions are misleading. Even post-mortem examinations would only show late stages of the changes". (Dr Parkes Weber in a private letter). With this I entirely agree.

The patient S.K. (fourth case) from whose leg the first sections were made, shows signs of vascular mischief in his cerebral vessels, viz:- the amnesia, weakness in the right arm, and changes in the retinal vessels.

One of Dr Parkes Weber’s cases died with symptoms of angina pectoris, possibly connected with thrombo-angiitis of one or both coronary arteries of the heart

He says it is possible that some cases of erythraemia may be due to a kind of thrombo-angiitis obliterans in the spleen and other viscera, giving rise to thrombotic infarctions in the spleen, etc.
ETIOLOGY.

The disease is not hereditary. No case has so far been reported where the disease was found in the parents or grand-parents. There seems to be no inherent weakness in vessels or any tendency to clotting of the blood. This is borne out by one of my five cases - M.R. - who tried to induce an attack of varicose veins by tying a tight elastic bandage round the thigh immediately above the knee. He used to keep this on for the greater part of the day until his leg would swell enormously. No bad effects followed after carrying out this manoeuvre for 6 weeks.

The disease is not associated with any particular diathesis, nor with any acquired disease, such as syphilis, alcoholism, malaria, albuminuria or gout. Excessive cigarette smoking has been offered as a cause of this disease by Dr Parkes Weber\(^2\); Willie Meyer\(^10\) of New York and others. This is not borne out in my cases. On enquiry it was found that none of them smoked more than about ten or fifteen cigarettes per diem. In one case I was told that as he was employed in a tailor’s shop where smoking was forbidden, he could only smoke for a few hours a day when he was off work. Moreover cases have been reported in people who were practically non-smokers.
Hebrew women from Eastern Europe certainly do not smoke, and this has been put forward as an added reason why their sex is not affected. Against it can be said that according to Duncan White⁸ "In China the women smoke almost as much as the men and smoke the same kind of tobacco." Osler and Macrae¹¹ say "It is difficult to believe that tobacco can have a very important influence". Were the disease due to cigarette smoking, it would be far more common and would not be confined to any one race or sex.

Hyperpiesis, a name given by Sir Clifford Allbutt⁶ to primary conditions of high blood pressure and the subsequent changes in the vessels following thereon, has no relation to Thrombo-angiitis obliterans, in which the blood pressure is usually low.

Occupation has been advocated as a cause. The squatting position of tailors is supposed to interfere with the free flow of blood. Against it can be said that the disease occurs in people of different walks in life. One of my cases was a solicitor who had to do a good deal of standing. Ergot of rye has not been found to have any connection with the disease as thrombo-angiitis obliterans is found among men who have never eaten rye bread.

Trauma/
Trauma seems to play only an indirect part in the causation of the disease; a slight injury or small operation such as removal of a toe-nail may bring on a train of symptoms of which there had only been the slightest suggestion.

The disease is very insidious in its onset. There is evidently a broad margin of safety in the irrigating capacity of the blood channels. We do not know when the pathological changes in the arteries and veins which begin with intermittent painful limping and culminate in gangrene, actually begin. The histo-pathological picture is of old standing. Long before the patient is aware of trouble in the as yet unaffected limb, pulseless vessels warn the observer of danger to come.

Chemical examination of the blood.

Dr Willie Meyer\textsuperscript{10} states that the chemical examination shews:

1. No retention of waste nitrogenous constituents.

2. No marked decrease of alkaline reserve of the blood by Van Slyke's method.

3. But a high sugar tolerance of the blood, and therefore he calls the condition "Glycophilia".
Increased coagulability.

"There are undoubtedly certain families in which a tendency to thrombosis exists—thrombophilic in contact to those haemophilic families in which a tendency to bleed is such a pronounced feature". (Osler and Macrae)

This is offered as a possible explanation of the thrombosis which is such a universal phenomenon in thrombo-angiitis obliterans.

One of my cases—S.K.—bled a good deal from a cut in his foot as a result of a bicycle accident. Severe symptoms of the disease followed rapidly after this slight injury.

In connection with the point raised here, it may be mentioned that in 1915 Mayesima of Japan, where a form of gangrene of the young is said to be prevalent, demonstrated that there was a constant high viscosity of the blood in all types of gangrene. The intravenous sod. citrate method of treating thrombo-angiitis obliterans is based on this fact.

Typhus Fever. Dr. Goodman who saw a number of cases in South Eastern Europe thinks the disease may be due to the typhus fever virus. With the doubtful exception of one, none of my cases had typhus. The lay people of Eastern Europe/
Europe make no distinction between typhus and typhoid. This may have misled Dr Goodman.

**Toxic Theory.** Agreeing with Leo Buerger, Dr MacCallum says: "The obstruction is generally accompanied by the formation of adhesions between the vessel and the surrounding tissue, and although no definite ideas as to its causation are to be found in the literature, it seems probable that it is of infectious or toxic nature."
TREATMENT.

(1) Drugs.
(2) Ionisation.
(3) Hyperaemia.
(4) Anti-coagulants.
(5) Surgical.

Drugs. There are no specific drugs for this disease. The late Dr Morgan Dockerell of St John's Hospital, Leicester Square, used to give enormous doses of Potassium Iodide for tertiary syphilitic conditions. My first case, which received marked benefit from his treatment, was given up to 200 grains of this drug per diem, in the hope of removing the obstructing tissue from the vessels. Nitroglycerine or some other vaso-dilator might be tried. Fibro-lysin has been tried; morphia for pain is often called for.

Iron tonics are strongly indicated when signs of anaemia and debility make their appearance. This may be combined with a little wine. As a local application after sloughing has appeared, which causes severe pain, there is nothing so useful as the ointment already described in connection with the first case. These patients stand wet dressings very badly as these aggravate the pain.

Ionisation./
Ionisation. This is very useful for the ischaemic ulcers. In my opinion zinc sulphate is the best drug. We know its value in trophic ulcers in tabetic conditions, and it certainly does good in this disease.

Passive Hyperaemia. My first patient - H.K. - discovered that keeping the leg in a dependent position gave great relief from the nagging pain. As the pain is of an ischaemic nature, the rationale of this procedure is easily seen. Sinkowitz and Gottlieb claim good results with Bier's suction cylinder. This they apply for five to fifteen minutes three times weekly.

Dr Ginsburgh ligated the femoral in the hope of slowing the venous return and so induce a constant hyperaemia.

Anti coagulants. Dr Koga and Dr Willie Meyer basing their practice on the researches of Mayesima who shewed that there was a constant high viscosity of the blood in all types of gangrene, administered 2% sodium citrate solution in conjunction with Ringer's solution hyperdermically.

Dr Meyer gives 250 cc. of a 2% sod. citrate at a temperature of 110°F. every second day. This is continued until improvement is noticed. He claims excellent/
excellent results in advanced cases. In the only case I have seen this method tried, the results were not encouraging.

Surgical. Various operations have been performed with a view to either increasing the arterial blood supply or inducing passive hyperaemia. The latter has already been described. For the former implantation of the proximal end of the femoral artery into the femoral vein has been performed. This has been an utter failure as it is based on a false pathology. The veins as we have seen, as well as the arteries suffer in this disease. Moreover we do not as yet know the exact starting point of the disease. For all we know, the common iliacs may be affected as well.

With regard to minor operations such as the removal of a nail or the amputation of a toe, great care has to be exercised. But according to Dr Parkes Weber and from what I have seen myself, these cases are best left alone. Several of my cases got decidedly worse after small operations. The disarticulation of the great toe at the metatarso-phalangeal joint in one of my cases led to a neuritis with contraction of the ham-strings resulting in permanent disability to straighten the knee.

H.K./
THROMBO-ANGIITIS OBLITERANS.

First Case.

Condition of feet 7 years after onset of disease.
Result of conservative treatment.
H.K., my first case, always got worse after operative interference. Last time I saw him, nature had amputated the right great toe. The wound was granulating nicely, and the patient was able to walk about. All pain had ceased.

As the disease has a tendency to become quiescent great patience has to be exercised. Even dry gangrene is not an indication for operative interference. After many years the affected members drop off and the disease causes no further trouble.

If an amputation has to be performed for moist spreading gangrene, the higher in the thigh the operation is performed, the better. Even then the main arterial channels may not bleed after the removal of the tourniquet and the stump may slough.
Popliteal Artery (6 cm. from termn.)
Weigert's Elastic Stain. X 30.

1. Elastica externa.
2. Media containing many elastic fibres in places which are dark.
3. Elastic lamella.
4. Boundary stripe.
5. Thin degenerated musculo-elastic between (3) & (4).
7. Organised thrombus occluding greatly reduced lumen.
8. Masses of elastic tissue in hyperplastic layer.
9. Masses of connective tissue in hyperplastic layer.
10. Small canalising vessel in organised thrombus.
11. New elastic lamina separating hyperplastic layer from organised thrombus.
12. Fault in staining section.
CONCLUSIONS.

(1) Ultimate etiology is unknown.

(2) The disease starts in the larger (viz:-popliteal arteries) and not in the smaller blood-vessels as Buerger claims.

(3) Immediate cause of symptoms is thrombosis secondary to hypertrophy and degeneration of intima; Buerger's says the thrombosis is primary and is not due to vascular changes.

(4) Operative interference should not be resorted to except in very extreme emergencies such as absolutely unbearable pain and moist spreading gangrene.

(5) The disease tends to become quiescent after the lapse of many years.
REFERENCES

17./