Resume of thrombo angiitis obliterans (buerger's disease)

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A RESUME

OF

THROMBO-ANGIITIS OBLITERANS

(Buerger's Disease)

- BY -

WILLIAM F. SRCL

UNIVERSITY OF NEBRASKA

COLLEGE OF MEDICINE

1932
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In this study of thrombo-angiitis obliterans, by a review of the more recent literature on the subject, I have in my own mind, made friends with a disease which well merits attention. It is of interest, not only from the standpoint of the disease itself, but from the insight which the study gives into the other allied affections of the extremeties. I quote Buerger (l) in this regard: "A careful consideration and investigation of all basic as well as the many clinical phenomena characteristic of thrombo-angiitis obliterans, will do more in a practical way to fashion and shape our concepts of the vasomotor and trophic neuroses and all allied organic affections of the vessels of the limbs, than the study of any other single or group of such diseases. And this is true because manifestations of almost all of the morbid conditions in question are represented in this one interesting malady." Of course, I have not gone into the study as deeply as Buerger suggests but I feel that I have made a slight acquaintance with what he suggests.

In the nineteenth century and during the early years of the twentieth century the medical profession began to recognize thrombo-angiitis obliterans as a definite disease having its own clinical manifestations. The past decade has witnessed radical changes in the treatment of this disease and altered the aspect of the prognosis although the pathology has remained
quite the same as described by Buerger in 1908.

The condition is one which is peculiar in many ways. In the first place, it is confined almost invariably to the male sex. However, some few cases have been reported in females. Second, it is a disease of young adult life (20 to 40 years). Third, it is more common among Jewish people than in any one other single race, although all other nationalities are also attacked, especially those of the yellow race. Fourth, the lesions occur in the lower extremities much more frequently than in the upper.

It is not within the scope of this paper to include any elaborate exposition of this disease. Suffice it here to give a general description of the disease, with slight elaboration on the general in some of its parts. Six case reports are presented which emphasize some of the more common symptoms and the various methods of treatment of the disease.

HISTORY

The historical development of our knowledge of thrombo-angiitis obliterans is at first intimately connected with that of all the vascular diseases of the extremities. The pioneer work was mainly done in connection with the study of gangrene. The first definite reference of the relationship of gangrene to disease of the arteries, to our knowledge, was that of Quesnay in 1739, but the idea of an obstacle to the course of the blood was not clearly stated until 1817 by Mébréard. Virchow later worked on embolism and thrombosis and clearly defined the mechanism for the genesis of gangrene due to embolism and thrombosis and thus gave a new direction to research in this field.

In 1862, Raynaud (2) published his these on the vascular
diseases and brought out conclusively that there is a form of
gangrene with demonstrable organic disease or occlusion of the
arteries. Then in 1876, Friedlander (3) first described a con-
dition which he called obliterator vascular disease of the ex-
tremeties. A. M. Graves (4) asserts that thrombo-angiitis
obliterans was first described by Charcot in 1856 but its
recognition clinically dates from the report of a case by Von
Winiwarter in 1879, who described the condition as a peculiar
type of endarteritis and endophlebitis. Being unfamiliar with
histopathology in the various stages of the disease, he in-
correctly named it "endarteritis obliterans". This term is
still often used by modern authors, as are also the non-descrip-
tive terms pre-senile gangrene, Buerger's disease, acro-cyanosis,
acro-asphyxia, dead finger, and many others. Weiss in 1895, and
Manteuffel in 1897 reported similar cases.

It was in 1908 that Leo Buerger (1), after an exhaustive
study, reported a large group of cases in the Jewish race, and
to him we owe the description of the pathologic changes, the
sequence of development and the description of this interesting
disease. He firmly established this disease as a definite clin-
cal and pathological entity, and properly termed it thrombo-
angiitis obliterans. This term, A. M. Graves (4) asserts is "a
no less complete definition of the condition than is the one
usually given in a few brief introductory sentences." Knowledge
of this disease clarified many of the doubtful cases which had
previously been diagnosed as Raynaud's disease. Todo in 1912
correlated the work of former investigators and described the
diffuse vascular inflammation with intimal proliferation and
thrombosis of the lumina of the arteries and veins. Since that time, especially during the last ten years, many cases have been reported in American and foreign literature.

ETIOLOGY

Confusion still exists as to the actual cause of this disease. Various current theories have been advanced, none of which is entirely satisfactory, in regard to the pathological changes which prevail in this condition. A microbial agent seems to be the probable one, since in the involved vessels early in the process of healing there occurs an inflammatory lesion which shows a specific and characteristic picture, and since in the acute stages certain purulent foci are usually in evidence. Thus the pathology indicates that there is an inflammation, although to date the organism has not been isolated. Difficulty in isolating the organism, if there is one, is to be expected, since the disease causes disabling symptoms only as a result of its healed process which obstructs the circulation.

Rabinowitsch (6) has isolated an organism from the blood in cases of thrombo-angiitis obliterans with which he produced vascular lesions in rabbits similar to those produced in man. Recently Buerger (7) succeeded in implanting clots from patients with "acute" thrombo-angiitis obliterans and thus produced typical lesions in the veins of inoculated persons. This work has not been corroborated by other investigators.

Syphilis was once thought of as a cause, but as positive Wasserman reactions are present in less than 10% of the reported cases, one may assume that its existence is merely a coincidence. Perla, Buerger, Kaliski, Allen, Brown, Adson and others all consider syphilis as not being a demonstrable factor.
Buerger (1) contended that the disease rarely attacks other than the Semetic male, especially those of Russian origin. Of 500 patients observed by him, only 10% were gentiles. Most of the cases reported shortly subsequent to that time were from Jewish hospitals, and thus the disease was erroneously interpreted as occurring mainly among the Hebrew race. In the Mayo Clinic up until 1931 (8) in a study of all cases of thrombo-angiitis obliterans, slightly less than 40% occurred among the Hebrews. This incidence however, exceeds many times the percentage incidence of registration in the Mayo Clinic for this race. The racial incidence depends entirely upon the section of the country, being higher in Jews in the urban districts and higher in the Gentiles in the rural districts. The remaining 60% in their series were distributed among many nationalities, i.e. Austrians, Finns, Norwegians, Germans, Scots, Irish, French, English, Dutch, Greeks, Native Americans, and those of mixed ancestry. Whyte has observed the disease in the Chinese, as have also Heleny and Miller. Ito and Koyana reported 120 cases occurring among the Japanese. Gemill reports one case found in a negro; Orr reports two cases in the male negro; others have also been reported. Thus it is evident that the disease in its geographical, climatic and racial aspects has a universal distribution. Noble in a recent article makes the statement that in all probability the disease is as common in the east as in the west. However, in the east it appears to be of a milder type than in the west.

Because of its widespread occurrence, diet and obesity can be eliminated as possible etiological factors.

Heredity has been suggested as a causative factor, but there is no proof that heredity plays an important etiological role.
S. Silbert, however, thinks that there may be some hereditarily transmitted defect, probably sex-linked in character, which plays an important role in its causation.

Occupation is apparently of no importance in the etiology although it is thought that cold and dampness may hasten its appearance in those predisposed.

As far as age is concerned, all men agree that it is a disease of early adult life. The age of onset as given by Perla is 20 to 45 years. Allen and Brown from their studies give it as 17 to 65, with the highest incidence between the ages of 30 and 50. Framenthal reported a doubtful case in a child of three years. Koyano observed a case whose symptoms began at the age of nine years, and there have been several other cases reported which began during the first decade of life. Buerger says that all age estimates will tend to be high, because it is very difficult to estimate the exact age, because of the insidious onset, and because it is overlooked in many cases. It must be borne in mind that remissions occur often, and have been known to last twenty years, that histories are inaccurate, and that a progressively increasing collateral circulation may delay the appearance of symptoms.

Of all the cases reported, there are only a very few which have ever been found in the female sex. According to Buerger the disease is almost wholly limited to the male sex. The Mayo Clinic up until the last three years has not had a proved case in the female sex. Meleney and Miller reported a case in a Chinese woman that was highly suggestive of thrombo-angiitis obliterans. Telford and Stopford (11) reported two cases in 1927 in white females which had most of the symptoms present. Buerger in his book (1) reports three cases in women. The strange thing about
the cases in females is that no pathological studies have been made
to confirm the diagnoses.

Tobacco smoking has been shown to be more prevalent in patients
with thrombo-angiitis obliterans, but one must not lose sight of
the fact that smoking might have been initiated in some cases in
order to make the painful and chronic disease less unbearable.
Allen and Brown (12) found that 20% of all the adult male patients
at the Mayo Clinic denied the use of tobacco, whereas only 1.5% of
those with thrombo-angiitis obliterans were total abstainers, but
not all were excessive smokers. Silbert (13) is convinced that
the etiologic background for this disease is intoxication from
tobacco smoking and that everyone having the disease shows a
decided improvement after discontinuation of the habit. He further
claims that there is a hereditary factor which makes these victims
susceptible to some intoxicant from the tobacco. This factor he
believes is influenced by the endocrine system. Many authors agree
and disagree with Silbert, but it is difficult to cast aside the
impression derived from case reports of the patients becoming
improved as a result of refraining from smoking.

There is always found to be a high blood viscosity in cases
of thrombo-angiitis obliterans and this is held by some observers
as a disease of the blood itself on this account. Stern, Koga and
Koyano all believe this to be a factor.

Most observers admit that there is usually found some focus of
infection somewhere in the body, when the patient first appears.
Orr (5) states that in all of his series of cases that there was
always found to be some focus of infection either in the teeth,
tonsils, sinuses or elsewhere. Allen and Brown suggest that the
prostate may serve as a focus of infection, but they state that
the theory lacks proof, as does the impression that any distant foci of infection are of etiological significance. Meyer's theory (14) with regard to sugar tolerance has not been borne out. Endocrine disfunction has also been brought into the discussion.

CLINICAL COURSE AND SYMPTOMATOLOGY

Thrombo-angiitis obliterans occurs frequently in one or more of the extremeties and first manifests itself when the circulation becomes inadequate for increased or prolonged activity of the part. This inadequacy depends upon the time element required to establish an adequate compensatory collateral circulation if such is possible. The early manifestations are variable and clear cut signs during the incipient stage are lacking. Brown and Henderson assert that the symptoms are usually pathognomic but are frequently erroneously interpreted.

The real beginning of the clinical course of this condition antedates by months and probably years the indications which bring the patient to the doctor. Long before there are any signs of passive congestion or pain, when the limbs are not being used, the pathological changes have started but give no indication of their existence until, and unless the patient speeds up his accustomed rate of locomotion, when he may be conscious of an ache or even a slight pain in the calves of the legs, not enough at first to stop him from walking, but merely enough to render him conscious of a sensation, more or less disagreeable, which should not be caused by so slight exertion. Often the symptoms may be coldness and numbness of the feet in cold or inclement weather, fleeting definite or indefinite pains in a toe, sole or ankle or calf. The pain is usually
non-characteristic, and may amount to little more than "rheumatic twinges". On this account most cases are at first diagnosed gout, myalgia, neuralgia, rheumatism, fibrositis, foot strain, broken arches, Raynaud's, varicose veins, trench foot, sprain, etc.; in the army "flat foot" is a common early diagnosis. According to Allen and Meyerding (15) in approximately 95% of the cases the complaint is referable chiefly to the lower extremities. In 30% there is some degree of arterial obliteration in the upper extremities, but the early symptoms are rarely referable to this region.

From this condition, the disease goes on by almost imperceptible gradations, to a state called "intermittent claudication", a state where "blood hunger" is so intense that one is obliged to pause and rest until the circulatory needs of the extremity have been satisfied. In many cases it is only later, when the true nature of the disease is suspected, that a history of intermittent claudication is obtained, often only as a result of careful questioning. Next comes the stage where elevation of the limb causes a blanching of the skin; and depression of the limb causes a purplish-red congestion of the toes and dorsum of the foot of varying intensity. If examined at this time, absence of pulsation, or at least a decidedly perceptible diminution in the arterial pulsation of one or more of the larger arteries supplying the limbs, may be noted, and the foot is cooler, both subjectively and objectively, than the normal one. When the thrombotic changes are in the part of the femoral artery above its division into the anterior and posterior tibial, the pain is less severe because the artery, vein and nerves are not so intimately associated and therefore do not become so tied up in the infiltrating process in the adventitia as is the case below this division. Absence of pulsation in one or other artery of the foot,
or in the radial artery if the upper extremity is first affected, may be a very early sign, and in certain cases be discovered only on routine examination prior to the onset of the characteristic symptoms; in some cases too, arterial changes may be far advanced in the clinically symptomless leg, while the patient complains of pain, etc., in the other in which the pulse may still be obtained. Wandering phlebitis occurs in about 25 to 40% of cases.

At first occurring only after prolonged or unwonted effort, the painful limp gradually follows less and less exertion until finally the patient is unable to walk even a few yards for fear of provoking it, and in consequence becomes bedridden or anchored to his chair.

Conservative treatment in the earlier stages may result in a remission and the patient be free of severe symptoms for a time or the condition may persist. After the lapse of weeks, months or even years the symptoms will recur, and usually evidences of trophic disturbances make their appearance. Following trauma, after the cutting of a nail or even without apparent cause, an abraded spot or hemorrhagic bleb, pustule or dry dead patch of skin develops near the tip of one of the toes or under a nail. Minor abrasions about the nails, ingrowing nails, and even trivial surgical procedures for their relief frequently start trouble by causing a wound in the soft parts which refuses to heal, and from this state it is often not long before a gangrenous condition develops.

Before trophic changes occur, the pain is usually absent or at least mild when the patient is at rest; but with the onset of trophic lesions or gangrene the pain becomes excruciating and continuous even at rest. Brown (16) presents a vivid description
of a patient at this stage: "The patient's morale is broken down and he becomes a pitiable wreck. Often one observes such a victim squatting tailor fashion, holding the diseased foot in his hands, moving it up and down, continuously rubbing it, and moaning most of the time. Relief from the pain is almost unattainable and opiates are attended by great danger because of the probability of habit formation".

Usually during the first attack of trophic disorder, but sometimes when only the intermittent claudication is present that a peculiar blush to the toes and foot, sometimes extending to the ankle or slightly above when the leg is in the dependant position appears. This is the "rubor" or "erythromelia" of thrombo-angiitis obliterans. Upon elevation the affected extremity rapidly becomes blanched (ischemia). Sometimes the superficial ulcer heals under conservative treatment, and the patient recovers completely, or the condition may become chronic, or sometimes progresses steadily to gangrene of one or more limbs, necessitating amputation as a life-saving measure.

Allen and Brown (17) state that pain of claudication was the first symptom in 51% of their cases, the longest history being 15 years and the shortest 2 months. Coldness of the extremities was the first symptom in 12%; abnormal fatigue in 11%; non-healing ulcer in 10%; sudden arterial occlusion in 7%; recurrent superficial phlebitis in 4%; edema in 3%; and spastic vasomotor disturbances in 2%.

Many other symptoms such as myokymia, anaesthesia, paraesthesia, etc., have been described in individual cases, but are not of sufficiently frequent occurrence to warrant more than a passing note.
The pathology of thrombo-angiitis obliterans was clearly described by Buerger (1) after a careful pathological study of 25 amputated limbs. Suffice it here to outline the most important pathological features of the disease, and refer the reader to Buerger's book for a complete comprehensive study of the pathology in all of its various phases.

Buerger summarized chronologically the pathological picture of thrombo-angiitis obliterans as follows: "An acute inflammatory lesion with occlusive thrombosis, the formation of miliary giant cell foci, the stage of organization or healing, with disappearance of miliary giant cell foci, the organization and canalization of the clot, the disappearance of inflammatory products, and the development of fibrotic tissue in the adventitia that binds the artery, vein and nerves." These various stages of the disease represent the study of material obtained from various positions of vessels from amputated limbs and from sections taken from superficial veins in which there was evidence of migrating phlebitis. From this latter material the acute stages of the disease can be found. In portions of the arteries and veins the other stages can be seen depending on the slow progress of the disease from one portion of the vessel to another. Meleney and Miller (18) especially stress the fact that the "pathologic process is patchy, and not an ascending one, as is the general impression. It does not begin in a single focus but in several at once.

G. E. Brown (16) describes the condition as a chronic thrombosing process usually involving the peripheral arteries and veins. The early pathologic picture shows a soft red cellular clot filling the vascular lumen, and containing erythrocytes, platelets and
fibrin. There are subsequent stages of fibroblastic organization and canalization. Aside from diffuse cellular infiltration of the arterial coats, suggestive of an infectious basis, there is no evidence of any changes involving the intima and media that characterizes endarteritis obliterans. Buerger was the first to point out this essential difference from arteriosclerosis in which the lumen of the vessels is gradually narrowed by proliferation of the intima. Mahorner (19) summarizes his pathological studies at the Mayo Clinic as follows: The result of this study suggest that thrombo-angiitis obliterans is fundamentally a chronic inflammatory condition of the vessels resulting in thrombosis with organization and canalization of the clot, fibrosis of the adventitia and an attempt on the part of the vasa vasorum and other vascular channels to establish a collateral circulation. At times acute inflammation is superimposed on the chronic process. The nerves are involved apparently by virtue of their relationship to the vessels and by ischemia in their distal portions." The process becomes chronic and has a tendency to heal as it spreads to other portions of the vessels or it may become quiescent, later to flare up again or even apparently remain healed in certain instances.

The interference with blood supply and nerve involvement gives rise to changes in the skin and skin appendages, and in long standing cases may get muscle atrophy. Thickening, hyperkeratosis and scaling frequently are seen. Alopecia may occur and the nails show changes varying from mild ridging to marked hyperplasia with deformation and incurvation. Ulcers commonly develop under the nail bed, over the tibia, on the plantar surface of the toes or immediately below the malleoli. The later developing gangrene is usually of the dry type, but secondary infection may develop above the gangrene.
Buerger has observed what he calls the acute lesions in territories other than the extremities, namely in the spermatic artery, veins of the spermatic cord, and in one case in the gastric arteries in a case of ulcer of the stomach. Lienenthal and Barron (20) believe that the disease may occur anywhere in vascular system and suggest that the symptoms of angina pectoris may be due to thrombo-angiitis obliterans. That arteriosclerosis may develop centrally in those affected with thrombo-angiitis obliterans is known, and it is likely that the development of this process may obscure a once present typical lesion of thrombo-angiitis obliterans.

Up to this time, few autopsies have been performed upon patients who were definitely known to have thrombo-angiitis obliterans (21). This is probably due to the fact that a pathologic diagnosis was made from the amputated extremity and the rather generally accepted idea that only vessels of the extremities were affected. In his book, Buerger (1) reported four autopsies and found coronary arteriosclerosis in one, thrombo-angiitis of the coronary vessels in another and central arteriosclerosis with blank thrombosis in two. Perla (22) reports that he found the typical lesion of thrombo-angiitis obliterans in the coronary vessels of one of his cases. Lemann's autopsy (23) was an elderly patient who had suffered for many years with thrombo-angiitis obliterans of the extremities. The coronary vessels showed clearly advanced arteriosclerosis with occlusion. Taube (24) reports 20 other cases affecting other "vascular territories". From his studies one is inclined to believe that in the future thrombo-angiitis obliterans may be thought of as attacking any part of the vascular tree.
DIFFERENTIAL DIAGNOSIS

In making a differential diagnosis of thrombo-angiitis obliterans it is necessary to differentiate all of the peripheral vascular diseases. In many cases the diagnosis may be quite obvious from some characteristic manifestation of the disease as sex, duration of symptoms, extremities involved, symmetry, presence of migrating phlebitis, etc. In other cases the difficulty is great. A classification has been attempted, but as yet none has completely included all of the peripheral vascular diseases. In about 90% of the cases, the vascular diseases can be divided according to Brown's classification (25) into vasomotor and organic groups, by the presence of absence of the pulsations of the arteries that are usually palpable and by careful analysis of the symptoms and physical manifestations. The Pachon oscillometer (26) also aids in determining the state of the pulsations in the peripheral arteries. Brown's classification is generally accepted in the literature as one of the best at present, and since a classification materially assists in differentiating the main types, I have embodied it into this thesis as table I. Tables II (27) and III (28) are copies of the main differential points used in the Mayo Clinic in the diagnoses of peripheral vascular diseases.

That the disease is frequently wrongly diagnosed is evidenced by the fact that more than 80% of the cases of thrombo-angiitis obliterans seen at the Mayo Clinic have been previously diagnosed incorrectly (29) and that many are frequently diagnosed as Raynaud's disease is shown by the review made by Allen and Brown in which 25 unselected cases in men or children were taken at random from German, English and American literature (30). They judged according to the symptoms and findings presented in the reports. All of
TABLE I.
TENTATIVE CLINICAL CLASSIFICATION OF ARTERIAL VASCULAR DISEASE

<table>
<thead>
<tr>
<th>Functional I or vaso-motor types</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vasoconstricting types</td>
</tr>
<tr>
<td>1. Multiple-phase color reaction. Raynaud's disease.</td>
</tr>
<tr>
<td>2. One-phase color reaction. acrocyanosis, dead finger, local syncope.</td>
</tr>
<tr>
<td>Vasodilating types</td>
</tr>
<tr>
<td>Erythromelalgia</td>
</tr>
</tbody>
</table>

| General distribution            |
| Vasoconstricting types          |
| Primary or essential hypertension, early stages |
| Vasodilating types              |
| Primary or essential hypertension |

| Local distribution              |
| 1. Arteriosclerosis, endarteritis obliterans with or without thrombosis; diabetic gangrene |
| 2. Thrombo-angiitis obliterans   |
| 3. Simple thrombosis or embolism |
| 4. Arteritis of known infectious origin (rheumatic, syphilitic) |
| 5. Aneurysm with or without thrombosis |

| II Organic types                |
| General distribution            |
| Arteriosclerosis                |
| 1. Primary                      |
| 2. Secondary to hypertension    |

In their experience this classification will cover practically all the usual forms of arterial vascular disease (25).
TABLE II
DIFFERENTIAL DIAGNOSIS OF DISEASES AFFECTING THE EXTERNALITIES

<table>
<thead>
<tr>
<th></th>
<th>Thrombo-angiitis obliterans</th>
<th>Arteriosclerosis</th>
<th>Raynaud's</th>
<th>Primary erythromelalgia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pulsation of Arteries</td>
<td>Pulseless 50%</td>
<td>pulseless 50%</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td></td>
<td>Diminished 45%</td>
<td>diminished 45%</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td></td>
<td>Normal 5%</td>
<td>Normal 5%</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>Increased rubor with dependency</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Excessive pallor with elevation</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Intermittent Claudication</td>
<td>usually present</td>
<td>usually present</td>
<td>absent</td>
<td>absent</td>
</tr>
<tr>
<td>Gangrene</td>
<td>Common</td>
<td>Common</td>
<td>Rare</td>
<td>Never</td>
</tr>
<tr>
<td>Rest pain</td>
<td>Usually very severe</td>
<td>Usually mild</td>
<td>Usually</td>
<td>Mild to severe</td>
</tr>
<tr>
<td>Type of rest pain</td>
<td>Sharp stinging</td>
<td>Aching</td>
<td>absent</td>
<td>burning</td>
</tr>
<tr>
<td>Appearance of gangrenous ulcer</td>
<td>moist, inflammatory</td>
<td>usually dry</td>
<td>small and</td>
<td>None</td>
</tr>
<tr>
<td></td>
<td>discharging</td>
<td></td>
<td>punched-out in early stage</td>
<td></td>
</tr>
<tr>
<td>Superficial Phlebitis</td>
<td>30% of cases</td>
<td>Absent</td>
<td>Absent</td>
<td>Absent</td>
</tr>
<tr>
<td>Age</td>
<td>mostly 25-45 yrs.</td>
<td>55-85 yrs.</td>
<td>17-35 yrs.</td>
<td>30-50 yrs.</td>
</tr>
<tr>
<td>Sex</td>
<td>99% in males</td>
<td>90% in males</td>
<td>95% females</td>
<td>70% females</td>
</tr>
<tr>
<td>Race</td>
<td>40% Hebrew</td>
<td>Any</td>
<td>Any</td>
<td>Any</td>
</tr>
<tr>
<td>Roentgenogram of arteries</td>
<td>Usually negative for sclerosis</td>
<td>Sclerosis present</td>
<td>Negative</td>
<td>Negative</td>
</tr>
<tr>
<td>Color change following exposure to cold</td>
<td>30%</td>
<td>15-20%</td>
<td>Always</td>
<td>Never</td>
</tr>
<tr>
<td>Temperature of extremities</td>
<td>Low</td>
<td>Low</td>
<td>Low</td>
<td>High</td>
</tr>
<tr>
<td>Edema</td>
<td>Frequent</td>
<td>Infrequent</td>
<td>Absent</td>
<td>Absent</td>
</tr>
</tbody>
</table>

# percentages are approximate. (27)

these cases had been reported as Raynaud's disease, but according to the Allen and Brown review, 16 of them were classical cases of thrombo-angiitis obliterans, 5 were other peripheral vascular conditions, on one there was insufficient data given, and the other three were of indeterminate diagnosis. None were cases which could be considered as
Table III. Chart of differential diagnosis based on our cases of arterial disturbances of the extremities. (There are necessarily exceptions to the rule.) (28).

<table>
<thead>
<tr>
<th></th>
<th>Vasomotor disturbances</th>
<th>Thrombo-angitis Obliterans</th>
<th>Monckeberg's Arteriosclerosis</th>
<th>Senile Arteriosclerosis</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Average Age</strong>.........</td>
<td>30</td>
<td>40</td>
<td>50</td>
<td>60</td>
</tr>
<tr>
<td><strong>Sex</strong>..................</td>
<td>Female</td>
<td>Male</td>
<td>Both</td>
<td>Both</td>
</tr>
<tr>
<td><strong>Nationality</strong>.........</td>
<td>All</td>
<td>Hebrew 40%</td>
<td>All</td>
<td>All</td>
</tr>
<tr>
<td><strong>Duration of Symptoms</strong></td>
<td>Years</td>
<td>Years</td>
<td>Months</td>
<td>Months</td>
</tr>
<tr>
<td><strong>Extremity</strong>...........</td>
<td>Upper</td>
<td>Lower</td>
<td>Lower</td>
<td>Lower</td>
</tr>
<tr>
<td><strong>Symmetry</strong>............</td>
<td>Bilateral</td>
<td>One side</td>
<td>Unilateral</td>
<td>Unilateral</td>
</tr>
<tr>
<td><strong>Gangrene</strong>............</td>
<td>Late</td>
<td>Late</td>
<td>Early</td>
<td>Early</td>
</tr>
<tr>
<td><strong>Vessels shown by Roentgen ray</strong></td>
<td>None</td>
<td>None</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td><strong>Pulsating vessels</strong>...</td>
<td>Normal</td>
<td>None</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td><strong>Response to Foreign Protein</strong></td>
<td>Marked</td>
<td>Marked</td>
<td>Slight</td>
<td>Slight</td>
</tr>
<tr>
<td><strong>Response to Novocaine block</strong></td>
<td>Rapid and Marked Slow and Mild</td>
<td>None</td>
<td>Slight</td>
<td>Slight</td>
</tr>
<tr>
<td><strong>Development of Collateral Circulation</strong></td>
<td>None</td>
<td>Inflamed media</td>
<td>Slight</td>
<td>Fair</td>
</tr>
<tr>
<td><strong>Pathological Section of vessels</strong></td>
<td>Normal</td>
<td>Thrombosis</td>
<td>Thickened irregular media</td>
<td></td>
</tr>
</tbody>
</table>

classical of Raynaud's disease.

If the symptoms presented in thrombo-angiitis obliterans were only those of an organic disease the diagnosis would be easier, but in about 30% of cases vasomotor disturbances are also present to some degree (31). One must also remember that gangrene may develop in this disease even when pulsations of the vessels are felt, because in these vessels the obliteration may take place distally to the area of palpation. This is
true in about 5% of cases and it is when either of these two conditions are present, according to Allen and Brown that the greatest difficulty arises in making the diagnosis.

As a further aid in deciding the functional or organic nature of the disease the circulatory efficiency test as described by Buerger (32) is valuable. In principle this consists in noting the color changes of the extremity following elevation to 180 degrees. In the presence of obstruction of the arteries a varying degree of pallor appears within a few minutes. When occlusion of the vessels is confined to the toes the pallor is limited to these areas. With the feet in the dependant position the color gradually returns, the extent of the collateral circulation is shown by the irregular advancing color and the foot after a variable time becomes intensely red and cyanotic. This is the so-called reactionary rubor. This simple test to determine the vascular obliteration yields data of greater value in the opinion of many than is obtained with more complicated methods. Other aids in diagnosis are: Viscosimeter (33) to determine the viscosity of the blood which is considered as an index by some authors. The capillary microscope to determine the extent of dilation of the capillaries and thus determine if a collateral circulation is being formed. Calorimeter and pyrometer (34) for color and heat tests. Salt injection (wheat) test (35) to determine the rate of absorption and thereby judge the rate of blood flow. The injection of radiopaque substances into the circulation to visualize the extent of circulation (36)(37). Vasomotor index (38) (39) spinal anaesthesia (40)(41) and paravertebral block (42) are used to determine the amount vasomotor involvement present. There are objections to all of these, some more than others and some strongly advocated by some authors and equally as strongly denounced
by others. Without a doubt the efficiency of the test as done will all depend upon the individual's own experience with the test and the proper interpretation after it is done.

Clinical examination carefully done yields most of the information necessary for a diagnosis of peripheral vascular disease. The accepted methods of physical examination, the appearance of the limb in the horizontal, the elevated and the dependent positions, the return of color after temporary local pressure and after elevation, the comparative warmth of the parts and the palpation of the arterial pulsations to determine circulatory impairment with the aid of the history, help in coming to a diagnosis.

PROGNOSIS

The prognosis as interpreted in thrombo-angiitis obliterans is in relation to the life of the affected extremity and not in relation to the life of the patient. Death rarely results unless some complication supervenes.

Until the last decade the prognosis of the extremity was generally recognized as being bad, since the disease was usually unrecognized or else allowed to progress until amputation was necessary because of the gangrene, infection of extreme pain. Former teachings gave rise to the impression that the ultimate outcome in almost every case of thrombo-angiitis obliterans was amputation of one or more of the affected extremities and even in many text-books the disease is described as a progressive series of amputations. Since the advent of modern methods of diagnosis it has been necessary to revise the concepts of this disease and adopt a more optimistic attitude as far as the prognosis is concerned.

S. Samuels declares that the percentage of patients with thrombo-angiitis obliterans who ultimately develop gangrene is remarkably small (43). This is probably due to the fact that the disease is now
recognized earlier, that the danger of surgical tinkering with affected digits is given more consideration, and also because the disease occurs most frequently in young males who have sufficient vis-a-tergo and "give" to be able to establish a compensatory collateral circulation. Other factors may be that the disease is more chronic, more slowly progressive, or that conservative therapy is of distinct value. Allen and Brown conclude that "Thrombo-angiitis obliterans is apparently a self-limiting disease, as the obliterative process eventually stops. Amputation seems inevitable at times, but frequently as the compensatory circulation increases and becomes established to a high degree the trophic disturbances disappear and the patient may be symptom-free for years or perhaps indefinitely."(44).

The economic factor greatly influences the prognosis. Patients who cannot afford long periods of rest with institution of conservative measures usually require high amputation performed early; or as Mueller (45) tersely expresses it, "We have nothing in the present methods of treatment to offer the patient except amputation which assures any reasonable promise of success." However, patients in whom the condition is diagnosed early and who cooperate with a physician in an attempt to establish a collateral circulation, may expect either a low amputation or perhaps a useful limb for years or even for life.

Optimistic views are held by many authorities as to the prognosis of amputation of the limb, and statistics are quoted by many. Silbert (46) claims that the disease can be checked by proper and newer therapeutic measures, whereas the earlier treatment resulted in 85% of the cases coming to amputation. In his studies of 155 untreated cases 77% came to amputation within five years of onset of symptoms, and in a further series of 225 cases treated by a single method only 9.3% came to amputation within 2 to 6 years. Some of these were far
advanced when they came for treatment. Horton and Brown assert that 20 to 30% will lose one or more limbs with treatment (47). In the Mayo Clinic in 424 cases from 1909 to 1929, 28% come to amputation (48). This percentage is said to be lower in the last five years. Thus, it can be seen that the prognosis as to amputation in late years is more optimistic.

The prognosis can best be determined by tests, such as Buerger's rubor and blanching test, palpation of arteries, use of pachon oscillometer, injection of radiopaque substances, intra- cutaneous salt solution test, fever test, and others, all of which aid in determining the amount of circulation in the extremity. Often the prognosis is best to be guarded until after the institution of some treatment for a time, to determine the probability of development of a better collateral circulation. If the blood supply to the extremity is exceedingly poor, the prognosis will necessarily be poor. In general, it can be said that where there are no trophic disturbances, and there are signs of collateral circulation developing, the prognosis will be good. However, in the absence of developed collateral circulation, the prognosis is not so good; and if trophic disturbances or gangrene are present in the absence of a developed or developing collateral circulation the prognosis is bad. Schleisinger (49) emphasizes that conservative therapy requires patience because quick cures are not possible. Spontaneous remissions are frequent and therefore proof of successful treatment is difficult to establish. The pain often stops of itself and less frequently the ulcer heals without treatment and occasionally the formation of collateral vascular channels or the reopening of occluded vessels will occur spontaneously.
The treatment of thrombo-angiitis obliterans in the eyes of the medical profession appears to be quite unsettled although certain individuals ardently advocate this or that method. The old prosaic truth that every therapeutic procedure must be measured by the yardstick of clinical evidence and final results is very evidently overlooked by many writers in their enthusiasm. Even though there is now a multiplicity of therapeutic measures, progress is being made toward conservatism.

According to some authors, it is unfortunate that the onset of the disease is usually insidious and that irreparable damage is done when the patient is first seen. According to others, due to the insidious onset, and to the long period of time between the first symptoms and the beginning of disability, the majority of individuals suffering from disorders of the peripheral circulation seek medical aid long before major amputation is the only obvious line of procedure. Is is due to disagreement of this kind and diversity of views that it becomes necessary to give consideration to the disease in all of its stages, and keeping in mind the various forms of treatment, to give therapy according to the variable conditions which are found in the patient after careful examination.

For purposes of simplifying the therapeutic measures as much as possible, I have divided the disease into four stages (after the plan of Graves) judging according to the presence of absence of gangrene, rest pain and trophic disturbances. The conditions may overlap, and when found to do so, the treatment is the combination as far as possible, but always with a tendency toward conservatism.

1. Extensive gangrene with or without pain. The treatment is high amputation.
2. Severe "rest pain" with or without moderate trophic changes. The treatment consists of measures for the relief of pain, methods to increase circulation, removal of foci of infection, and, in a limited number of cases, lumbar ganglionectomy and rami section may relieve pain and increase circulation. If these measures fail, amputation is indicated.

3. Mild trophic changes without "rest pain". The treatment should be designed to increase circulation. Foci of infection should be removed and prolonged rest enforced. Lumbar ganglionectomy and rami section are valuable in certain cases.

4. Neither "rest pain" or trophic changes. The treatment consists of removal of foci of infection, rest, and conservative measures to increase circulation.

Certain general measures should be applied in all cases under treatment. Septic foci should be removed as toxic absorption may be a causative factor in the production of symptoms, and certainly can be said to act as an aggravating factor in the disease. Abstinence from alcoholic beverages, highly seasoned foods and a diminished protein diet are recommended. Smoking is interdicted and Silbert goes so far as to state that satisfactory results often are gotten only if the patient stops using tobacco. (46). Rest in bed, cleansing baths and inbibation of lots of water are as important here as in any other disease. Protective measures to the other foot are also of paramount importance since if the disease is present in one foot, it will have a tendency to occur also in the other at a later date.

1. Physical Measures to improve the circulation. Heat in its various forms is of benefit. It may be administered by baking, heat tents, radiant light and other means, but is probably most
effective when administered as hot sitz baths. Contrast baths have been recommended by some observers, especially in the early stages of intermittent claudication, but cold, if continued too long, is dangerous in these cases and therefore is contraindicated. They are also contraindicated in the presence of gangrene or open lesions. Diathermy and galvanization are useful for their vasodilator effect on the small arterioles and capillaries (50).

2. Mechanical measures to improve the circulation. Buerger's postural exercises are of benefit in the young, but are often too exhausting in elderly patients. They are done in the following manner; With the patient lying in bed, the affected extremity is elevated from 60 to 90 degrees above the horizontal allowing the part to rest upon a support for from 30 sec. to 3 minutes in order to produce ischemia. As soon as blanching occurs the patient then hangs the leg down over the edge of the bed for 1 to 3 minutes, or long enough for the characteristic rubor to set in. The limb is then placed in the horizontal position for 3 to 5 minutes during which time heat should be applied. This procedure should be repeated for one hour as many times daily as is practicable, usually 2 to 4 times. A. W. Allen thinks it well to have the patient routinely forcibly flex, extend, evert and invert the feet, flex and extend the toes once. This serves a double purpose; it makes it possible to assume the position longer and at the same time keep the joints and ligaments active (52). Samuels advises against allowing the foot to hang over the edge of the bed if ulceration is present since the dependant position soon produces an intense edema of the foot that is not conducive to resolution or healing. He advises that the foot be kept horizontal in such cases (43).

Hyperemia induced according to the method of Bier is another method included in this group.
3. Measures affecting the vasomotor system.

Various methods of medical treatment have been advocated as mercury, iodides, arsphenamine, intravenous sodium iodide, nitro-glycerine and the nitrites, all of which are of questionable value. Cowadias treats the arterial spasm with nitrites, aspirin, and acetylcholin as well as local measures.

The use of typhoid vaccine to induce fever and a vasodilating action in the collateral channels of the diseased extremity have been shown by Adson and Brown to be of distinct value (25). These observers have demonstrated by calorimetric methods that during fever there is a distinct increase in blood flow through the affected extremity. This treatment is chiefly valuable to carry a patient through one of the critical periods of exacerbation.

The initial injection should contain 40,000,000 killed organisms and should be repeated five times at daily intervals in doses which are increased sufficiently to produce a chill and 2 to 4 degrees elevation of temperature. Although exhaustive in repeated courses, its beneficial effect on pain and trophic changes warrant its use within conservative limits in practically all cases.

Waller (53) has used 2 cc. of 2% suspension of sulfur in olive oil for intramuscular injections to produce a foreign protein reaction and regards it superior to typhoid vaccine, even the special "H" typhoid vaccine. His claims are that it produces a prolonged fever, less chill, maximal peripheral dilatation and that repeated injections cause no decrease in the reaction. Also it is not so apt to produce the untoward effects as often are found with typhoid vaccine.

4. Measures to affect the blood directly.

This type of therapy includes the administration of various solutions as infusions and clyses. Koga (54) in 1913, hoping to increase the
blood viscosity advised hypodermoclysis of Ringer's solution. This method immediately became popular and various modifications are still being used with presumably favorable results. Steel (4) advocated the use of sodium citrate intravenously reasoning that clotting would be decreased. Buerger states that the results obtained by this therapy hardly warrant its use. However, Jablons (55) reports favorable results from the employment of an elaborately prepared citrate solution.

Twenty grains of sodium citrate are dissolved in 100 cc. of distilled water to which 3 gm. of sodium chloride are added. The addition of one gram of dibasic potassium phosphate is usually required to render the solution iso-electric as well as isotonic. This latter acts as an anticoagulant, and when present in certain concentrations, prevents the occurrence of severe chills which follow the use of sodium citrate in distilled water. 250 cc. of the solution are given intravenously for ten days, and then at two day intervals for six months. After this, improvement usually warrants an interval of a week for the next year. Of Jablon's 120 cases treated in this way for one to three years, 60 have been symptom free.

Silbert (46) and Samuels at Mt. Sinai Hospital in New York, have reduced the percentage of amputations from 77% to 10% by the intravenous use of hypertonic salt solution. This consists of 300 cc. of a 5% sodium chloride solution given three times week over a long period of time. The purpose is to increase the blood volume, dilute the blood, increase the blood pressure, allow a greater distention of the vessels and therefore a better and earlier collateral circulation. The treatment is contra-indicated in patients over sixty years of age and those who show signs of an injured myocardium or poor renal function.

Allen et al have used radium chloride intravenously and found that it relieved pain in about 70% of cases. However, they found it to be an expensive procedure and no more efficacious than the administration of typhoid vaccine (56).
5. Surgical procedures on vessels.

These procedures have been reviewed in a large series of cases by Zitto and Stelton (57), who reported failures in over 70% of cases. These procedures are ligation of the femoral vein, as advocated by Oppel, Morton and Lienthal, and arteriovenous anastomosis as practiced by Weiting, Goodman and Davies.

Ligation of the femoral artery as practiced by Lewis and Reichert (58) in arteriosclerosis hardly seems a rational procedure to institute in a disease which itself includes the arteries. Ligation of the femoral vein has not been of great benefit in most cases.

Since Pearse (59) has shown experimentally that simultaneous ligation of the artery and vein results in improved circulation peripherally, it seems that ligation in this disease should produce like results. Pearse and Morton have utilized this procedure for some time and report gratifying results from it. Van Gorder in Peking reports that of nine patients so treated, eight were improved or actually relieved of their gangrene (60).

Arterio-venous anastomosis is generally considered an illlogical procedure since both veins and arteries are thrombosed.


Any procedure which increases the circulation lessens the pain. Analgesic drugs give only partial relief, and very often none. Morphine is usually considered as contraindicated since the condition is so prolonged and the pain so intense that the massive doses would lead to addiction.

White and Smithwick inject alcohol into the anterior and posterior tibial nerves and lateral cutaneous branches of the peroneal. Also six inches above the ankle between the tibia and fibula. The middle cutaneous branch of the peroneal may be ex-
posed and injected. This produces a paralysis of the intrinsic
muscles of the foot, but gives relief for about six weeks, and
allows improvement in that the necrotic areas may be attended to
without pain. This measure does seem of value, but ulceration
may occur at the site of the injection.
7. Local Treatment.
Trophic ulcers are treated on general surgical principles. For
local pain Buerger suggests an analgesic ointment containing 5%
novocaine and 10% orthoform or anaesthesin in lanolin and glycerin
(51). Migrating phlebitis is best treated by the application of
hot wet dressings.
Local measures such as diathermy, radiant heat, ultra-violet rays,
Bier's hyperemic therapy, etc., have within limits, proved useful
in some cases.
8. Surgery of sympathetics.
Adson and Brown (12) have shown that lumbar ganglionectomy and rami-
section produce definite and persistent vasodilation of the vessels
of the feet when vascular dilatation is obtainable. In about 30%
of cases there is in addition to occlusion also a vasomotor factor
which is probably due to the impulses arising in the inflamed
vessel walls and being carried to the spinal cord reflexly produce
a vasoconstriction or prevent maximum vasodilation. If the lumbar
reflex is broken, there results a diminution on the vascular tone
and a vasodilatation permitting an increased flow in certain cases.
Brown has determined that this procedure is applicable in only one
out of seven cases. He first calculates their vasomotor response by
giving typhoid vaccine and determines the rise of surface temperature
and oral temperature. If the increase in oral temperature is sub-
tracted from the increase in surface temperature, and the result
divided by the increase in oral temperature, a so-called "vasomotor
index" is obtained. If this index is 1.5 or more, a favorable result may be expected from lumbar ganglionectomy and ramisection. Periarterial sympathectomy, as originally practiced by Leriche has given uncertain results, and appears to have fallen into disfavor among surgeons and even Leriche now limits its usefulness (61). Bernheim (62) terms it as a tiding over process which should be used in certain selected cases as it frequently relieves pain and is easy to execute. Brown and Allen feel that the results are so slight or transient that the operation is not worth while (12). Recently a combination of periarterial sympathectomy with lumbar ganglionectomy has been introduced by Adson (63) and performed by him on several cases with apparent success.

Surgery of the sympathetics is still in an experimental field and must necessarily remain so until we learn more of the function of the whole sympathetic nervous system. Recently Leriche, the sponsor of several sympathetic operations, is quoted as saying; "Briefly, I am more and more led to think that no sympathetic operation is of value in Buerger's Disease".

9. Roentgen ray therapy. Philips (64) reports relief of pain and improvement in circulation in cases subjected to radiation of the lumbar segments of the spine. Beall and Jagoda (65) report an apparent cure following such therapy.

10. Surgery of the extremeties. That surgical tinkering with the toe or nails frequently precipitates gangrene is a well known fact among all observers and this is always to be avoided in the presence of any possibility of thrombo-angiitis obliterans.

Formerly high amputations of the extremeties were performed early without regard to the state of the circulation. That it is futile
to attempt a radical operation without the presence of dilating vessels is obvious. Now with the advent of conservatism one finds that the indication for amputation are not nearly so clearly defined. Cases have been reported in which medical treatment has reestablished the function of involved extremities. Gangrenous lesions have been seen to heal and Hills reports that function remains in feet of stoic Chinamen whose toes have undergone auto-amputation. To generalize, one might say that cases should be treated medically provided that pain can be relieved and economic conditions permit it. Those treated surgically have the benefit of postoperative medical treatment to facilitate healing. Incision of toes and removal of toe nails usually results in spreading gangrene, and therefore, should never be practiced.

The level at which amputation should be performed can only be determined by an investigation of the status of the circulation. If in an attempt at low amputation, vessels are found to be diseased, a higher level should immediately be tried rather than re-amputation at a later date. However, Allen and Brown (67) state that amputation below the knee is successful in 80% of all cases regardless of the condition of the pulsations in the polliteal artery, provided that the gangrene does not involve the leg and that extensive lymphangitis or edema are not present. The extent of patency of the femoral artery may be of significance. They also add that intensive medical treatment has made possible such results.

Fingers can usually be amputated successfully regardless of obliteration of ulnar or radial arteries while toes may be amputated successfully in that small group of cases in which either one or both main vessels of the foot are pulsating normally (43). Amputation of the distal one-half of the foot or above the knee offers no functional advantage. Amputation below the knee joint
offers a distinct functional advantage and should be preferred. The age of the patient, extent of patency of the arteries, general condition, and the condition of the tissues at the site should all be adequately considered before amputation is performed.

11. Miscellaneous measures.

Willy Meyer (14) claimed beneficial results by flushing the intestinal tract daily with eight to ten quarts of Ringer's solution through a duodenal tube, and supplementing this with daily hypodermoclysis of the same solution.

Treatment with muscle extract is reported by Schwartzman (63). He reported five cases in 1931 with good results.

Left suprarenalectomy has been performed on some cases in Russia, but according to Leriche, this procedure has not been employed much outside that country (69).

Insulin therapy (70) has been considered by some to be efficacious.

All in all, there is a multiplicity of therapeutic measures which can be used in the treatment of thrombo-angiitis obliterans. Many are successful only in certain hands, and many others have not seen sufficient time and experience to determine their worth. Patient conservative therapy seems always recommended, and over-hasty amputations to be avoided.

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Case 1. J. V., patient number 33626, a white, male, laborer, aged 54, entered the University Hospital on November 28, 1930 complaining of pain in the right foot and lower leg, swelling of the right foot, and a purple discoloration of the toes of the right foot.

**ONSET AND DEVELOPMENT** - Patient had never been troubled with his feet until two weeks before admission when he was laboring on his feet most of the day, noticed some tenderness in the big toe of the right foot but paid little attention to this at the time. About three days later he noticed that the big toe and the second toe were somewhat red and swollen. This swelling gradually involved the other toes and climbed up the foot. The redness extended just above the swelling and on Nov. 21, 1930, (6 days later) he was unable to work any longer. About this time he noticed that this toe was getting dark and cyanotic. The pain continued to increase until on Nove. 26 (11 days later) he was forced to go to bed. By this time the redened area extended to the middle of the lower leg and all the toes and lower one half the foot were cyanotic. Doctor was consulted and the patient sent to the hospital.

**Local Examination:** The right foot is swollen to the level of the junction of the middle and lower thirds. The foot is very edematous with the big and first toes quite black. The entire foot is cold as far as the ankle. There are some red streaks up either side of the leg above the ankle. The entire foot is quite cyanotic. There are many enlarged and tender inguinal lymph glands.

**General:** A very strong and muscular man of about stated age
sitting on the edge of the bed with both legs hanging down, moaning and holding the right knee.

**Physical Examination:** Essentially negative except as mentioned.

**Diagnosis:** on admission. Moist gangrene of the right foot secondary to arterial thrombosis.

**Course in Hospital:** The patient almost constantly complained of severe excruciating pain in his right foot. Large amounts of morphine and sodium amytal were required to keep him in any degree of comfort. The foot was kept warm by means of a light cradle. On Nov. 30, 1930 (two days after admission) an attempt was made to cause an artificial aneurysm of the femoral artery in hopes of bettering the collateral circulation to the right leg by the operation. The operation was unsuccessful and the femoral artery was finally ligated. The patient was free from pain for a few hours following the operation, but thereafter more morphine and sodium amytal were required. The gangrenous area was less black than before the ligation, but the leg was still cold and showed little evidence of improving. On Dec. 3rd the right leg was amputated in the mid thigh. The recovery was uneventful and the patient was dismissed on Dec. 31, 1930 with a well-healed stump. On dismissal he was instructed to watch the left leg and foot carefully for the same symptoms as were in the right previously.

**Gross Pathological Examination** of the amputated Extremity:

Amputation three inches above the patella. Foot edematous, necrotic and discolored up to the metatarsal region. Fibrous adhesions found around the popliteal vessels - all banded together. Anterior tibial artery and its point of origin
greatly thickened with a narrowed lumen. The popliteal vessels are thrombosed. The peroneal artery has a roughened intima and shows intermittent areas of thrombosis. This is also true of the anterior tibial artery. Posterior tibial artery appears normal from its origin to the malleolus, but beyond that the lumen is narrowed. The intima is roughened and the vessel is thrombosed. Most of the veins show thrombosis.

Microscopical Examination: Atheroma of intima of large vessels and entire lumen blocked by a red thrombus.

Final Diagnosis: Thrombo-angiitis obliterans involving the veins and arteries of the leg and resulting in moist gangrene of the foot.

Re-admitted: on March 25, 1931. Patient had noticed some discoloration of the left leg since last hospital entry. Has had no trouble with left leg until three days before entrance when the leg became swollen and reddened. Onset of swelling was rapid, and has subsided during the last twenty-four hours. There has been no pain in the left leg as there had been in the right one.

Examination: Left leg - Toes cyanotic, moderate amount of pitting edema of foot and ankle - more marked on medial side. Superficial veins distended. Posterior tibial artery pulsates. No evidence of gangrene. Small hemorrhagic areas over toes.

Course in Hospital: The patient was placed in bed, hot packs applied, and he rested fairly easily for the most part. Occasionally complained of a small amount of pain. Postural exercises given. The foot would be very little discolored when the foot was elevated. The patient was given 500 cc. doses of hypertonic (3%) salt solution intravenously during his stay at the hospital. Discharged upon May 10, 1931 in a much improved
condition and advised to return immediately if further exacer-

When last heard from, this patient was still getting along

nicely and the trouble had not recurred.

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Except for the rather sudden onset in this case the history

is quite that of a typical case of thrombo-angiitis obliterans.

Case II. A. S., Patient number 28005, a white, male, laborer,

aged 40, entered the University Hospital on March 18, 1929, com-

plaining of painful and swollen left foot and a large carbuncle on

his back.

Onset and development: Five years ago, while working as a mech-

anic on a cement floor, the patient first noticed a burning sen-

sation on the ball of the right foot, and later on the left foot

which he attributed to the cement floor. He went to several doctors

at the time and a diagnosis of chillbains was made. The foot would

get well for a time and then relapse again. This continued for about

four years. A year ago the toe nail of the large right toe was re-

moved when the toe became injected and painful. At that time the

rest of the foot was somewhat swollen and tender, and became worse

when working. After that time the foot felt very sensitive. There

were chilly sensations and more or less numbness and tingling in the

left foot upon standing which continued until he could get the blood
to circulating with cold water. About eight weeks before entrance

the foot began to act as before. One week ago the nail of the large

toe of the left foot became loose and painful and the patient had

the nail removed. Since that time the rest of the toes, foot and

leg have become swollen and painful, and there is constant throbbing

in the big toe.

A sore on the patient's back began about two weeks ago as a
small boil which rapidly increased in size and then broke. The patient tried to take out the core but was unsuccessful. Since then it has become larger and more painful until at present it covers the greater part of the back.

Physical Examination: Large reddened area upon the back centrally placed in lumbar region and about twelve inches in diameter. Left foot is swollen, discolored and edematous to the ankle, and from there up to the knee it is less discolored and swollen but very tender two-thirds the distance to the knee. Large toe has the nail half removed and a large dark ulceration is present on the medial side. The adjoining two toes are also swollen and discolored. The patient has much pain and constantly moves the foot about. Otherwise the examination is essentially negative.

Course in Hospital: The carbuncle on the back increased in size and was incised. Foot became more gangrenous, infection set in, the pain became more excruciating. Leg amputated at lower one-third of thigh on March 25, 1929 (seven days after admission). Stump became infected. General erysipelas developed and patient died on April 5, 1929. Autopsy not performed.

Diagnosis: Thrombo-angiitis obliterans. Erysipelas.

This case illustrates the insidious onset and wrong diagnosis which is frequently made early in the course of the disease. The history is fairly typical of that of a case of thrombo-angiitis obliterans. Pathological findings were not available.

Case VI. W. S., patient number , a male, married, negro, aged 44, meat cutter, entered the Douglas County Hospital on Nov.
14, 1930, complaining of pain in feet on walking, only able to walk a short distance without resting because of pain, coldness and numbness of feet.

Onset and Development: Patient was bothered with rheumatism in his legs about five years ago. This then let up and he did not notice his rheumatism until about a year ago when he would occasionally have pain in his legs after working real hard all day. At this time he was working on a cold cement floor at a packing plant. About seven months ago his feet began to swell and pain him so that he was unable to walk. He took hot foot baths and rubbed them frequently. His feet did not improve and in August 1930 he went to Creighton Medical School to be treated. After an explanation of the treatment and the estimation of the financial output, he sought admittance to the Douglas County hospital. His feet continued to pain him and the pain became constant. He was able to walk only a short distance without resting. His toes began to turn bluish about two weeks ago and this color has slowly increased up to the time of his admittance on Nov. 14, 1930.

Local Examination: Both feet are slightly swollen and cold. The great toe of the right foot shows slight discoloration about the size of a silver quarter at the tip. The feet both feel cold. Patient has several small scars about the ankles which he says were due to burns about three years ago (six weeks in healing). Knee jerks positive. Gait is very cautious. Weight placed upon feet only after care. Pulsation in anterior tibial artery and posterior pedis artery of the right leg are barely perceptible. Both are palpable in left leg but not easily felt.
General: Small pox and measles during childhood.

Gonorrhea at age of 29. Soft chancre at age of 20.

Family history is essentially negative. Father, aged 76, is living and well. Mother died at age of 30 of pneumonia. No brothers. One sister died at the age of 16 from burns. There was no history of tuberculosis, epilepsy, carcinoma or insanity in the family.

Physical Examination: Eyes reacted to light and accommodation, no nystagmus, no discharge. No deformity, obstruction or discharge from nose. No ulcerations, fissures or mucous patches in mouth. Considerable pyorrhoea of teeth. Tonsils out. Palate reflex present. No laryngeal involvement. Neck negative except for slight anterior cervical adenopathy. Heart and lungs negative. Abdomen negative except for an indirect inguinal hernia. Prostate not enlarged. Inguinal glands slightly enlarged. Arms are strong and muscular, and radial pulses are distinctly felt. Blood pressure 128/31. Weight 140 lbs. Patient has been losing weight for the last six months.

Wasserman positive (four plus).

Urinalysis negative.

Blood count, r.b.c. 5,100,000; w.b.c. 3,600; Hb. 93%.

Diagnosis: Thrombo-angiitis Obliterans, Indirect inguinal hernia, Lues.

Progress: During his six weeks stay at the hospital the pain gradually decreased. He was gradually able to walk about the hospital for longer distances without causing severe pain. The discoloration disappeared. Treatment was supportive, and heat was applied to the feet and legs.

This is a case which from the symptoms presented is quite
typical of thrombo-angiitis obliterans in the early stages. No treatment was given him, other than the bed rest and hot applications. The patient may have had a remission.

Case III. Man, aged 41, admitted to the hospital on Feb. 7, 1928. He complained of pains in the left calf and in the plantar region of the foot with trophic disorders and gangrene of the great toe and the extremity of the third toe. He had been subject to bronchitis since the age of fifteen. He had been jaundiced when he was young. He used alcohol to excess between the ages of 20 and 35 years. He was a hearty eater. A blister appeared on the left great toe in 1922 and disappeared after treatment for three weeks.

The disease began in December 1927 with sharp pains in the foot and difficulty in walking. A small vesicle appeared on the external edge of the great toe at the end of fifteen days. The patient incised this vesicle and pus was discharged. The wound did not heal and there was a hard black crust one month later. The foot then became swollen, red and painful. Hot oil was applied but the swelling increased and the black crust enlarged. The pains were continuous but were more severe during the night. He decided to consult Dr. Dupre.

Examination of the left leg showed an edema extending from the foot to the knee with erythematous areas on the leg. The foot was cold and violet in color. The great toe was hard, black and gangrenous. There were hemorrhagic blisters and black crusts on the extremity of the third toe. The anterior surface of the instep was red and edematous. The Wasserman reaction was negative. The urine was normal. A blood count was also normal.
The redness disappeared when the leg was elevated.

Treatment consisted of hot applications, diathermy and analgesics. No results were obtained. Insulin was tried on February 23 and ten units were given daily for ten days, also without any improvement. Sympathectomy of the left femoral artery was performed on March 2, but did not give any relief.

The circulatory disorders extended to the entire lower part of the leg and on April 9 an amputation at the thigh was proposed. The patient refused to allow this operation, but he requested that the two toes be amputated first. This was done on April 10, under local anaesthesia. The tissues did not have any vitality. The incision was not closed with sutures but was left open. The patient had relief for a few days and then the wound became gangrenous and the pains were just as severe as before the operation.

The leg was amputated on May 1. The postoperative course was normal. The wound cicatrized slowly. This appeared to be a classical case of thrombo-angiitis obliterans.

This is a case as described by Dr. Dupre in the Bulletin Med. de Quebec, 29:329-334, (Nov.) 1923. The case illustrates the diversity of treatment which can be tried, and despite all that is done they frequently make a straight progress toward amputation.

Case IV. D., a clerk, married, aged 43. No history of venereal disease. Moderate smoker. Wasserman reaction of blood and cerebrospinal fluid negative.

1919, symptoms of intermittent clausication.

1926, shooting pains in left foot.

January, 1927, ulcers broke out on right foot.
April, 1927, periarterial sympathectomy of right femoral artery
(Mr. G. Mullally, Westminster Hospital). Gangrene of right
little toe a fortnight after operation.

April, 1927, amputation of right foot above ankle. (Mr. G. Mullally.)

May, 1930, readmitted to Westminster Hospital with advanced
gangrene of the left toes. Soft tissues of big toe partly
sloughed off. Also black ulcers on two or three toes. Foot swollen,
stone cold, and deeply blue. Offensive discharge. Distal portion
of left big toe necrosed. Amputation stump (right) ulcerated.
Left dorsalis pedis and posterior tibial arteries pulseless.

The patient was given daily injections of skeletal muscle
extract until the beginning of July, 1930. Pain ceased, swelling
subsided. Discharge disappeared, color improved, and the surface
of the foot became normal. Healthy granulations appeared.
Blood pressure, 130/90. Treatment continued for another three
months. Wounds completely healed. No pain or discomfort. Patient
can now ride a bicycle for a few hours a day.

This is one of Dr. Schwartzman's cases which he treated by
the use of skeletal muscle extract. He also presented in April
1931, four other cases before the Royal Society of Medicine, all
equally as severe, and with the same results. This is one of the
newest forms of treatment, and whether the good results in his
cases are merely coincidental with remissions of the disease or
due to the treatment rendered still remains to be proven by
further experience. Dr. Parkes Weber ventures the opinion that
Dr. Schwartzman's results seem hopeful.
Case V. J. G., a Russian Jew, aged 45, admitted to Johns Hopkins Hospital, June 18, 1922, and discharged improved July 6, smoked ten cigarettes a day. He had been an active athlete, having boxed, run and wrestled. He served in the Russian army, but developed scurvy. In 1912, the little toe of the right foot became gangrenous. This was amputated in the John Hopkins Hospital Dispensary. The foot was supposed to have been badly frostbitten. In 1915, the great toe on the right foot was amputated for gangrene, and in 1916, the remaining toes of the right foot were removed for the same lesion. The blood pressure was: systolic, 120; diastolic, 70. The radial pulses were of equal volume, but small. The vessels were just palpable; the brachial pulses could not be felt. The left dorsalis pedis was just palpable. No pulsation could be felt in the right dorsalis pedis or in the right posterior tibial artery. At the time of admission the left leg was normal in appearance. On the right side the first and second toes were gangrenous. In 1917, the fourth left toe became discolored and painful, dry gangrene developing. This toe was amputated at the Hebrew Hospital. At the same time the right leg was amputated above the knee, because of the gangrene of the right foot. In the Hebrew Hospital the left third toe was removed. A small ulcer remained at the base of the second toe. In June 1921, the left foot became slightly discolored. After rubbing and massage the color became more normal and remained so until five weeks before admission to Johns Hopkins Hospital. Then admitted, the big toe was purplish. The pain became very severe. Examination on admission revealed discoloration of the left foot just above the ankle - purplish on foot, pink at ankle - toes dead, dry and black. Amputation was done, June 20,
1922, through the lower third of the left thigh.

June 29, nine days after operation, the thumb on the right hand became quite painful and the right radial pulse was no longer palpable. Under treatment the pain subsided, the amputated stump healed nicely and the patient was discharged on July 6, in a very much improved condition.

This case is one of a group reported by Dean Lewis and F. L. Reichert in the Journal of the American Medical Association, July 31, 1926. This case shows the chronic progressive course of the disease. In this case resulting in amputation of both legs in the mid-thigh region, the skliogram of the amputated foot of which the popliteal artery had been injected with Bismuth oxychloride is most interesting. Fig. 1 demonstrates the normal arterial tree of a normal foot. Fig. 2 shows the arterial tree in this case of thrombo-angiitis obliterans. The collateral
circulation development was great, but nevertheless insufficient to prevent severe gangrene and loss of the extremity.

CONCLUSION

The past decade has witnessed great changes in our concept of thrombo-angiitis obliterans. The etiology is still unknown, and the symptomatology is usually pathognomic but often erroneously interpreted. Cases should be diagnosed early and rightly, and diagnoses of chill-bains, foot strain, flat feet, etc., etc., should not be made until the patient has had a thorough examination of his extremities. The main line of therapeutic procedure consists of a thorough and intensive exploitation of conservative therapy, and a careful and proper selection of cases for surgical procedures.
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