*THE CRIPPLES' CLINIC, COPENHAGEN.*
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# THROMBO-ANGIITIS OBLITERANS (BUERGER)

BY

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During recent years diseases of the vessels of the extremities have aroused an increasing interest and an incidental better understanding of a number of facies morborum that have not been differentiated previously.

One of these diseases is thrombo-angiitis (T. A. O.), also called *Buerger's* disease. It occurs chiefly in young males from the age of 17 to 40, beginning with acute, disseminating inflammatory processes of the vessels of the lower extremities followed by a chronic inflammation which in the course of a few years leads to obturation of large parts of the peripheral system of vessels.

The interest in this disease is increasing, among other things because the number of cases seems to become greater and because this disease, beginning as a benign disease without any alarming symptoms, as time goes on causes the most serious invalidism. Within the course of 5 years after the occurence of the disease 64 per cent of 460 patients with untreated T. A. O. had one lower extremity amputated; within the first 10 years 46 per cent had the other lower extremity amputated *(Silbert)*.

Investigations made by American, German, Russian, and a few French authors have elucidated the clinical picture and increased the knowledge of the anatomy of the disease; but we have not succeeded in arriving at an explanation of the etiology of the disease. These investigations have given noteworthy results not solely from a scientific point of view, but also with regard to treatment — especially the early treatment — impor-

tant advances have been made since the disease was described in detail for the first time in 1874 by von *Winiwarter*, at that time assistant to *Billroth* at Vienna (von *Winiwarter* draws, however, the attention to the fact that, already in 1866, *Larivière* in the Journ. de Bordeaux, published a case of juvenile gangrene which, judged by the case record, must have been one of T.A.O.).

In the Scandinavian literature only a few positive cases have been described. The Danish literature comprises 8 cases, all occurring in young males. *Viggo Christiansen* (1903), *Wimmer* (1905), *Kraft* (1911), *Jens Schou* (1911), *Meisen* (1917) have reported one case each and *Kjærgaard* (1916 and 1918) has reported 3 cases. In all these cases the disease had advanced so much that it was easy to establish the diagnosis. *Christiansen* and *Kjærgaard* describe in detail the facies morbi in its late stage.

This article is an attempt at supplementing the above papers, especially with a view to early diagnosis and treatment.

In Norway only one case has been published by *Böe* and a questionable one by *Harbitz*.

I have not been able to find any case in the Swedish literature, but Dr. *Albert Ahnberg* of Malmö has kindly informed me that he has found 3 cases in all, the case records of which will be published in a near future.

Most of the cases occur in the parts of Europe where the Jewish element is especially predominant, e. g. in Poland and in Russia. Especially in Russia numerous cases are said to have been observed after the war, a fact that perhaps may be associated with poor social conditions, which seem to be predisposing factors.

In the French literature, too, a number of cases have been described (*Camuset, Gilbert, Leriche, Guillaume,* and *Leibovici*).

The greatest number of cases published is found in America, where a great work has been performed in order to study this disease, the work has even been carried to such a length that special consulting stations and clinics for the treatment of this disease have been established. The frequency of the disease may

be due to the heterogeneous descent of the American population and, doubtless, to the great number of Polish Jews living in the eastern states.

*Leo Buerger,* Surgeon to the *Mount Sinai Hospital,* a special Jew Hospital in New York, has contributed a full share of the study of the disease and among other things published a very authoritative monograph (1924) based on more than 500 cases. It is rather peculiar to see how this disease, nearly always described by surgeons because it leads to gangrene and amputation, now belongs to the border-land between medicine and surgery.

When I consider the publication of the case record of a patient with T. A. O. expedient it is because I believe that it might be of interest to some to have the facies of this disease, and especially the first phases of the disease, revived. Moreover the disease is not so rare in this country as one is inclined to believe. Thus, in going through the case books of the surgical wards C and D of the »Rigshospitalet« for 1920—29, I found 5 cases in all of T. A. O. Amputation was performed in all the cases.

T. A. O. may be mistaken for sciatica, rheumatism, arthritis, and pes planus. There are, doubtless, patients who are treated to-day with insets for pes planus but whose complaints are due first and foremost to an obliterating vascular disease of the peripheral vessels, be it a dysbasia angiosclerotica or a T. A. O. — questions which I shall discuss more thoroughly in the paragraph on diagnosis.

Finally the knowledge of T. A. O. and of the other obturating diseases of the vessels might cause the disappearance of the diagnosis of juvenile gangrene without a more exhaustive history, because such a diagnosis does not inform us about the nature of the causative disorder.

*Case record:*

Gripples' Clinic. 2290—30. Sailor, aged 31, not of Jewish family. As a boy the patient had uncomplicated rheumatic fever twice. Never any tropical diseases. Uncomplicated urethritis gon. three times, the last 5 years ago. During the last 10 years the patient has smoked about 50 ci-

garettes daily. Denies abus. spirit. Lived in U. S. A. these 12 years. For the most of the time he has worked as a window-cleaner.

2 years ago the pt. was suddenly taken ill with fever, swelling of the right ankle-joint and crus. During the time following this there appeared — especially on the left foot and calf tender, red infiltrates of the size of a pea in and under the skin. The infiltrates disappeared spontaneously in the course of 1—7 days. The pt. was confined to bed with fever for a couple of months. When he got up there was no tenderness of the legs; but when he walked he got, after a little while, a sensation of tension in the calves and the feet. This sensation disappeared when he stood still. In the course of the following months the sensation was changed into pain and whilst being able during the first 6 months of the disease to walk without pain for about half an hour he can only walk about 50 metres now. The pain is aggravated if he tries to walk on. During the last year he has suffered much from cold feet and toes, the latter being said to be red in the evening. During winter the attacks of pain are especially marked. Ulcerations have never occurred. During the last year the pt. has had sensations in the left hand similar to those in the legs. The right hand is apparently well. During the last 18 months the pt. has been treated in several hospitals in New-York with various injections, among other things with typhoid vaccination, but without any improvement.

On objective examination the lower extremities appear to be natural, only the dorsum of the left foot has a bluish mottled appearance in spots. The feet are cool. No pulsation in the art. dorsal pedis, tib. post., and popliteae on either side. But pulsation is good in the art. femoralis. The muscles of the calves are of a peculiar, pasty consistence. In some parts tenderness and nodular infiltrates are found in the deep layers corresponding to the vessels.

On elevation of the extremities both feet become waxy pale, the left foot most readily and most markedly. There is reactive erythromelia of the left foot to the level of the scaphoid bone, of the right foot to the 1st and 4th toes. After pressure of he finger on the foot the anæmic spot remains longer than normally.

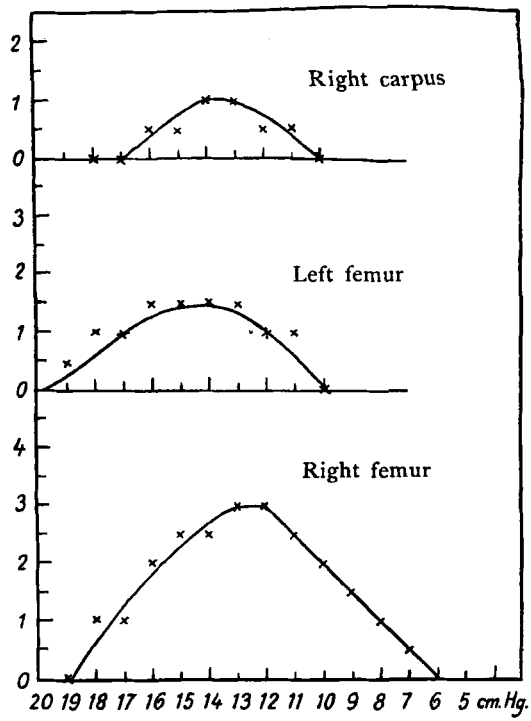
On Moskowicz' test the limit between the hyperæmic and anæmic parts of the left crus is ill-defined and found at the level of the border between the lower and intermediate thirds.

On the right foot, too, the limit is ill-defined and found at the line between the 1st intermetatarsal joint of the 1st toe and the metatarsophalangeal joint of the 5th toe. Oscillogram, see the curves!

The remaining objective examination did not reval anything of interest, especially the prostate gland was found to be natural on eploration.

The medical ward A. of the »Rigshospitalet« kindly admitted the patient from Sept. 18, 1930, to Nov. 29, 1930.

The following appears from the case book: — Wassermann's test ÷. Blood sugar 0,097—0,082. Time of hæmorrhage 3 minutes. Sedimentation of the red blood corpuscles (Westergren): 3 mm (1 hour). Blood pressure 125—80. Apart from a slight anisocytosis the blood picture showed no abnormal conditions. R. B. C.'s = 5.03. W. B. C.'s = 8540. X-raying: no arteriosclerosis of the peripheral vessels.




Oscillogram Sept. 8 for *Jens Körner*.
Right and left crus: 0.
Right and left ankle: 0.
After foot-bath (39°) for 10 minutes: 0.
Left wrist: 0 on Sept. 8., 1930.

The pt. got 10 intravenous injections in all of a 5 per cent Nacl. solution (300 cc.) which were well tolerated. After some of the injections there were, however, slight sensations of chill and a few times there was a rise of the evening temperature after the injections. The pt. was free from symptoms during the treatment. The urine was free from albumen, sugar, and blood all the time. The subjective complaints and the objective

symptoms remained uninfluenced by treatment. During the last few days (Feb. 1930) localized tenderness and infiltration have occurred corresponding to a limited part of the v. saphena of the left crus. The patient walks more poorly than formerly, but there is no pain when the legs are kept quiet. The pt. was discharged before his time owing to bad conduct (Nov. 29. 1930).

Resumé: — associated with an acute inflammation of the vessels of the lower extremities a sailor, aged 31, who smokes much, gets the symptoms of an obturating disease of the vessels. The disease is uniformly progressive with a few acute aggravations of short duration. Diagnosis: thrombo-angiitis obliterans *(Buerger)*.

*Morbid Anatomy.*

It is difficult, not to say impossible, sharply to draw the anatomicopathological picture of T. A. O. It is not because the macroscopic and the histological findings present pecularities which it is difficult to describe, on the contrary, but because the picture we find has elements in common with the pictures known from other inflammatory (syphilis, tuberculosis, simple inflammation) and degenerative (the polymorphous picture of atherosclerosis!) vascular diseases.

It is, therefore, quite natural that the question arises, is T. A. O. a specific disorder which we are justified in defining as a special disease with a definite, pathological picture? The answer must be affirmative, even if we do not, as yet, know the etiology of the disease. The clinical picture and the pathological alterations present such peculiarities that for the time being it seems to be justifiable to regard the disease as a nosological unit.

The descriptions of the morbid anatomy in the literature correspond in their main features; only details have been added after von *Winiwarter*'s elaborate description.

The following account based on examinations by von *Winiwarter, Buerger,* »*Brown, Allen* and *Mahorner*«, *Leibovici, Gans, Kjærgaard* and *Böe.*

*The Macroscopic Picture.*

The changes of the vessels in T. A. O. are as a rule localized to the peripheral arteries and veins of the lower extremity, but the disease may also occur in the vessels of the upper extremities.

Cases of T. A. O. have also been communicated in which the disease was localized to the mesenteric vessels and the coronary arteries. It seems to me to be doubtful whether such cases, displaying the same anatomicopathological picture as T. A. O. but not corresponding to T. A. O. as regards the clinical picture, may be grouped under this term. Perhaps such disorders should rather be referred to the group of endarteriitis obliterans.

T. A. O. is chiefly localized to the small and medium sized peripheral vessels and especially to the arteries. The veins and the arteries are lying firmly welded together in a sclerous, fibrous tissue. The disease of the vessels is found to be unevenly distributed over the vascular area in question, sound parts alternating with diseased parts and fresh and old processes being found side by side.

It is, however, rare that fresh processes can be demonstrated if the disease has been going on for several years. *Buerger* draws the attention to the fact that the process begins peripherally and spreads proximad. *Meleney* and *Miller* do not agree, as they have demonstrated in several cases that the process has begun in the middle of the leg, the peripheral vessels being completely unimpaired.

If a diseased vessel be examined when cut open its wall is found to be thickened and the lumen is unevenly strictured as a consequence of thickening of the intima. In some places the lumen may be fine as a hair, in other places there is complete obturation as a consequence of plugging of the vessel by a red thrombus or by a plug of granulation tissue, which is soft and sometimes brittle and through which the blood can be squeezed, the tissue being traversed by fine, sanguiferous canals. Resting on such an obturating mass of tissue there may perhaps be seen a red thrombus adherent in some places to the thickened wall of the vessel. The vessel itself is of a rigid consistence but not brittle as in atherosclerosis.

*The Adventitia.*

At the earliest stage of the disease small, dispersed, frequently perivascular lymphocyte infiltrates are found. Thickening of the endothelium is seen in the vasa vasorum. At this stage there are no alterations of the other coats of the blood-vessel, apart from thickening in some parts of the intima. As the disease advances the alterations of the vessels become more marked, the fibrous tissue of the adventitia increases and a *increase of the perivascular fibrous tissue* is seen simultaneously. If the process is so advanced that the passage of the blood is interfered with, or there is a complete occlusion of the vessel the vasa vasorum are seen to be dilated, thus reflecting the attempt of the organism to establish a compensating, collateral circulation.

It is worth mentioning that the above lymphocyte infiltrates do not disappear but are found constantly in the adventitia, even if the disease has been going on for a long time and the sclerosis is very marked; but it is rare to find accumulations of polynuclear leucocytes in the adventitia, even if they can be found in the media or the intima.

*The Media*

is characterized by the fact that it is the seat of exudative and proliferative processes at the same time. The cellular infiltrates — lympho-leucocytes and possibly *Langerhans'* giant-cells — are highly varying and not infrequently present as small abscesses in the wall of the vessel. I shall revert later on to the importance of these inflammation elements, as they play a certain part in the discussion of the clinic and pathology of T. A. O.

The proliferative processes with increase of the fibrous tissue are on the other hand constant. Not solely the fibrils but also the number of fibroblasts is increased, however, without atrophy of the nonstriated muscle cells — they are on the contrary unusually well-preserved.

In the media there are, in conclusion, the vasa vasorum which are hardly ever found under normal conditions in vessels of this order; only in atherosclerosis a few vasa vasorum may be found

sometimes, but never to the same extent as in T. A. O. These alterations differ from the atherosclerosis, where a general atrophy of the muscle cells is found together with a marked sclerosis replacing the myogenic elements.

In atherosclerosis chalky deposits are also found and round the latter lymphocyte infiltrations and a few giant-cells can be found; but such a round-cell infiltration as is seen in T. A. O. forming veritable abscesses of giant-cells is not seen in atherosclerosis. The picture of

*The Intima*

is highly varying and is to some extent associated with the duration of the disease. In the parts where there is only a slight stricture of the lumen of the vessel the intima is hyperplastically thickened, the cellular elements, endothelium — and connective tissue cells and the elastic fibrils being increased in number. If on the other hand the case is of long standing the thickened intima consists of tissue with few nuclei. It is worth mentioning that the lamina elastica interna *frequently is much thickened, consists of several layers and is not split and fissured as seen in atherosclerosis.*

In other parts, where the process in the intima is of longer standing, an irregular, indented mass is seen growing into the lumen with incipent depositing of red blood corpuscles as the initial stage of the ensuing thrombus. In conclusion there areparts where the intima has grown into the thrombus, which obturates the lumen of the vessel completely. The thrombus, thus being secondary in connection with the disorder of the intima, is recanalized and gradually replaced by granulation tissue. This picture is in points essential different from atherosclerosis in which we find thickening of the intima — but no cellular hyperplasia — proliferation of the other tissue elements together with degenerative processes, such as fatty degeneration, hyaline degeneration, and chalky deposits.

As mentioned above the irregularities found in the membrana elastica are characteristic of atherosclerosis. The proliferation of the intima which is seen in atherosclerosis and which, owing to thrombosis, may lead to a secondary occlusion of the

vessel should not be termed endarteriitis obliterans but should be perceived as the sequels of a disorder of nutrition in the wall of the vessel. Obliterating endarteriitis can be found in syphilitic arteriitis, in the vessels in cases of tuberculous cavern, in kidneys with chronic nephritis, in inflamed tissues, and near by healing wounds. It is these diseases of the vessels, occurring in connection with inflammation in and round the vessels, which *Friedländer* (1876) described under the name of endarteriitis obliterans. The alterations of the intima in these cases are the same as are seen in T. A. O. It can be difficult, not to say impossible, in the initial stage to determine the nature of such disases of the vessels. If on the other hand the T. A. O. is of longer standing and the processes are marked the difficulty will only be to distinguish between T. A. O. and atherosclerosis.

*Buerger* is of the opinion that it is possible to distinguish between T. A. O. and other diseases of the vessels, because it is said to be a distinctive feature of T. A. O. that it is possible in the initial stage to demonstrate the existence of acute foci of infection with round cells and giant-cells in the media and sometimes also in the intima. There are varying opinions about the value of this picture. Some authors, e. g. *Leibovici,* think that the alterations described by *Buerger* are nearly always found on careful serial examination of the vessels, whilst others, *Brown, Allen* and *Mahorner,* are of opinion that the acute foci of inflammation are found sometimes, but that these alterations cannot be demonstrated in the great majority of cases. They disagree absolutely with *Buerger* that the acute inflammatory alterations are the first stage of the disease, because they have been able themselves in such cases together with the acute inflammatory alterations to demonstrate the existence of lymphocyte infiltration, fibrosis in the adventitia and thickening of the intima indicative of the long standing of the alterations of the vessels.

Whilst there are divergent opinions, then, as regards the picture in the initial stage there is a general concord as regards the final stage. The adventitia and the perivascular tissue display an increase of the connective tissue, a perivascular fibrosis solder-

ing together arteries, veins, and nerves. Some leucocytes may still be found in the adventitia. The vasa vasorum are larger and more numerous than normally. The media is thickened with an increase of the interstitial connective tissue. The muscle cells are as rule well preserved, and numerous small blood-vessels can be seen in the media. The lumen is obturated by a tissue rich in cells consisting of fibroblasts and sometimes of leucocytes, and in the tissue there are numerous blood-vessels — some with walls consisting of three coats — through which the blood is flowing, the vessel thus becoming partially permeable again. Also round the perivascular nerves there is an increased production of connective tissue and the nerve fibrils are the seat of degenerative processes with a decrease of the myelin and thickening of the perineurium, alterations that in all probality are due to an ischæmia of long standing, as a similar picture is seen in atherosclerosis.

With regard to the histological diagnosis the difficulty is to differentiate the picture from atherosclerosis, as it must be considered that the histological picture of the normal vessel is dependent on and varies according to the age and to some extent according to the part of the body. Endarteriitis has a characteristic picture which makes a distinction possible, whilst in atherosclerosis and in T. A. O. it may be extremely difficult to distinguish them from each other, when there are no marked alterations.

It has been proved by investigations that the characteristic, histological picture corresponding to the clinical picture of T. A. O. is not always found, but on the other hand a picture corresponding to atherosclerosis, i. e. a presenile atherosclerosis is found (*Leibovici*). As we know that the atheroschlerotic process is developing gradually from childhood to old age and toxic or infectious influences may hasten this process it is quite natural that such an early atherosclerosis clinically can present the same picture as T. A. O. The diagnosis becomes especially difficult in the cases where it is the atherosclerotic vessel that becomes the seat of a T. A. O. It may be difficult, not to say impossible, to draw the limit between such cases.

## RESUMÉ

T. A. O. is a chronic inflammatory process in arteries and veins characterized by proliferation of the intima, sclerosis of the wall of the vessel, and thrombosis. The thrombi become organised and re-canalized. In the media and the adventitia there are numerous new-formed vessels leading the collateral circulation round the obturating thrombus. Together with the chronic inflammation there are sometimes found acute inflammatory processes, frequently localized to the media. The surrounding nerves are also altered and there is a marked and very characteristic perivascular fibrosis.

*The etiology*

is not comprehended with certainty, but the course of the disease and the anatomicopathological picture seems to justify our conception of the disorder as an infectious toxic disease localized to the wall of the vessel — during the acute stage it is actually a pyæmic arteriitis.

As yet no convincing results have been arrived at on attempts at cultivation of virus from the diseased vessels. The portal of entry of the infection is not known, but the Americans believe that infectious foci round the teeth or in the tonsils should be of importance. As the disease practically is found in males exclusively the possibility of an infection of the prostate gland has also been considered. It is at any rate peculiar that *Mac Callum* in 50 per cent. of the cases has demonstrated infection of the prostate gland.

Even if we do not know the cause there is, however, a number of factors which seem to be predisposing.

T. A. O. occurs especially in the Jewish race, but this viewpoint which was the common one formerly and also a just one — only 4 of *Buerger*'s 500 cases were not Jews — cannot be maintained to-day. Only 50 per cent. of the material from the *Mayo* clinic (200 cases) were Jews. None of the pts. were Jews in the 5 cases from the »Rigshospitalet« plus the case described here. Gradually as the interest in the disease has increased in the various countries an increasing number of cases is communi-

cated in which the pts. are not Jews. This displacement of the distribution is perhaps due to the fact that the disease was of special interest and originally was described in the eastern part of Central Europe, where the Semitic race is prevailing. But the increasing number of cases (*Buerger*) may of course also have caused a displacement.

*The sex* seems absolutely to be of importance, few cases being found in the literature in which the disease has been diagnosed with certainty in females.

According to *age* the disease occurs during the interval from 15 to 65 years; the greatest number is found between the ages of 30—50 years.

Of extraneous factors which seem to be predisposing the *tobacco* must be mentioned first and foremost, however, without regarding tobacco as a primary, etiological factor, as *Silbert* and *Weber* were inclined to do. For there is not a small number of patients who never smoked tobacco. But it appears among other things from *Silbert's* results of treatment that tobacco plays a certain rôle, as the treatment failed when the patient continued to smoke.

*Cold* and *wet* are apparently predisposing elements in $^2/_3$ of the cases from the *Mayo* clinic. On the whole poor social conditions seem to be of importance, compare Russia; but this does not hold good absolutely, which appears from the fact that the disease also occurs in tropical districts and is seen among the members of social classes living under good conditions.

On the other *the nature of the profession* does not seem to be of any importance, which appears to be strange as the disease is localized chiefly to the extremities, a fact which one should think beforehand had to be considered when estimating the etiological factors.

It has been emphasized that the blood sugar percentage and the coagulation time and viscosity of the blood were increased, but it seems as if it is impossible to confirm this statement by control examinations.

Disturbances of internal secretion have been discussed and the attention was especially drawn to the suprarenal glands

(juvenile atheroma). Neither the experimental examination nor the operative results (epinephrectomy) indicate that these glands are of any importance in this disease.

*The course of the disease.*

In about ¾ of the cases there is a characteristic facies morbi and course of the disease, whereas the remaining number of cases displays such a polymorphous picture that the course of the disease is best illustrated by means of examples.

The disease develops by stages with symptoms of acute inflammation, and between the stages long quiet periods intervene, often with apparent improvement.

It may be practical to distinguish between 4 types of T. A. O.

1. T. A. O. localized to the lower extremity alone.
2. T. A. O. complicated by thrombophlebitis or phlebitis migrans.
3. T. A. O. localized to the upper extremity.
4. T. A. O. complicated by atherosclerosis.

This classification is of course an artifical one, as there are transition forms; but it has the advantage that it affords a survey of the localization of the disease and of the combinations that are of importance to the clinical aspects of T. A. O.

The onset of the disease is as a rule insidious. Cold feet are often the first symptom. Some time after the patient complains of fatigue or rheumatic pain in feet or calves, a fatigue which is aggravated especially on exertion, as walking or running. These inconveniences may last for a long time, from months to years, before the patient displays the typical intermittent claudication: the patient drags his leg, gets spasmodic sensations in the muscles of the calves preventing him from going farther, but after a short rest the patient is enabled to walk again, and in this manner painless and painful periods on exertion or walking interchange. In the early stage of the disease sensations of fatigue are not infrequently of intermittent type.

At some time or other at the beginning of the disease numerous patients display symptoms of localized superficial phle-

bitis (phlebitis migrans). Cases of deep phlebitis and arteriitis and ædema of the extremity are not infrequently seen either. The symptoms correspond to the acute stage of the disease as described in the section on the morbid anatomy of the vessels. These acute symptoms of inflammation are of great diagnostic value, because the demonstration of an obturating vascular disorder in connection with such a period gives great support to the diagnosis T. A. O.

At the time of commencement of these symptoms, or some time afterwards, the extremity displays other symptoms of disturbances of circulation. The foot is red in the evening when the patient has been walking the whole day. When the symptom is more marked the foot turns red as soon as it is placed in a declivous position. The redness disappears when the extremity is elevated, and the skin becomes waxy pale — which is not seen under normal conditions — as a consequence of the ischæmia. This redness, which *Buerger* calls *erythromelia,* corresponds to the rubor seen in senile peripheral atherosclerosis and termed »le signe de la chaussette« by *Vaquez.* The hyperæmia which is localized to the foot or a little up the crus is either uniformly diffuse or seen in patches.

Sooner or later following this period boring pain occurs in the legs, pain which is present, even if the patient is resting completely (rest pain). The pain may be so intense that it influences the mind of the patient and it becomes necessary to perform amputation of the painful, diseased part in order to relieve the patient. It is characteristic that this pain frequently is alleviated when the leg is dependent. Therefore these patients cannot make themselves comfortable in bed but have to sit up with the legs hanging over the bedside the greater part of day and night. Such pain is nearly always the precursor of trophic disturbances in the foot or the toes, occurring either as superficial ulcerations or as partial gangrene requiring amputation in most cases.

There are thus two phases of the disease, a *medical phase* from the onset of the disease up to and including the period of claudicatio intermittens and erythromelia, and a *surgical phase*

beginning from the time of onset of the intense pain (rest pain).

About ⅓ of the cases are complicated by vasomotor disturbances, especially spasms of the vessels, symptoms that may be misleading and give rise to confusion with other vasomotor disorders.

Before I begin the discussion of the diagnosis I consider it expedient to refer more thoroughly to the single symptoms, also because these symptoms are common symptoms of peripheral, obturating diseases of the vessels. As regards atherosclerosis and T. A. O. it is important out of regard to treatment that the diagnosis is established as early as possible.

*Symptoms.*

Absence of pulsation in the peripheral arteries (a. dorsalis pedis, a. tib. post., a. poplitea) is one of the most important symptoms indicating that the circulation in the peripheral vessels is compromised.

Absence of pulsation may be due to: — 1. Obturation of the vessel in question; it is then felt as a hard, rolling cord under the fingers. 2. Partical occlusion of the vascular trunk above the part that is examined, for which reason the blood from the collateral arteries and the eventually re-canalized thrombus oozes through the vessel. 3. A local vascular spasm. Repeated examinations in a well-tempered room will prevent such a mistake.

It is, however, not in all cases of T. A. O. that a suspended pulsation is found in the peripheral vessels even if the other symptoms are found. Thus, in 5 per cent of the cases of the *Mayo* clinic, good pulsation was found in the vessels. This may be due to the localization of the vascular disease to the more peripheral arteries, e. g. to the a. plantaris. If there is an opportunity to watch such cases it will be found after some time — perhaps 6 months — that for instance the a. dorsalis pedis does not show pulsation any more, the disease spreading from the most peripheral vessels in a central direction.

One may be tempted to believe that when the extent of the pulseless vascular area is estimated we have a clue to the prog-

nosis. This is only correct to a certain extent, as there are cases with absence of pulsation in the arteries of the foot and in the popples, even in the a. femoralis, in which the course has been comparatively benign, several years passing before gangrene occurred. Such a course is only seen when the thrombosis begins peripherally and progresses slowly, so that it is constantly possible to create an effective collateral circulation.

If on the other hand the course of T. A. O. is rapid a total gangrene of the foot will soon occur — which is rare in T. A. O. as contrasted with atherosclerosis — and it becomes necessary to perform amputation above the knee, whereas in the slow, progressive form an economic amputation below the knee as a rule is sufficient.

*Pachon*'s oscillometer is a good aid in the examination of the pulsation of the vessels, as it is highly sensitive to fine pulse waves. Only in the ankle region one should not infer too much from absence of pulsation, as the apparatus is not always able to register sure pulsation in this region.

*The cutaneous disturbances of circulation* in T. A. O. are of the greatest importance to the diagnosis. *Buerger* has especially drawn the attention to the characteristic redness of the foot that is not infrequently seen in the erect posture. This cutaneous, passive hyperæmia is found when the deep vessels have been occluded, and it should be perceived as an indication of a compensating collateral, cutaneous and subcutaneous circulation through the dilated, superfical veins; but the symptom is not so constantly present in atherosclerosis as in T. A. O. in which it is usually very marked. If the patient is sitting with his legs hanging over the bedside it will be seen in about half a minute that the toes, especially the great toe, become red whence the redness spreads on to the foot and possibly on to the crus. (*Buerger*'s erythromelia should not be confused with *Pick*'s erythromelia corresponding to *Herxheimer*'s acrodermatitis atrophicans chronica progressiva). In the mild degree of T. A. O. the erythromelia is only brought about when the extremity has been elevated and lowered a number of times, the so-called *reactive* erythromelia, whilst in the severe degrees of T. A. O. the

erythromelia is found, even if the extremity is placed horizontally: *chronic erythromelia.*

The colour is not always uniformly red, the skin is frequently of a reddish mottled appearance and the colour may sometimes be masked by cyanosis owing to vascular spasm. Another indication of the sensitiveness of the veins to weight is seen on elevation of the extremity, the foot, or more properly the part of the vascular area that is diseased, becoming the seat of a marked *ischæmia* owing to a disproportion between the afflux and the efflux of blood. As is known the foot retains its pink colour on elevation under normal conditions.

The rate at which the ischæmia occurs and the number of degrees of the angle of elevation may be used for expressing the degree of the vascular disease. Sometimes peripheral cyanosis may render it difficult to decide whether there is ischæmia or not. If so *Buerger's* compression test is a good aid, consisting of pressure with the finger-tip on the suspected part — often the nail of the great toe — calling forth an ischæmic spot. If the ischæmia continues it indicates that the circulation has become compromised.

For purposes of measuring the insufficiency of circulation the level to which the leg must be raised or lowered in order to call forth ischæmia or erythromelia *(Buerger)* is stated in degrees. The angle thus arrived at, the circulation sufficiency angle, can be used as an objective standard in estimation of the course of the disease. (Fig. 1).

*Pain* is a common symptom and often causes the patient to seek medical advice and the diagnosis to be established. There is, however, a number of cases which do not present any symptoms of pain despite an extensive T. A. O. in the peripheral vessels. The type and the occurrence of the pain are in reality not especially characteristic of T. A. O. but are symptoms common to all obturating vascular diseases.

Two types of pain may be outlined:

1. intermittent pain, occurring as claudicatio intermittens in its most marked form,

2. constant or paroxysmal pain, present even when the extremity is kept quiet (rest pain).

1. In its marked form the claudicatio intermittens *((Charcot, Erb)* is such a well-known symptom that further description

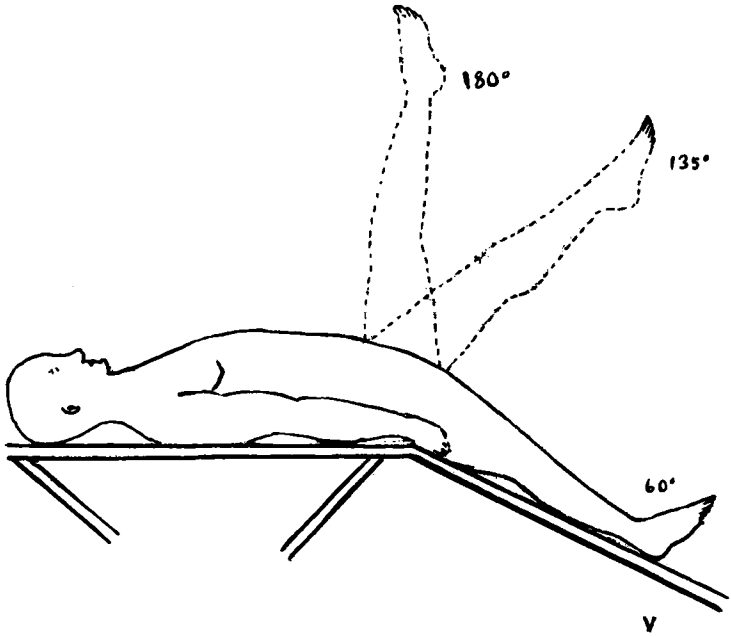



*Fig. 1.*

The circulation sufficiency angle. Normally the colour of the foot is only sligthly altered at 180° and only sligthly red at 60° and below. In case of arterial obturation: ischæmia on elevation and abnormal rubor in dependent position.

will be unnecessary. In T. A. O. there is, however, a form characterized by intermittent visible circulatory disturbances. After exertion of short duration the foot becomes pale and pulseless, as contrasted with the true claudicatio the patient is not aware of any circulatory disturbances, but the circulation is re-established.

It would perhaps be reasonable to emphasize that it is not correct to establish the claudicatio intermittens as a facies morbi — as it is sometimes seen — it is and will remain a symptom common to a number of diseases. If it is desired to use the symptom as an indication of a disease it should be further characterized, e. g. dysbasia angiosclerotica.

In T. A. O. the intermittent cladication occurs simultaneous with or after the other vascular symptoms being demonstrable. But there has been a preceding period during which the patient has had vague sensations of fatigue in the calves and in the soles of the feet, and sometimes intermittent sensations of cold and cramp. In the earliest stages of the disease burning pain is not infrequently present in the deep parts of the leg, as is also tenderness of the deep vascular trunks. It is this vague pain at the onset of the disease that is of far greater importance to the diagnosis than the intermittent claudication, because this pain can and should lead the examination in the proper direction thus causing the diagnosis to be established at an early point of time.

2. *Rest pain.* If the patient begins to complain of pain in the legs, even when he is lying in his bed, and states that he is only relieved when sitting up in the bed with the legs dependent over the bedside it is a most serious symptom, because this pain heralds the onset of gangrene. The pain corresponds entirely to the classical pain of decubitus. When localized to a single toe it is actually pathognomonic of the coming gangrene. Only few patients are able to bear this sort of pain and to await the spontaneous demarcation; most of them require amputation before. If the patient is able to endure the period of pain a partial gangrene of a toe or of part of the foot occurs, and the pain becomes more intense.

The Americans have been much inclined to use a high amputation, but *Buerger, Leibovici* and *Kjærgaard* prefer an economic amputation below the knee, as it is unnecessary to be too radical in this disease which has so long remissions. If the pain is not alleviated by amputation it is a symptom of impending

gangrene at the seat of the amputation, either because the latter has been too economic or because the vascular disease has spread.

*The trophic disturbances:* ulcerations or partial gangrene occur during the last phase of the disease. In about half the number of cases the ulcerations have been provoked either by a trauma or as a consequence of an operation on the foot, as the pain in a toe, the marked redness, or a small fissure in the nail-fold cause the surgeon wrongly to establish the diagnosis of unguis incarnatus or panaritium, and the result of the operation will then be a flaccid small ulceration with a foul bottom healing slowly at best. If the wound does not heal, gangrene will develop. Otherwise the trophic ulcerations are localized to the heel, the dorsum of the foot, and about the malleoli. The gangrene often begins in the great toe which to begin with is painful, cold, cyanotic or waxy pale, later on becoming black, shrivelling up, and ultimately coming off.

*Various types of the disease and prognosis.*

About ¾ of the cases follow the course referred to above, but the clinical picture of the remaining cases is highly varying. Cases are seen which could be termed »les formes frustes« and in which the patient complains of cold feet or fatigue in the calves. This is the only symptom for months until one day the patient displays other symptoms of an obturating disease of the vessels. Other patients only display a single symptom, either pain or trophic lesion or only red feet in the erect posture; there are even patients who have never displayed any symptoms before the occurrence of gangrene. In conclusion there are cases displaying no symptoms whatever. Such cases ore seen where there is T. A. O. in one leg without any symptoms in the other leg, despite the fact that the objective examination reveals complete occlusion of great vascular areas.

The intensity of the pain or the abruptness of the latter may cause one to think of embolemia, but in reality the cause is multiple angiitis with massive thrombosis. The acute T. A. O. is

frequently associated with phlebitis and is only seen during youthful years. The prognosis is bad, the disease rapidly leading to gangrene. On the whole it may be said that the earlier the disease occurs the more rapid is the course, ending with gangrene and amputation. The typical T. A. O. has a chronic course with remissions of long duration. The symptoms may cease spontaneously during the first period of the disease. Such spontaneous remissions are frequently seen during the hot periods of the year and when the patient uses remedies improving the peripheral circulation. Recovery may be spontaneous but this is rare. Recovery is clinical but not anatomical. The average period from the onset of the disease to the occurrence of gangrene is 2 years, and within five years a little more than half of the untreated patients have been amputated. It is, however, an exception that the disease involves death.

*Diagnosis.*

The early diagnosis is of the greatest importance to the prognosis of the disease. It should be fully realized that abnormal fatigue after exertion, especially when unilateral in calf or foot, is frequently due to circulatory disturbances. It should not be supposed at once that it is a case of pes planus or insufficientia pedis or an arthroitis, but the attention should be directed towards the static pain which is not alleyiated when the patient stands still as contrasted with sensations of fatigue in circulatory disturbances; for cases of arthroitis display symptoms both during rest and on movements. The orthopedist is as a rule the one who has the greatest chance of establishing the correct diagnosis, because several of the patients are sent to him owing to pes planus.[1])

80 per cent. of the patients from the *Mayo* clinic had been treated with insets before the diagnosis had been established. It is rather a good — though somewhat agitating — rule that

[1]) From Dec. to Feb. 1931 we have a diagnosed dysbasia angiosclerotica three times in patients who either had been treated for or had been sent to treatment of pes planus.

if a well-fitted inset does not alleviate the so-called flat-foot pain of soft feet the diagnosis was wrong.

Erythromelia is characteristic of the obturating vascular disorders as contrasted with the active hyperemia which is seen in the vasomotorial vascular disease erythromelalgia. Just as the diagnosis of sciatica should not be made without a preceding exploration, the diagnosis of pes planus or rheumatic pain of the foot should not be made without examination of the peripheral circulation.

The Arterial Vascular Diseases*)

- Vasomotorical vascular diseases
  - localized
    - Vascular spasm
      1. *Raynaud's* disease
      2. Acrocyanosis, acrosphyxia, acroparæsthesias
    - Vascular dilatation: Erythromelalgia
  - universal
    - Vascular spasm: Hypertension (essential)
    - Vascular dilatation: Hypotension (essential)
- Organic vascular diseases
  - localized
    1. Atherosclerosis — with or without trombosis—diabetic gangrene (juvenile atherosclerosis)
    2. Thrombo-angiitis obliterans
    3. Thrombosis. Embolism
    4. Arteriitis (Endarteriitis obliterans: etiology known: syphilis, tuberculosis etc.
    5. Aneurysm
  - universal: Atherosclerosis

*Fig. 2.*

With a view to the differential diagnosis the point is first and foremost to know whether the disorder is of a vasomotorical or of an organic nature. This can be decided in 95 per cent. of the cases by the estimation of the pulsation of the vessels: variable or constant. The influence of the temperature on the complexion and the pulsation, especially when the latter is measured by means of *Pachon*'s oscillometer, will also give good information. The measurements of the temperature of the skin give no better information than the general clinical examination. Arterial injection of lipiodol can only be used in immediate con-

*) (adapted from Brown and Allen)

nection with amputation and is, therefore, of no noteworthy practical importance.

In the table, fig. 2, the diseases are tabulated which can be mistaken and which, therefore, are of importance to the diagnosis. In the group: vasomotorical vascular diseases it is only the localized vasomotorical disturbances, and among these first and foremost *Raynaud*'s disease, that most frequently give rise to confusion.

This disease, which in its classical form is characterized by painful vasomotorical crises occuring in paroxysms and localized symmetrically to the peripheral parts of the body, most frequently to fingers and toes, begins with periods of local asphyxia, which in the late stages of the disease is transformed into a well-defined, symmetrically localized gangrene, which is frequently localized to the digital pulp.

The pain does not correspond to definite nerve areas. The course is intermittent, often with pain-free intervals. During these periods the pulsation of the vessels is completely normal, there is, however, not infrequently a constant vasomotorical lability. The duration of the attacks is highly varying, from a few hours to several weeks. In the course of single attacks the disease may pass through all the phases and end with gangrene; as a rule several consecutive attacks are seen. On objective examination no sensory disturbances or paralyses are found, although other symptoms of vasomotorical disturbances of innervation, aphasia, hæmoglobinuria, arthropathies, may be demonstrable. As a rule the disease occurs in neuropathic females from 20 to 30 years of age.

It has moreover been stated that there is an atypical *Raynaud's* disease without any periods with positive, local circulatory disturbances but with an asymmetrical, localized gangrene. *Leriche* is, however, of opinion that such atypical forms do not exist, but that in these cases we have to do with obliterating arteriitis with complicating vasomotorical disturbances.

Localized vascular spasms are also seen in *acrocyanosis, acroasphyxia* and *acroparæsthesias* which are characterized by

pain occurring in attacks and accompanied by œdema, alterations of the colour of the skin, and sometimes trophic ulcerations. The alterations are localized to one or more toes but there is no symmetry. Between the attacks there is good pulsation and a normal oscillogram.

Vasomotorical disturbances with vascular dilatation are seen in the facies of *erythromelalgia (Weir Mitchell),* a motor neurosis with marked, active hyperæmia occurring in attacks and accompanied by burning pain localized to feet and hands. There is, therefore, no ischæmia on elevation of the extremity. The pulsation of the vessels is natural, also during the attacks. The disease is most common in females.

The difficulties in distinguishing between the various cases are to a certain extent due to the fact that there are types which are combinations of organic and vasomotorical disturbances.

Among the organic, localized vascular disorders one must first and foremost form an opinion on the most frequent type, the atherosclerosis. It is diagnosed by means of palpation of the arteries, by means of the general condition of the patient and the blood-pressure, which is not increased in a non-complicated T. A. O. The age of the patient will also be of importance, but too much weight should not be given to the age, cases of presenile atherosclerosis being known. In conclusion a skiagram can give valuable information.

*The embolemia,* which is of an acute unilateral occurrence with intense pain, may perhaps be confused with an acute T. A. O., but symptoms of a disease of the heart, atherosclerosis, or a preceding disease may prevent such a mistake. Confusion with the other organic vascular disorders will hardly be possible.

### *Treatment.*

Of recent years a change of the viewpoint concerning treatment has taken place. Before that time medical treatment was considered to be of no value worth mentioning, and it was almost exclusively the treatment during the surgical phase that was recorded in the literature. It has now been realized that

a prophylaxis carried through in a rational manner and medico-physical treatment clinically restore a good deal of patients to health thus saving them from amputation. But the treatment is of long duration, frequently going on for years, a fact which it is necessary to consider when the choice has to be made between medical treatment and amputation, it would for instance be inexpedient only to recommend medical treatment of a small gangrenous ulcer on a toe. As the principles of treatment — apart from the medicinal treatment — are common to the obturating vascular diseases I believe that a more detailed reference to treatment will be justified.

The prophylaxis is of paramount importance during the earliest stage of the disease: foot-baths, anointing of brittle nails with lanolin ointment. The nails should be pared straight in order to avoid ingrowing or lesion of the nail fold and should be cleaned by means of a wooden instrument and not by means of cutting instruments. The foot-wear should fit irreproachably. Thick wollen stockings keep off the influence of cold, and the extremity should at all costs be preserved from trauma. Tobacco should be absolutely forbidden.

The medial treatment requires confinement to bed for weeks, whereby the nutrition of the tissues is improved, the pain alleviated, and the ulcerations, if any, will perhaps heal. If the extremity is placed either in an elevated or declivous position the pain may be alleviated considerably. Care should be taken that the feet are kept warm and that pressure of the blankets on the foot and pressure on the heel is avoided.

By means of physical methods and medication it is tried to improve the peripheral circulation: incandescent light baths for 1 hour 2—3 times a day. Ultra-red rays seem to be especially effective in alleviating the pain. Sun-baths and diathermy also seem to be beneficial (diathermy 1—1½ hour a day). Hot foot-baths seem to be less beneficial, not solely out of regard to the posture, which impedes the circulation, but also out of regard to the danger of maceration of the delicate skin. The heat-treatment must not be given during the acute periods, or when there

is ulceration. Diathermy is especially indicated during the initial stage as part of the ambulatory treatment.

*Buerger* has recommended gymnastic exercises based upon the same mechanism as engenders erythromelia. The patient elevates the leg for 1 minute and then keeps it in a dependent position over the bedside for 1 minute, placing it in a horizontal position for 2 minutes afterwards. The exercises should be performed 3 times a day for a quarter of an hour each time, and by this means an alternating draining and filling of the collateral vessels is attained. *Bier*'s stasis treatment is also said to be beneficial *(Kraft)*, but this treatment should, of course, only be used during the quiet periods of the disease. Massage should be dissuaded most positively. It goes without saying that massage of a vascular area in which the thrombotic processes are characteristic of the facies morbi is fraught with risks.

Among the various medicinal methods of treatment that have been recommended there are as yet only 2 which it seems to be possible to employ with some chance of a good result, viz. intravenous injection of typhoid vaccine and intravenous injection of a 5 per cent. solution of sodium chloride.

The typhoid vaccine therapy was recommended by *Goodmann* and *Gottesman* and has been employed with apparent success by *Brown* and *Allen*. Of 43 patients 25 became free from pain. The number of amputations decreased and the trophic ulcerations healed rapidly. Numerical information about the latter two facts is, however, lacking. This form of intravenous protein therapy seems partly to be anodynous, partly actively creative of hyperæmia in the peripheral vascular area simultaneous with the patient becoming febrile. The typhoid vaccine consists of typhoid bacilli and paratyphoid A and B. The initial dose is 20 to 50 millions and the dose is gradually increased by 50 millons up to 300 millions. Injections are made every 4th or 5th day, 4—6 injections in all, then there is a pause for 3—4 weeks and eventually a repetition of the injections.

*Brown* and *Allen* are content with the treatment, so much so that they maintain that no amputation should be performed until this treatment has been tried.

The only mehod that seems to have been tested thoroughly for a sufficiently long period is *Silbert*'s method, in which intravenous injections of a 5 per cent. newly prepared, sterilised solution of sodium chloride are made. *Silbert* maintains, and is doubtless justified in doing so, that the only satisfactory criterion of the value of the treatment is, not whether the pain disappears, but whether the number of amputations decreases.

In a group of 450 cases, which have been observed for up to 5 years but not treated 64 per cent. amputations were found. In another group comprising 225 typical cases and 64 borderland cases, also observed for up to 5 years, in which all the cases were treated the amputation percentage was 83. In this group 64 per cent. of all the ulcerations healed. 67 per cent. returned to their original work and 84 per cent. displayed improvement. Many reasons warrant reservation with regard to these figures. But considering the relatively large number of cases it seems to be justifiable to suppose, as *Silbert* does, that this treatment has a beneficial influence on T. A. O.

*Technique.* A trial dose of 150 cc is administered intravenously; then for 2 months 300 cc are administered three times a week. The injections must of course not be given in the affected extremities. Heat-treatment is given simultaneously. *Silbert* emphasizes that the treatment will fail, if the patient goes on smoking tobacco. The injections are well tolerated. The patient may complain of heat of the face and thirst, but no real disturbances are seen.

Insulin has been recommended, but neither *Leibovici* nor *Brown* and *Allen* have seen any results after treatment. Acetylcholine has also been tried without positive effect. *Philips* and *Tunick* have used X-raying of the lumbar column in 50 cases which, however, were only of 1 year's standing. In most of the cases an improvement was seen, possibly owing to action on the paravertebral, sympathetic ganglia. *Brown* and *Allen* on the other hand have not observed any effect from X-raying. In case of intense pain *Silbert* has been successful in injecting absolute alcohol into the sensitive nerve trunks of the nerve segment in

question; after this treatment there is said to be absence of pain without complications for up to 6 months.

Neither sympathectomy nor resection of the paravertebral ganglia and epinephrectomy (von *Oppel, Leriche, Herzberg*) have given results encouraging further experiments.

Conservative methods, such as ligation of the vena femoralis (von *Oppel*) or ateriovenous anastomosis, must also be dissuaded. Despite the fact that good results have been communicated after ligation of the vena femoralis this procedure cannot be recommended, among other things because *Leibovici* after a number of good experimental investigations has proved the absence of a physiologic basis of the method and because *Buerger* only has had poor results in the clinic.

The radical, surgical treatment, amputation above the knee, has had a number of supporters in America. *Buerger, Leibovici, Kjærgaard* and others maintain, however, that an economic amputation should be performed as the disease ceases after the course of some time. In case the disease does continue and necrosis of the flap occurs, an amputation can always be performed at a higher level.

Infection and gangrene at the amputation wound in T. A. O. do not involve the same danger to the patient as does the amputation gangrene in senile gangrene.

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