Cerebrovascular Thrombosis in Patients with Buerger's Disease

By Heinz I. Lippmann, M.D.

Nine cases of cerebrovascular thromboangiitis obliterans were observed among 1700 cases of peripheral thromboangiitis obliterans. These, with 30 acceptable cases from the literature, are analyzed. Smoking appears to activate the disease, which is characterized by recurrences and remissions of focal cortical signs due to thrombosis of cerebral arteries and cortical granular atrophy. Of my patients, one died. Eight have been followed for 35 to 3 years, and with one exception all are ambulatory. Cessation of smoking is necessary. No other effective treatment is known.

CEREBRAL manifestations in patients with thromboangiitis obliterans are rare. In over 1700 cases of this disease followed for years by Silbert and his group, involvement of the brain was found only in 12 cases.

The impression gained from perusal of all published cases of cerebrovascular thromboangiitis obliterans is that the diagnostic criteria of cerebral manifestations in this condition need further clarification. Since Buerger's report in 1915 of a pertinent case,1 more than 250 case reports have appeared in the medical literature. Many cases have been described in patients suffering from conditions commonly associated with arteriosclerosis and vascular diseases other than thromboangiitis obliterans.2-5 Patients with multiple sclerosis6 and malignant glioma7 have been presented as instances of cerebral involvement in thromboangiitis obliterans. The belief that cerebral involvement in this disease is a well defined anatomicopathologic entity2-5, 12, 17, 22-26 has led to confusion, as a result of which a variety of diseases has been described under the collective name of cerebral thromboangiitis obliterans.

Most authors state that cerebral thromboangiitis obliterans follows a progressive course uninfluenced by therapeutic procedures.21 My experience with several patients suffering from this condition does not confirm this opinion. Until recently27 many observers were pessimistic concerning the prognosis of peripheral thromboangiitis obliterans. Silbert,28, 43 having followed a large number of cases over more than 25 years, maintains that peripheral thromboangiitis obliterans is arrested when the use of tobacco has been discontinued, and this view is now accepted by others.29-31 Since smoking is the main factor which causes active peripheral thromboangiitis obliterans, it is reasonable to assume that this holds true in the cerebral form.

Some of the case histories presented below illustrate this point.

Twelve clinical case reports are presented.* In nine of these cases the diagnosis of cerebral thromboangiitis obliterans can be made with reasonable certainty. One case is reported in detail.

Case 1, H. R., $35510 M.H., a Jewish male, aged 34, admitted in 1919. The patient had been a heavy cigarette smoker since early adulthood. In 1915, when he was 29 years old, he developed intermittent claudication in his left leg. Two years later, in 1917, when he was 32 years old, gangrene of the left foot developed and a left thigh amputation was performed. In 1918, at the age of 33, he suffered a spontaneous right hemiplegia and aphasia which developed over a period of two days. After four months, his right arm regained some of its power and his speech improved. A few days before hospitalization, over a period of a few days, his speech deteriorated again to the point that he could utter only a few stereotyped words.

Examination in 1919 revealed a blood pressure of 130/80. He presented the picture of a right spastic hemiplegia, motor aphasia, right hemianesthesia, right central facial palsy and right hyper-reflexia. The left femoral and iliac pulses were absent. The right dorsalis pedis pulse was small, the posterior tibial pulse was absent, the right popliteal and femoral arteries were patent, as were the wrist

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* A table summarizing the 12 case reports will be supplied, upon request, with the reprints.
arteries. No abnormality of the carotid arteries was recorded. There were no signs indicative of arteriosclerosis. Blood Wassermann reaction was negative. The urine was free from albumin and sugar. At that time, the patient gave up smoking upon medical advice and has never resumed this habit, to date. He was put under the custodial care of the hospital.

From 1919 to 1938 the clinical course was stationary. The blood pressure ranged from 120 to 140 systolic over from 75 to 80 diastolic.

In 1939 he developed a spontaneous right iliofemoral thrombophlebitis. The blood pressure for the first time was found elevated to 150/102. The electrocardiogram, except for left axis deviation, showed no abnormality. In 1940 a complete re-evaluation of his clinical status revealed some improvement in the motor power of his right arm, but unchanged findings in all other respects. The blood pressure was 140/100. Basal metabolic rate was plus 4 per cent. At this time, the diagnosis of a thrombosis of the left middle cerebral artery on the basis of Buerger's disease was entertained. The absence of any signs of arteriosclerosis for 20 years was commented upon by several observers.

From 1941 to 1947, the status was unchanged; the blood pressure stayed elevated. In 1943 the patient was discharged to an Old Age Home for permanent custodial care. In 1947 he developed a post-traumatic ulcer over the right tibia which healed with penicillin injections.

In September, 1948 re-examination by me revealed an obese male patient, 63 years of age, grey-haired, cheerful and with a youthful facial expression. He was confined to a wheelchair on which he moved about with great agility. He understood spoken and written words and was oriented as to time and place; he answered questions with gestures. His aphasia was complete. There was no arcus senilis. The eye grounds and papillary reactions were normal. Chest and heart, except for an accentuated second aortic sound, were normal. The abdominal organs were normal. There was a healed left, high thigh amputation stump. Both carotid arteries were patent, as were all wrist arteries. The right femoral artery was open, the right popliteal artery could not be felt, the right dorsalis pedis and anterior tibial arteries could be felt weakly pulsating, the posterior tibial artery was closed. No iliac or femoral pulse could be found on the left side. Oscillometric readings were 2.0 at the right ankle, 4.0 at the right calf, trace at the left thigh stump. There was no albumin or sugar in the urine. Blood sugar was normal. The electrocardiogram was normal. The blood pressure was 170/100 at the right and 185/105 at the left arm. Re-examination in May, 1950 revealed the same findings.

Comment
This is a 36 year follow-up of a male patient, now 66 years old, who at the age of 29 developed occlusive peripheral vascular disease resulting in gangrene of the left foot. A left thigh amputation was carried out two years later. Another two years later, when he was 34 years old, he developed a right-sided hemiplegia and motor aphasia in two episodes at a few months interval. At this point, the patient gave up smoking. Since then, namely for the past 31 years, his peripheral vascular disease and cerebral involvement have failed to manifest any progressiveness. The neurologic and peripheral vascular findings were identical in 1919 and 1950. The blood pressure was normal at the time of the hemiplegia and for 20 years thereafter. Subsequently, the patient developed essential hypertension without altering the benign clinical course for the past 11 years. The absence of detectable signs of arteriosclerosis such as an arcus senilis, tortuosity of peripheral arteries, retinal artery changes, albuminuria, and electrocardiographic changes is noteworthy.

He was a heavy smoker when the disease was active. After cessation of smoking, the disease came to a standstill and has been arrested for 31 years.

In this patient, a remarkable psychologic and physical adjustment has taken place considering the widespread damage caused by active occlusive vascular disease in its initial stages.

Discussion
The name thromboangiitis obliterans, as proposed by Buerger and accepted in this country for 40 years, denotes a clinical-anatomic entity. The disease involves the large and medium-sized arteries and veins of the extremities and may involve visceral vessels. It is conceivable that thromboangiitis obliterans may start in the visceral vessels and later manifest itself in the extremities. However, in the present state of our knowledge, one cannot be certain that a disease process involving the visceral vessels alone is thromboangiitis obliterans, no matter how much it resembles the lesions in the extremities either in gross or in microscopic appearance.

When thromboangiitis obliterans is considered from the anatomic standpoint alone, the findings are not sufficient to establish the diagnosis. The lesions of the acute stage described by Buerger in superficial and deep veins are rarely found in arteries. Isolated instances of acute lesions in visceral vessels have been described. However, lesions of identical histologic appearance are also seen in conditions other than thromboangiitis obliterans. It has been known for a long time
that, at least in part, the histologic picture of acute thromboangiitis obliterans is due to non-specific reaction of the vessel intima.

Later stages of thromboangiitis obliterans produce anatomic lesions which are more characteristic. The signs of a subsiding inflammation, the preservation of the internal elastic membrane of the involved blood vessel together with the absence of evidence of degeneration and calcification are distinctive features of thromboangiitis obliterans past the acute stage. Nevertheless, some pathologists insist that there must be a clinical history of involvement of the extremity vessels before a diagnosis of thromboangiitis obliterans in the visceral vessels can be accepted. 

Thromboangiitis obliterans past the subacute stage may lead to an anatomic picture which is interpreted by most observers as arteriosclerosis superimposed upon the lesion of thromboangiitis obliterans. This belief has recently been challenged by von Albertini who maintains that thromboangiitis obliterans produces lesions which ultimately resemble but can be distinguished from arteriosclerosis; he furthermore contends that the transition from the picture of acute thromboangiitis obliterans to the end stages of the disease may be completed in less than two months.

From a clinical point of view, the diagnosis of thromboangiitis obliterans in a nonsmoker is open to doubt. The overwhelming experience has shown that all patients with thromboangiitis obliterans are smokers. A follow-up of 1400 cases of many years has demonstrated that the disease is arrested when smoking has been discontinued, provided tissue damage has not advanced irreversibly, or has not involved vital organs.

The diagnosis of thromboangiitis obliterans should not be made in patients with conditions associated with arteriosclerosis, in patients in whom the onset of symptoms in the extremities occurs after 50 years of age, in those suffering from other arteritides and phlebitides (syphilis, tuberculosis), and in those with vascular injuries (frostbite, immersion foot). Each of these conditions can produce clinical and anatomic manifestations similar to thromboangiitis obliterans.

A low basal metabolism, high blood cholesterol, low blood volume and signs of relative concentration of the formed elements of the blood are often found in thromboangiitis obliterans. However, in otherwise characteristic cases, the absence of any of these tests is of no significance. Special studies such as the observation of the nail fold capillaries, determination of arterial and venous oxygen content and capacity, the heparin tolerance test, to name only a few, have not proved to be helpful in arriving at a diagnosis of thromboangiitis obliterans.

The Diagnosis of Cerebral Thromboangiitis Obliterans

I. Anatomy

The anatomicopathologic lesions that are said to be characteristic of the cerebral form of the disease are cortical cerebral atrophy and encephalomalacias, thrombosis of one or more major cerebral arteries and structural changes of the cervical sympathetic chain.

According to Spatz and collaborators and pupils cerebral thromboangiitis obliterans manifests itself in two anatomic forms: granular atrophy of the cortex in a sickle-shaped distribution and discontinuous foci of cerebral softening. The first of the two was described in cases of thromboendarteritis of the anterior, medial and posterior cerebral arteries, singly or in combination, which grossly appear wormlike and histologically reveal intimal proliferation and thrombosis. Patients suffering from this type are said to present various emotional disturbances such as depression, forced crying, fatigue and alsoaphasia. The second of the two, discontinuous cortical encephalomalacias, was described in thrombosis of the larger brain arteries. These patients are said to suffer from various forms of cortical symptoms and signs, mono- and hemiplegias, pareses and aphasia.

Re-study of the case material on which this anatomic description is based leaves no doubt that many cases have been included which do not fulfill the criteria for the diagnosis of thromboangiitis obliterans. Even from the standpoint of descriptive anatomy and histology only, the distinctiveness of the cerebral form of the disease has been questioned by von
Albertini. The same author pointed out that the first anatomic description of cerebral thromboangiitis obliterans by Spatz was based on a case suffering from recurrent cerebral emboli and not thromboangiitis obliterans. Other diseases in which granular cerebral atrophy of encephalomalacias have been observed are arteriosclerosis, chronic rheumatic cerebral disease, chronic heart failure, hypertension and chronic kidney disease, carbon monoxide poisoning, and embolism. Subendothelial bleeding into the involved cerebral artery was described as the first anatomic sign of cerebral involvement but not as a distinctive feature of thromboangiitis obliterans since it is found in arteriosclerotic involvement as well.

Thrombosis of the internal carotid, vertebral, medial cerebral, anterior and posterior cerebral arteries has been described in patients with thromboangiitis obliterans in order of frequency. It appears to account most frequently for cerebral complications in Buerger’s disease. Among 30 acceptable cases, it was encountered 21 times. It is well known that in many pathologic conditions other than thromboangiitis obliterans, thrombosis of the carotid and cerebral arteries may be found. Attempts at establishing an etiologic diagnosis have been made in such cases by means of biopsy and arteriography, but it appears doubtful at the present time that either method has yielded findings specific for thromboangiitis obliterans.

Structural changes in the cervical sympathetic chain in thromboangiitis obliterans with cerebrovascular complications have been described. This should be accepted with caution, since the interpretation of the histologic appearance of the sympathetic ganglia and periganglionic tissues, with the available methods, has been controversial even among experienced observers. Likewise, reports on structural changes of the sympathetic chain in involvement of the extremities have been contradictory.

In conclusion, there is no proved characteristic anatomic picture of cerebrovascular involvement in thromboangiitis obliterans. Most patients suffering from Buerger’s disease who actually developed cerebral complications had thromboses of one or several cerebral arteries and some had cortical granular atrophy.

II. Clinical Course

Of more than 250 case reports of cerebrovascular thromboses in the literature, only 30 can be accepted as being caused by thromboangiitis obliterans, if the above-mentioned diagnostic criteria are applied. A considerable number of those that might be due to cerebral complications fail to include sufficient clinical data to establish a diagnosis. This is particularly true for some detailed anatomic histologic and clinical reports on cerebral thromboangiitis obliterans. Finally, many cases reported as cerebral thromboangiitis obliterans suffered from diabetes, hypertension, chronic kidney disease and other diseases.

The following discussion is based on 39 cases (see table 1), 30 cases from the literature and 9 of the 12 cases observed by me. In three cases of my series, the diagnosis is open to doubt.

All cases in the literature here discussed were males, and four among the nine cases of my group were females. The relatively high incidence of cerebrovascular complication in female patients with thromboangiitis obliterans in this group was first pointed out by Silbert.

Nineteen of the 30 cases from the literature and three of my nine cases, that is 22 of 39 cases (56 per cent), first developed peripheral vascular and then cerebrovascular disease within a few years. If cerebral thromboses develop when the peripheral vascular disease has been quiescent for many years, one cannot be certain of the diagnosis, since arteriosclerosis may have supervened. My cases 7 and 9, in whom cerebral thrombosis developed 20 and 27 years following peripheral thromboangiitis obliterans, have not, therefore, been included in the discussion of the clinical course.

Six of the 30 cases in the literature and six of my nine cases, that is 12 of 39 cases, first developed cerebrovascular and then peripheral vascular disease in fairly short order (see table 2). In my cases, three out of six of this last

* A table summarizing 12 case reports observed by the author will be supplied, upon request, with the reprints.
<table>
<thead>
<tr>
<th>Year</th>
<th>Author</th>
<th>Case no.</th>
<th>Sex</th>
<th>Onset age PVD*</th>
<th>Onset age CVD†</th>
<th>Clinical data</th>
<th>Site of occlusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>1915</td>
<td>Buerger¹</td>
<td>9</td>
<td>M</td>
<td>?</td>
<td>?</td>
<td>Incoherent speech</td>
<td>Malacia in stratum subcallosum and putamen</td>
</tr>
<tr>
<td>1926</td>
<td>Cserna⁴⁴</td>
<td>M</td>
<td>20</td>
<td>35</td>
<td></td>
<td>Recurrent right hemiparesis</td>
<td>Left common carotid, right external carotid arteries</td>
</tr>
<tr>
<td>1927</td>
<td>Lewis⁵⁵</td>
<td>M</td>
<td>40</td>
<td>47</td>
<td></td>
<td>Left hemiplegia</td>
<td>Left arteria fossae Sylvii, Malacia of right temporal lobe</td>
</tr>
<tr>
<td>1928</td>
<td>Stahnke⁵⁶</td>
<td>M</td>
<td>21</td>
<td></td>
<td></td>
<td>Died suddenly</td>
<td>Left middle cerebral artery</td>
</tr>
<tr>
<td>1929</td>
<td>Nordmann and Reuys⁷⁷</td>
<td>M</td>
<td>41</td>
<td></td>
<td></td>
<td>No cerebral symptoms</td>
<td>Right middle cerebral artery</td>
</tr>
<tr>
<td>1929</td>
<td>Barron and Lilenthal⁸⁷</td>
<td>1</td>
<td>M</td>
<td>48</td>
<td></td>
<td>Right hemiparesis</td>
<td>Left middle cerebral artery, Left cerebral cortical atrophy</td>
</tr>
<tr>
<td>1932</td>
<td>Bauer and Recht⁹⁸</td>
<td>M</td>
<td>38</td>
<td>44</td>
<td></td>
<td>Recurrent left hemiparesis</td>
<td>Right middle cerebral artery</td>
</tr>
<tr>
<td>1933</td>
<td>Foerster and Guttmann¹⁰⁸</td>
<td>M</td>
<td>34</td>
<td>31</td>
<td></td>
<td>Recurrent right hemiparesis, amaurosis</td>
<td>Left middle cerebral artery</td>
</tr>
<tr>
<td>1933</td>
<td>Merkelbach⁹⁹</td>
<td>M</td>
<td>31</td>
<td>30</td>
<td></td>
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<td>Right middle cerebral artery</td>
</tr>
<tr>
<td>1933</td>
<td>Livingston¹¹</td>
<td>M</td>
<td>34</td>
<td>36</td>
<td></td>
<td>Died suddenly</td>
<td>Left middle cerebral artery</td>
</tr>
<tr>
<td>1934</td>
<td>Averbuck and Silbert¹²</td>
<td>M</td>
<td>37</td>
<td>44</td>
<td></td>
<td>Hemiplegia</td>
<td>Left middle cerebral artery</td>
</tr>
<tr>
<td>1934</td>
<td>Poetzl¹³</td>
<td>M</td>
<td>29</td>
<td>29</td>
<td></td>
<td>Recurrent right hemiparesis</td>
<td>Right middle cerebral artery</td>
</tr>
<tr>
<td>1935</td>
<td>Essen¹⁴</td>
<td>M</td>
<td>31</td>
<td>45</td>
<td></td>
<td>Left hemiplegia</td>
<td>Left middle cerebral artery</td>
</tr>
<tr>
<td>1936</td>
<td>Cabot¹⁵</td>
<td>M</td>
<td>48</td>
<td>48</td>
<td></td>
<td>Dizziness</td>
<td>Left middle cerebral artery</td>
</tr>
<tr>
<td>1938</td>
<td>Hauser and Allen¹⁶</td>
<td>M</td>
<td>37</td>
<td>37</td>
<td></td>
<td>Right hemiplegia, aphasia</td>
<td>Right middle cerebral artery</td>
</tr>
<tr>
<td>1938</td>
<td></td>
<td>3</td>
<td>M</td>
<td>39</td>
<td></td>
<td>Left hemiplegia</td>
<td>Right middle cerebral artery</td>
</tr>
<tr>
<td>1938</td>
<td></td>
<td>4</td>
<td>M</td>
<td>43</td>
<td>28</td>
<td>Right hemiparesis, aphasia</td>
<td>Right middle cerebral artery</td>
</tr>
<tr>
<td>1939</td>
<td>Meves¹⁶</td>
<td>2</td>
<td>M</td>
<td>37</td>
<td>39</td>
<td>Recurrent left hemiparesis</td>
<td>Left middle cerebral artery</td>
</tr>
<tr>
<td>1939</td>
<td>Straussler Friedmann and Scheinker¹⁷</td>
<td>2</td>
<td>M</td>
<td>37</td>
<td>39</td>
<td>Recurrent left hemiparesis</td>
<td>Left middle cerebral artery, Left middle cerebral artery</td>
</tr>
<tr>
<td>1939</td>
<td>v. Hasselbach⁵⁵</td>
<td>3</td>
<td>M</td>
<td>22</td>
<td>35</td>
<td>Recurrent left hemiplegia</td>
<td>Right middle cerebral artery</td>
</tr>
<tr>
<td>1939</td>
<td></td>
<td>6</td>
<td>M</td>
<td>37</td>
<td>37</td>
<td>Recurrent hemiplegia</td>
<td>Right middle cerebral artery</td>
</tr>
<tr>
<td>1941</td>
<td>Sunder-Plassmann¹⁸</td>
<td>3</td>
<td>M</td>
<td>40</td>
<td></td>
<td>Headaches, fatigue, visual disturbances</td>
<td>Basilar and vertebral arteries</td>
</tr>
<tr>
<td>1941</td>
<td>Nils Antoni¹⁹</td>
<td>2</td>
<td>M</td>
<td>36</td>
<td>37</td>
<td>Right hemiplegia, spastic quadriplegia</td>
<td>Left internal carotid artery</td>
</tr>
<tr>
<td>1944</td>
<td>Krayenbuehl and Weber¹⁰</td>
<td>16</td>
<td>M</td>
<td>46</td>
<td>46</td>
<td>Right hemiplegia</td>
<td>Left internal carotid artery</td>
</tr>
<tr>
<td>1947</td>
<td>Davis and Perret¹⁰⁷</td>
<td>11</td>
<td>M</td>
<td>53</td>
<td>53</td>
<td>Recurrent left hemiparesis</td>
<td>Left middle cerebral artery</td>
</tr>
<tr>
<td>1948</td>
<td>Llaverco²⁰</td>
<td>10</td>
<td>M</td>
<td>33</td>
<td>25</td>
<td>Recurrent dizziness on effort, Epilepsy, Right hemiplegia</td>
<td>Left middle cerebral artery</td>
</tr>
</tbody>
</table>

* Peripheral vascular disease  † Cerebrovascular disease
group (cases 4, 5 and 11) developed the arterial occlusion in the paretic limb. Patients with spastic hemiparesis are known to exhibit spastic vascular phenomena on the involved side. It has been suggested that the same mechanism may lead to organic vascular occlusion in the extremities. The vascular occlusion in the extremities was of sudden onset in two of my cases and without detectable preceding vasoconstriction on the involved side. In one additional case, thromboangiitis was observed as well. In one case (case 12) peripheral occlusion developed in the nonparetic leg, and in two other cases (cases 3 and 10) the involvement of the peripheral vessels was bilateral.

All cases of cerebral thromboangiitis obliterans described in the literature, with the exception of two where data concerning the use of tobacco are not given, were smokers. All patients in my series were smokers. The material here reported offers data which illustrate the causal relationship between smoking and disease activity in the cerebral form of thromboangiitis obliterans (cases 1, 4 and 6). Of these, one patient developed gangrene of one leg and hemiplegia in short order. Only a short time after he gave up smoking did his disease become inactive. Today, the patient reveals the same peripheral vascular and central nervous system findings as he did 31 years ago. One patient (case 4) continued to smoke after the onset of his cerebral symptoms and within a period of four years developed hemiplegia, aphasia, and peripheral arterial occlusion as well as thromboangiitis. Another patient (case 6) alternated between several months’ periods of abstinence from smoking and resumption of this habit against medical advice. During this period, he experienced the development of thrombosis of a cerebral artery, two recurrences of a brachial artery thrombosis and coronary artery thrombosis. In each instance the resumption of smoking had preceded the onset of a thrombosis by some weeks. When this patient was last examined, he had given up smoking for more than four months and his symptoms were rapidly improving.

It is generally recognized that smoking may cause constriction of the peripheral blood vessels especially in patients with thromboangiitis obliterans. Several reports in the literature give suggestive evidence of cerebral blood flow disturbance in patients with thromboangiitis obliterans who smoke.

Of the nine cases reported here, two (cases 1 and 2) stopped smoking after cerebral paresis had developed. In none of these was there a thrombotic closure of cerebral or other arteries during subsequent observation for a long time; the first of the two patients was observed for 31 years without any further disease activity. In contrast to this course in the nonsmokers, those who continued to smoke after the onset of cerebral paresis, six (cases 3, 4, 5, 10, 11 and 12) developed peripheral artery occlusions, and one (case 6) developed a thrombosis of the brachial artery in two episodes and a thrombosis of the coronary artery. This suggests that cerebral thromboangiitis obliterans remains an active disease as long as the patient smokes, although the activity is not limited to the cerebral vessels.

Of the three cases with doubtful diagnosis, cases 7 and 9 had a cerebrovascular accident 20 years and 27 years respectively after the peripheral vascular disease had become manifest. It is reasonable to suggest that arteriosclerosis

### Table 2.—Sequence of Cerebrovascular and Peripheral Vascular Involvement in Thromboangiitis Obliterans (Thirty-nine Cases)

<table>
<thead>
<tr>
<th>Cases</th>
<th>After years 1-5</th>
<th>After years 6-10</th>
<th>After years 11-20</th>
<th>Total</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>No.</td>
<td>%</td>
<td>No.</td>
<td>%</td>
</tr>
<tr>
<td>A. CV after PV involvement</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Literature</td>
<td>10</td>
<td>25.6</td>
<td>6</td>
<td>15.4</td>
</tr>
<tr>
<td>This series</td>
<td>2</td>
<td>5.1</td>
<td>1</td>
<td>2.6</td>
</tr>
<tr>
<td>B. PV after CV involvement</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Literature</td>
<td>3</td>
<td>7.7</td>
<td>2</td>
<td>5.1</td>
</tr>
<tr>
<td>This series</td>
<td>5</td>
<td>12.8</td>
<td>1</td>
<td>2.6</td>
</tr>
<tr>
<td>C. No data available</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Literature</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>This series</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td></td>
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</table>
had supervened in both cases. Case 8 reveals a bizarre course suggestive of retinal artery spasm, peripheral occlusive arterial disease, transient hypertension and a cerebral thrombosis after subsidence of the hypertension. A final diagnosis is deferred in this case.

For reasons unknown, the most frequent site of cerebral arterial occlusion in patients with thromboangiitis obliterans is the left middle cerebral artery (see table 3) and its branches.

Not unlike the development of the peripheral lesions, which follow a characteristic pattern of recurrent segmental arterial closures, cerebrovascular thromboangiitis obliterans manifests itself in recurrent attacks of cortical signs such as fleeting monoplegias, hemianopia, hemiplegia and paresis, aphasia interrupted by remissions of unpredictable duration. The transient character of these initial signs of cerebral involvement has led some observers to believe that spastic phenomena account for the development of the cerebral manifestations. However, with each recurrence of the cerebral signs, more extensive and longer lasting damage can be noted. Twenty recurrences of hemiparesis were reported in one case in the literature; the attacks increased in intensity and extensiveness and climaxed in a permanent hemiplegia.12 In my series four such attacks preceded the establishment of hemiparesis in case 4, three in case 2 and two in cases 1 and 6.

Even if the recurrent attacks of paresis do not continue until permanent irreversible hemiparesis results, there are clinical signs suggestive of organic rather than spastic vascular occlusion. Thus, in case 2 a transient left hemiparesis was observed which subsided after two days and never recurred, while a positive Babinski reflex of the involved side persisted for many months. Whether widespread vaso-spastic phenomena accompany the onset of recurrent small vascular occlusions could not be established in this series, since I did not make use of arteriography in my patients.

It is a distinctive feature of this disease that with each recurrent cerebral insult the site previously involved is damaged again. There is no dissemination of the pathologic process as found in multiple sclerosis.

Some observers mention that attacks of prostration, perspiration, dizziness, and transient visual disorders such as scotomas may precede the development of the above described focal cerebral signs and that these prodromal symptoms are entirely reversible.12, 75 Such symptoms were not observed in any of the cases reported here.

Table 3.—Site of Arterial Occlusion in Cerebrovascular Thromboangiitis Obliterans (thirty cases from the literature and nine of this series*).

<table>
<thead>
<tr>
<th>Artery</th>
<th>No.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Left middle cerebral artery</td>
<td>16</td>
<td>41</td>
</tr>
<tr>
<td>Right middle cerebral artery</td>
<td>9</td>
<td>23</td>
</tr>
<tr>
<td>Left internal carotid artery</td>
<td>2</td>
<td>5.2</td>
</tr>
<tr>
<td>Left common carotid artery</td>
<td>1</td>
<td>2.6</td>
</tr>
<tr>
<td>Right common carotid artery</td>
<td>1</td>
<td>2.6</td>
</tr>
<tr>
<td>Left and right vertebral arteries</td>
<td>1</td>
<td>2.6</td>
</tr>
<tr>
<td>Total</td>
<td>39</td>
<td>100%</td>
</tr>
</tbody>
</table>

* Including the postmortem findings in seven cases of the literature. In the remaining 23 cases of the literature and the nine cases of this series, only clinical data were available to determine the site of cerebrovascular occlusion.

Transient contraction of the retinal vessels, causing temporary amaurosis, has been observed86 in patients with cerebral thromboangiitis obliterans. In the only patient in this series in whom this happened (case 8), a definite diagnosis of cerebrovascular thromboangiitis obliterans cannot be made. Sheathing of the retinal veins has been reported in patients with cerebral manifestations87 but could not be seen in this series. Interestingly, both phenomena of retinal artery spasm and retinal vein sheathing have also been reported in patients with multiple sclerosis.77, 78a, b The similarity of the clinical course in both diseases has been pointed out.75

Apart from the occasional occurrence of a central retinal artery thrombosis in patients with thromboangiitis obliterans,79 permanent changes of the retinal arteries are probably rare.66 This is in keeping with the experience that thromboangiitis obliterans involves middle-sized and large rather than small arteries.60 Older reports to the effect that thromboangiitis obliterans may and frequently does involve the retinal blood vessels82 and may be associated
with cerebral involvement are probably accounted for by a faulty interpretation of anatomic and histologic findings and the selection of patients disregarding the diagnostic criteria for thromboangiitis obliterans.

It has been pointed out that cerebral manifestations of this disease may lead to epilepsy and petit mal. Significantly, these attacks involve the limbs previously involved, paralyzed or paretic and, if jacksonian in nature, do not spread over other parts of the body. One of the cases discussed here (case 2) developed attacks of petit mal brought on by physical effort. They were stopped for 18 months when the patient avoided physical exertion. Following a long automobile trip which entailed considerable exertion, the patient had an epileptic seizure lasting for several days, followed by massive thrombosis of one femoral vein and artery with gangrene, to which she succumbed.

**Prognosis of Cerebral Thromboangiitis Obliterans**

Seven of 30 cases described in the literature died from cerebrovascular disease. In this series of nine, one died. This corresponds to an overall lethality of 21 per cent.

Those in my series who survived have been followed over a number of years (see table 4). With the exception of one patient who did not present himself again, and one who has been confined to a wheelchair since the onset of his cerebrovascular disease, all patients are ambulatory. This would suggest that cerebral thromboangiitis obliterans does not have a grave prognosis for life and does not follow a progressive course. If the initial damage inflicted upon the brain has been extensive, the prognosis for life is altered for the worse; in the one patient of this series who succumbed, evi-

| Table 4.—Prognosis of Cerebrovascular Thromboangiitis Obliterans |
|---|---|---|---|
| Patient No. | Follow-up after onset of PVD in years | Follow-up after onset of CVD in years | Present condition |
| 1 | 35 | 31 | same as 31 years ago—wheelchair |
| 2 | 12 | 7 | died |
| 3 | 17 | 10 | working |
| 4 | 4 | 11 | working |
| 5 | 5 | 8 | working |
| 6 | 14 | 1 | unknown, last seen in 1945 |
| 7 | 25 | 3 | retired, ambulatory |
| 8 | 6 | 6 | working |
| 9 | 27 | 1 | working |
| 10 | 11 | 12 | working |
| 11 | 12 | 14 | working |
| 12 | 1 | 3 | working |

The persistence of symptoms in patients with cerebral thromboangiitis obliterans

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Paresis</th>
<th>Aphasia</th>
<th>Year followed</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>unchanged</td>
<td>unchanged</td>
<td>31</td>
<td>none</td>
</tr>
<tr>
<td>2</td>
<td>unchanged</td>
<td>unchanged</td>
<td>7</td>
<td>none</td>
</tr>
<tr>
<td>3</td>
<td>mild, unchanged</td>
<td>mild, unchanged</td>
<td>12</td>
<td>none</td>
</tr>
<tr>
<td>4</td>
<td>improved</td>
<td>improved</td>
<td>9</td>
<td>none</td>
</tr>
<tr>
<td>5</td>
<td>unchanged</td>
<td>improved</td>
<td>2</td>
<td>none</td>
</tr>
<tr>
<td>6</td>
<td>improved</td>
<td>improved</td>
<td>4</td>
<td>on a-s basis</td>
</tr>
<tr>
<td>7</td>
<td>improved</td>
<td>improved</td>
<td>1</td>
<td>on a-s basis</td>
</tr>
<tr>
<td>8</td>
<td>improved</td>
<td>improved</td>
<td>2</td>
<td>on a-s basis</td>
</tr>
<tr>
<td>9</td>
<td>improved</td>
<td>improved</td>
<td>3</td>
<td>on a-s basis</td>
</tr>
<tr>
<td>10</td>
<td>mild, unchanged</td>
<td>mild, unchanged</td>
<td>12</td>
<td>none</td>
</tr>
<tr>
<td>11</td>
<td>mild, unchanged</td>
<td>mild, unchanged</td>
<td>14</td>
<td>none</td>
</tr>
<tr>
<td>12</td>
<td>mild residue</td>
<td>none</td>
<td>3</td>
<td>none</td>
</tr>
</tbody>
</table>

The presence of bilateral widespread brain damage was present.

Once hemiparesis or hemiplegia have been present for more than a few months the chances that functional recovery will take place are very slight (see table 5). Those who developed aphasia have shown not more than slight speech improvement or none at all over many years. Attempts at speech re-education in one case (case 2) have been unsuccessful.

Smoking has a deleterious effect upon the prognosis of the cerebral form of the disease since there is reason to believe that the cerebral thromboses in patients with thromboangiitis obliterans occur only when the patients smoke.
Moreover, those in my series who gave up smoking after their cerebral accident have presented no evidence of further vascular occlusion. Those who continued smoking developed thromboses in peripheral or visceral arteries. The conclusion appears justified that cerebrovascular thromboangiitis obliterans is an active disease only in smokers.

TREATMENT OF CEREBROVASCULAR THROMBOANGITIS OBLITERANS

Cessation of smoking is a necessity. The rationale for this has been discussed above.

Cervical sympathectomy has been performed in two cases by Foerster and Guttman in 1933 and additional cases have been reported by Foerster's pupils and others without notable success. I doubt that blocking of the cervical sympathetic outflow as recently voiced by DeTakats for treatment of the cerebral insult can be of help in cerebrovascular thromboangiitis obliterans. Its effect was studied in one case of this series (case 4) and exerted no effect on the neurologic signs or the electroencephalographic pattern. Likewise, the adrenergic blocking agent, Dibenamine, administered intravenously, was ineffective. Whether these procedures are of value in patients treated in the acute stage of cerebral thrombosis remains a matter of future trial. Likewise, the resection of a thrombosed artery (Leriche) and periarterial sympathectomy have been inconclusive. 

I do not have enough experience in the use of anticoagulants as therapeutic agents in cerebrovascular thromboangiitis obliterans. They were used in one patient of this series, with no result (case 2). The use of vasodilators (e.g., papaverine) by mouth has been recommended for a long time and has been employed in several patients of this series with no untoward effects. I do not believe they were of any value. The more logical use of vasodilators administered into the carotid artery (provided it is patent) has not been tried to my knowledge. In all other respects, patients with cerebrovascular thromboangiitis obliterans ought to be treated according to the same principles as other patients with cerebrovascular thromboses.

SUMMARY AND CONCLUSIONS

Of 1700 cases of peripheral thromboangiitis obliterans studied by Silbert and his associates, only 12 with cerebrovascular involvement were encountered. A diagnosis of cerebrovascular thromboangiitis obliterans could be made in only nine of these cases. In two, superimposed cerebrovascular arteriosclerosis and in one, cerebral thrombosis of unknown origin were diagnosed. Four cases in this small series occurred in women, a relatively high incidence. The over-all incidence of cerebrovascular complications in thromboangiitis obliterans amounts to less than 0.5 per cent.

It appears from a study of the literature that cerebrovascular thromboangiitis obliterans is diagnosed too often. Diagnosis of the disease is justified only if peripheral thromboangiitis obliterans is present. The diagnostic criteria of peripheral thromboangiitis obliterans are summarized. Survey of the literature discloses that cerebrovascular involvement presents no distinctive pathologic anatomic picture. The nonspecific structural lesions most frequently encountered have been thrombosis of one or more large or medium-sized brain arteries or their branches and cortical granular atrophy.

Thirty acceptable cases of cerebrovascular thromboangiitis obliterans in the literature and nine personal cases are discussed.

Clinical data are given which suggest that smoking activates the cerebral manifestations of thromboangiitis obliterans. The clinical course is characterized by frequent recurrences and remissions of the same focal cortical signs which terminate in permanent damage. The most frequent signs are hemiparesis or hemiplegia and partial or complete aphasia.

If cerebrovascular thrombosis is seen in young people in whom rheumatic heart disease or other sources of embolic disease, hypertension, diabetes, brain tumor or multiple sclerosis have been ruled out, the diagnosis of cerebrovascular thromboangiitis obliterans should be suspected. The patient should be examined and followed-up for the presence of occlusive peripheral vascular disease. Such a patient should be forbidden to smoke.

The prognosis for life is favorable provided the initial damage to brain tissue has not been too extensive and the use of tobacco has been discontinued. Aphasia and hemiparesis tend to persist with slight or no improvement.

Apart from the cessation of smoking, there
is no known effective treatment of cerebrovascular thromboangiitis obliterans. Blocking or removal of the cervical sympathetic chain, the use of sympatholytics and anticoagulants have not proved to be beneficial. Vasodilators were innocuous but their therapeutic value in the cerebral manifestations of thromboangiitis obliterans is questionable.

I wish to thank Dr. S. Silbert for his permission to report on cases 3, 10, and 11 from his personal files and for his constant interest and assistance in preparing this report.

REFERENCES


5. Ibid. Cases 1 and 2.


10. Ibid. Cases 2 and 5.


16. Ibid. Case 5.


18. Ibid. Case 3.


22. Ibid. Cases 1, 2, 3, 4, 8, 10, 12, 13, 14, 15.

23. Ibid. P. 234.

24. Ibid. Case 16.


29. Ibid. Case 1.


32. Ibid. P. 230.

33. Ibid. P. 119.

34. Ibid. Case 10.

35. Ibid. P. 234.


37. Ibid. Case 5.

38. Ibid. Case 3.


40. Lueers, Th.: Weitere Mitteilungen zur Klinik und Anatome der zerebralen Form der Thrombo-angiitis Obliterans (v. Winicwarter-
CEREBROVASCULAR THROMBOSIS WITH BUERGER'S DISEASE


SILBERT, H.: Personal communication.


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