Editorial

The Case for Retention of the Diagnostic Category
"Thromboangiitis Obliterans"

IN THE February 1961 issue of Circulation there appeared an editorial by Dr. Stanford Wessler entitled "Thromboangiitis Obliterans: Fact or Fancy." In this editorial Dr. Wessler reiterated some statements and concepts that had appeared in an article published by him and his associates in the New England Journal of Medicine during the past year. My experiences, observations, and concepts based on more than 30 years of special interest in peripheral vascular diseases, including a considerable study of the pathology of these diseases, appear to be somewhat at variance with those of Dr. Wessler. I believe that my observations and concepts regarding the disease in question are shared by a considerable number of other physicians who also have had extensive experience and similar interest.

It is agreed that the diagnostic category "thromboangiitis obliterans" was somewhat abused in the past and that in it were included many cases that would not be so included today, but during the past 20 years my associates and I have, as Dr. Wessler has suggested, reviewed critically our criteria for the clinical diagnosis of thromboangiitis obliterans on numerous occasions.

There has been and still is being encountered, not commonly but not rarely either, a group of patients who have the following clinical manifestations in common: evidence of objective and persistent ischemia of one or both feet, objective evidence of segmental arterial occlusions distal to the popliteal arteries without evidence of proximal arterial occlusion, persistent objective ischemia of one or more fingers and objective evidence of segmental arterial occlusions distal to the brachial artery, recurrent thrombophlebitis of small or medium-sized superficial nonvaricose veins of the extremities, and onset of these manifestations prior to the age of 40 and frequently prior to the age of 30. There is another group of patients who have the above-mentioned clinical manifestations with the exception of either superficial thrombophlebitis or the evidence of occlusive arterial disease in the upper extremities. In both of these groups, the patients are otherwise in good health and have no evidence of organic heart disease, arterial aneurysms, diabetes mellitus, hypercholesteremia, roentgenographically demonstrable calcification of peripheral arteries, or scleroderma. The occluded segments of the arteries and veins that have been obtained from amputated specimens and biopsy specimens from the patients described above have almost invariably shown the following histopathologic changes: occlusion of the lumen by a very cellular organized thrombus, diffuse thickening of the intima without deposits of sudanophilic material or calcium, a completely or almost completely intact internal elastic lamina, slight to moderate diffuse infiltration of the medial coat by foreign cells.
without significant destruction of the muscle or elastic tissue or calcium deposits, and moderately intense diffuse cellular infiltration of the adventitia. In amputated specimens obtained a number of years after the onset of clinical manifestations of the disease, the lesions are usually less cellular and more fibrotic but the cellular lesions can frequently be found also if a number of sections are made of the involved arteries and veins of an amputated leg. In some amputated limbs and at some necropsies, simple thrombotic occlusion has been found in the arteries of a leg in association with the more characteristic lesions. This is not surprising when one considers the marked alteration in circulatory dynamics that must occur in a limb where the circulation is so badly compromised by arterial occlusions that amputation is necessary, or that must occur as a result of circulatory failure just prior to death.

The above-mentioned clinical and pathologic descriptions can be considered an observed fact and the patients that fall into the groups described have been and are being diagnosed by my associates and myself as having thromboangiitis obliterans. The remainder of the discussion of the issue, if it can be called an issue, involves interpretation, analogy, definition, and diagnostic categorization.

For a number of years we have thought that the distinctive clinical manifestations in the patients described above were the superficial thrombophlebitis, the involvement of the upper as well as the lower extremities, and the localization of the occluded segments, at least during the early course of the disease, in the small and medium-sized arteries and veins. By comparison, these three manifestations have not been encountered in patients who have occlusive peripheral arterial disease due to proved atherosclerosis. Most of the patients that we have classified as having thromboangiitis obliterans live for a considerable number of years after onset of the clinical manifestations, hence data from necropsy examination are unfortunately rarely available during the active stages of the disease.

Dr. Wessler apparently believes that the peripheral vascular disease of the patients described above can be interpreted as a manifestation of either atherosclerosis, embolic arterial occlusion, or nonspecific reactions in the blood vessels to simple intravascular thrombosis. The lesions in the arteries themselves are not atherosclerotic, since among other differences they lack that hallmark of atherosclerosis: the intimal plaque that contains cholesterol and sudanophilic material. The lesions in the veins are certainly not of atherosclerotic origin. Neither can the arterial lesions themselves be interpreted as distal thrombotic manifestations of more proximal atherosclerosis. It is true that some of the patients develop clinical manifestations of coronary or cerebral atherosclerosis a number of years after onset of the peripheral vascular lesions and die as a result of the complications of this coronary or cerebral atherosclerotic disease as do many patients who do not have clinical peripheral vascular disease. It is also probably true that the patients under consideration have early atherosclerotic lesions in the aorta even though these are not detectable clinically or radiographically at the time of onset of the vascular lesions in the extremities. A relationship of this early aortic atherosclerosis to the peripheral arterial and venous occlusive lesions is highly improbable, however, since such aortic lesions develop in almost all adults during the third and fourth decades of life. In my experience the significant clinical manifestations as described above have not been encountered in relatively young patients who have advanced and occlusive atherosclerotic lesions of the abdominal aorta.

The ease for considering that the arterial lesions under discussion are manifestations of arterial embolism cannot be supported, since at the time the lesions develop and for many years thereafter no evidence of a source for arterial emboli exists. The patients do not have histories, symptoms, or objective evidence of organic heart disease, proximal arterial aneurysm or aortic atherosclerosis of sufficient degree to give rise to primary aortic thrombosis. Also, an embolic origin for the

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arterial lesions could hardly explain the lesions in the veins.

It has been suggested that the cellular proliferation seen in the thrombi and vessel walls obtained from amputated specimens, particularly those of digits, are the result of regional gangrene and secondary infection. This does not account, however, for the very similar changes seen in the superficial veins removed from patients who have neither gangrene nor local infection. Also, similar changes have not been observed in the arteries of digits of patients who have gangrene and infection complicating occlusive atherosclerotic peripheral arterial disease nor in those who have digital gangrene and infection associated with scleroderma.

The contention that both the arterial and venous lesions under discussion can be interpreted as the result of nonspecific intravascular thrombosis cannot be dismissed so easily. The question here depends in part on what is considered "nonspecific." My observations apparently differ from those of Dr. Wessler in that in my experience the very cellular appearance of the thrombi and the proliferative changes in the intima, media, and adventitia that are seen in the superficial veins of patients with thromboangiitis obliterans have not been seen in the veins from patients with postoperative thrombophlebitis nor in the superficial thrombophlebitic lesions that are complications of visceral carcinoma. Neither have I seen them in the thrombophlebitic lesions that develop in varicose veins. I have been unable, however, to distinguish histopathologically the superficial thrombophlebitis of thromboangiitis obliterans from that occurring in the condition known as recurrent idiopathic thrombophlebitis or idiopathic thrombophlebitis migrans. I do not interpret this latter condition as a nonspecific thrombotic disease but as a disease that is closely related to thromboangiitis obliterans. In fact, I have observed a number of patients in whom segmental peripheral arterial occlusions developed months or years after the lesions in the veins first appeared. There is a small group of cases of occlusive peripheral arterial disease in relatively young persons that is characterized by sudden dramatic occlusions, usually of large arterial trunks such as the iliac or femoral, in which associated atherosclerosis is not found. Neither in this type of thrombotic occlusion, which has been designated as simple arterial thrombosis, nor in arterial embolism with distally propagating thrombosis have I encountered the very cellular reactions in the thrombi and arterial walls that are seen in the arteries of patients having thromboangiitis obliterans.

From the standpoint of pathogenesis the problem whether the lesions of thromboangiitis obliterans are primarily thrombotic or primarily angiitic has never been satisfactorily settled. In either event, I believe that the intense cellular proliferation seen in the thrombi, endothelium, and vessel walls is peculiar and distinctive. Also, the localization of the lesions in segments of small and medium-sized arteries and veins of both upper and lower extremities is peculiar and distinctive. These two characteristics alone suggest a primary focal morphologic or biochemical change in the endothelium. Accelerated blood clotting may be an additional factor in some or even all cases.

Dr. Wessler has suggested that the diagnostic category "thromboangiitis obliterans" be abandoned because in the patients so classified the etiology of the vascular lesions is unknown and the morphologic pathology is nonspecific. By this same reasoning, one might suggest the abandonment of such well-established entities as rheumatoid arthritis and multiple sclerosis. Strictly speaking, the etiology of the condition that has been classified as thromboangiitis obliterans is not known, but a strong case can certainly be made for a peculiar individual reaction to tobacco smoking as a dominant or even necessary etiologic factor. It is almost universally agreed that patients who have this condition are almost without exception moderate to heavy smokers, that they very rarely develop new vascular lesions if they stop smoking and that they almost always develop new vascular lesions sooner or later if they resume smoking. It is
quite conceivable that these patients develop peculiar focal vascular changes involving the endothelium as a result of an antigenic effect of tobacco smoking. To me the histopathologic changes in the occluded arteries and veins are distinctive and not duplicated by the simple reactions to thrombosis that occur in atherosclerosis, embolism, simple arterial thrombosis, or other types of venous thrombosis.

I, too, have regretted my inability to find the histologic picture of what I would consider to be a very fresh or acute arterial lesion. This is to be expected, however, when one considers the source of the available material. I doubt that any pathologist can say, on the basis of histologic examination alone, that any vascular lesion is acute—that is, that it is only a few hours or a few days old. Clinically, the evidence does not indicate that the episodic progress of the arterial disease includes a great many episodes, and statistically the pathologist would be very fortunate if he could encounter a truly acute lesion. As the late Dr. Russell Holman has stated, the histopathologist gets a look at only a very few small areas of a very few frames in a very long movie strip. Without detracting at all from the importance of histopathologic study of the lesions in question, the judgment whether or not the pathology in the cases under question is specific involves a broader concept of morphologic changes. This includes the anatomic distribution of the primary vascular lesions, which is certainly distinctive in the patients under consideration.

Finally, since the basic question here seems to involve diagnostic categorization, one might discuss at length the value of our system of diagnostic categorization in general, oversimplified as it is and based as it is sometimes on known etiology, sometimes on morphologic pathology, sometimes on metabolic, biochemical, or physiodynamic abnormality, sometimes on a clinical syndrome, and sometimes simply on human behavior. Actually, the purpose of diagnostic categorization is to lead to a better appraisal, at least on a statistical basis, of what is going to happen to the patient in the future and of what may be expected in the way of modification of such future events by certain therapeutic procedures. Secondarily, our system of diagnostic categorization has been of some value in teaching and in clinical and basic scientific investigation. Even if one disregards all other considerations, the use of the diagnostic category "thromboangiitis obliterans," though it may have been abused in the past, has served many of us and many patients reasonably well during the past 20 years. "Thromboangiitis obliterans" is a good descriptive term for the lesions under question. If this term is abandoned, how is it proposed that we should classify this group of patients? Should we classify them simply as cases of nonspecific occlusive peripheral vascular disease or as cases of nonspecific peripheral arterial and venous thrombosis—syndrome X? This would seem to be a long step backward. I believe that in the light of our present knowledge and experience the diagnostic category "thromboangiitis obliterans" should be retained during at least the immediate foreseeable future.

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A rare and precious gift is the art of detachment.—Sir William Osler. Aphorisms From His Bedside Teachings and Writings. New York, Henry Schuman, Inc., 1950, p. 84.
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