The Pathogenesis of arterial narrowing

D.C. 616.13-002.2:616-005.6

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The Pathogenesis of Arterial Narrowing

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Before we can with any certainty identify the causes of atherosclerosis we must have a fair understanding of the nature of the processes concerned. Let us ask ourselves what, for instance, we mean by the term coronary atherosclerosis; do we mean the condition which pathologists describe as fibrous thickening of the intima with fatty change and calcification, or do we mean the one which clinicians recognise as coronary insufficiency and which we assume is associated with narrowing of the arteries? It may be contended that the two are identical, but if so why is it that we sometimes find the most extreme fibrous thickening, fatty change and calcification without any narrowing, and why on the other hand do we also find examples of extreme narrowing with little fatty change and no calcification? Until we can answer these questions we cannot claim to have a very clear knowledge of the nature of atherosclerosis.

It is of course obvious that the process we seek to understand, and possibly prevent, is narrowing of the arteries, since it is so largely responsible for the high death rate from cardiac disease, but narrowing is a condition about which there is much confusion. We have been taught that it is brought about by swelling or proliferation of the intima encroaching on the lumen and so reducing it, but when one considers the functional activities of arteries it is difficult to see how this could occur in life. Arteries are elastic tubes, supporting a high internal pressure of blood which is constantly pulsating. The aorta and coronary arteries have to expand and recoil with each pulse wave, and whilst the expansion is a movement imposed on them by the pulse pressure, the recoil is a function of their own elasticity. Thus anything like a fibrous growth, which must impair their elasticity, must interfere with their ability to recoil, and leave them in the more or less dilated position, at the mercy of the blood pressure. In such case the tendency would be towards progressive dilatation rather than narrowing.

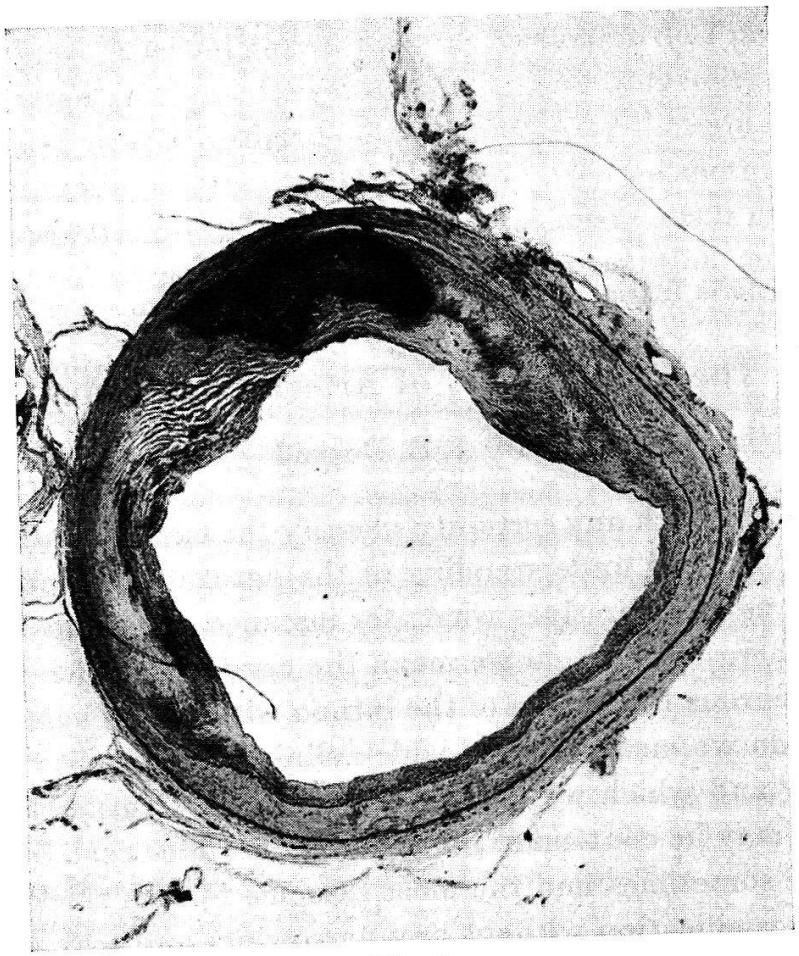

Fig. 1.

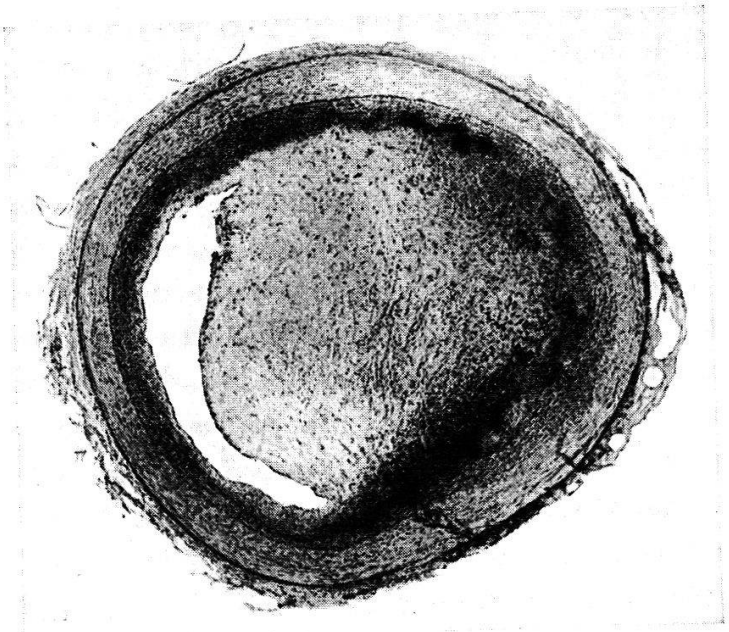

Fig. 2.

The foregoing may seem a rather involved theoretical argument, but it is in fact fully borne out by the vast majority of atherosclerotic lesions. Fig. 1 for example shows a very large fibrous thickening of a coronary artery with much fatty change and calcification, but beneath the thickened intima the media is stretched to a thin band, so that the lumen is probably wider than it would have been in the normal vessel. This is more or less the state of affairs in nine out of ten atherosclerotic lesions, and since the change is not one which would seem likely to offer any obstruction to the blood flow, we might conclude that atherosclerosis is not a very disabling lesion. There remains the fact, however, that from time to time we find atherosclerotic arteries narrowed almost to the point of occlusion, as in fig. 2, and this is a phenomenon which has long puzzled pathologists. A possible explanation is to be found in the following two sections.

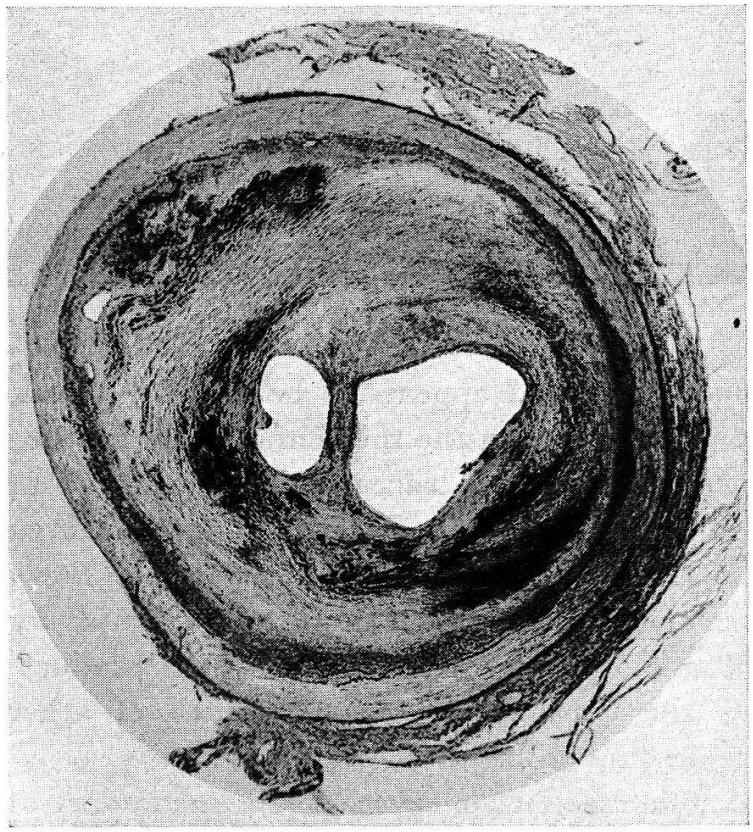

Fig. 3.

Fig. 3 shows an organised thrombus in a coronary artery with two channels running through it, and it will be noticed that the fibrous band which separates the channels, and which obviously represents the thrombus, merges into the intima so as to be practically indistinguishable from it. Fig. 4 is a section from the same lesion about 2 mm further along the vessel, and in it the two channels have joined to form a single

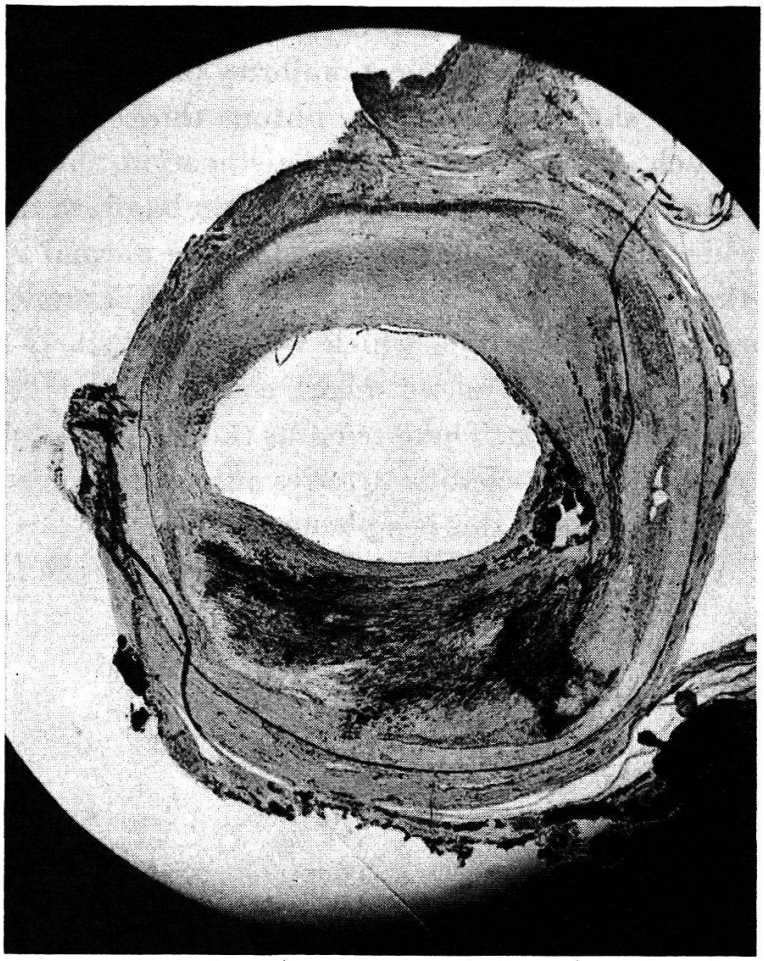

Fig. 4.

lumen surrounded by what appears to be a greatly thickened intima. Since there is fatty change in the thickening it has all the characters of atherosclerosis, yet when it is traced back through the series of intervening sections it is found to be still a part of the same organised thrombus as seen in fig. 3. We thus have a demonstration of how an artery can become thickened and at the same time narrowed, simply by the development of a thrombus in its lumen, and since the product is typical of atherosclerosis the question arises—how much of atherosclerosis in general can be accounted for in this way?

When we examine sections of severe aortic or coronary atherosclerosis with this question in mind we find that arterial thrombosis is much commoner than has generally been suspected. Thrombi of all kinds can be found from large masses of fibrin almost filling the lumina of the arteries (fig. 5), to small surface deposits as seen in fig. 6. Some are freshly formed, and others partly organised so that they are difficult to distinguish from the intimal tissues (fig. 7), and from a comparative study of these various examples a new principle in arterial pathology seems to emerge. When a mural thrombus forms in an artery it becomes

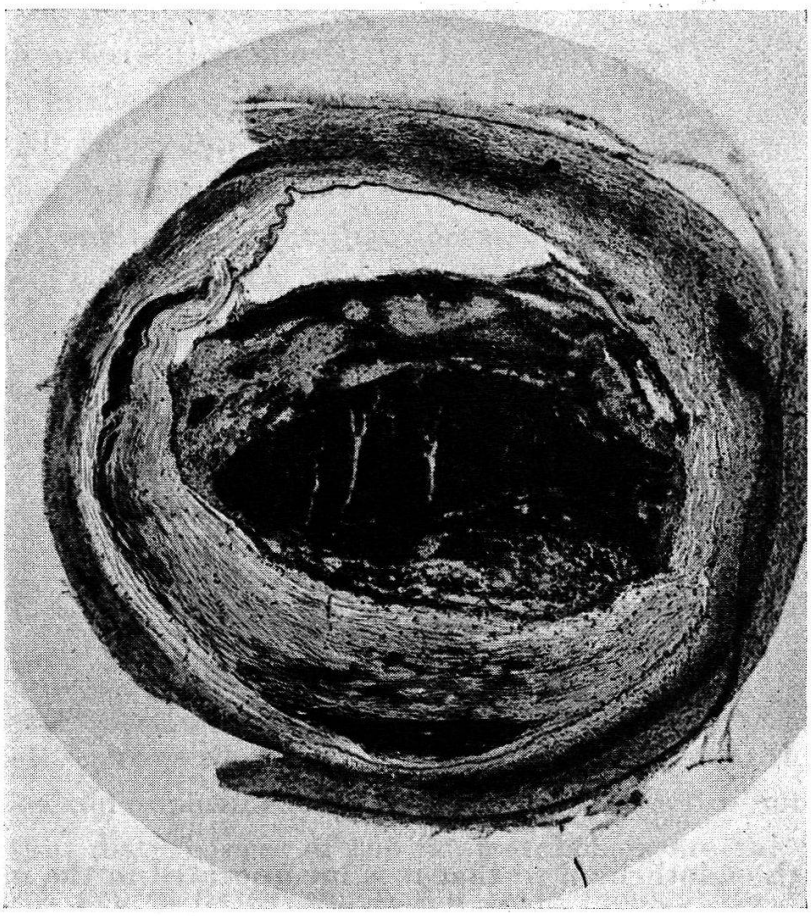

Fig. 5.

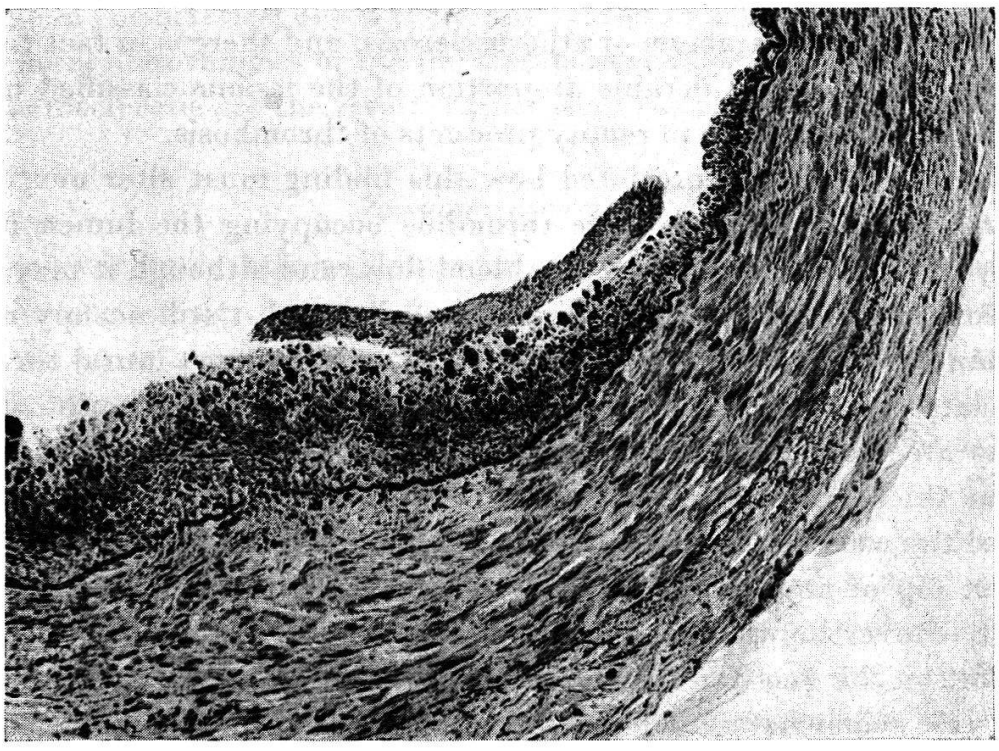

Fig. 6.

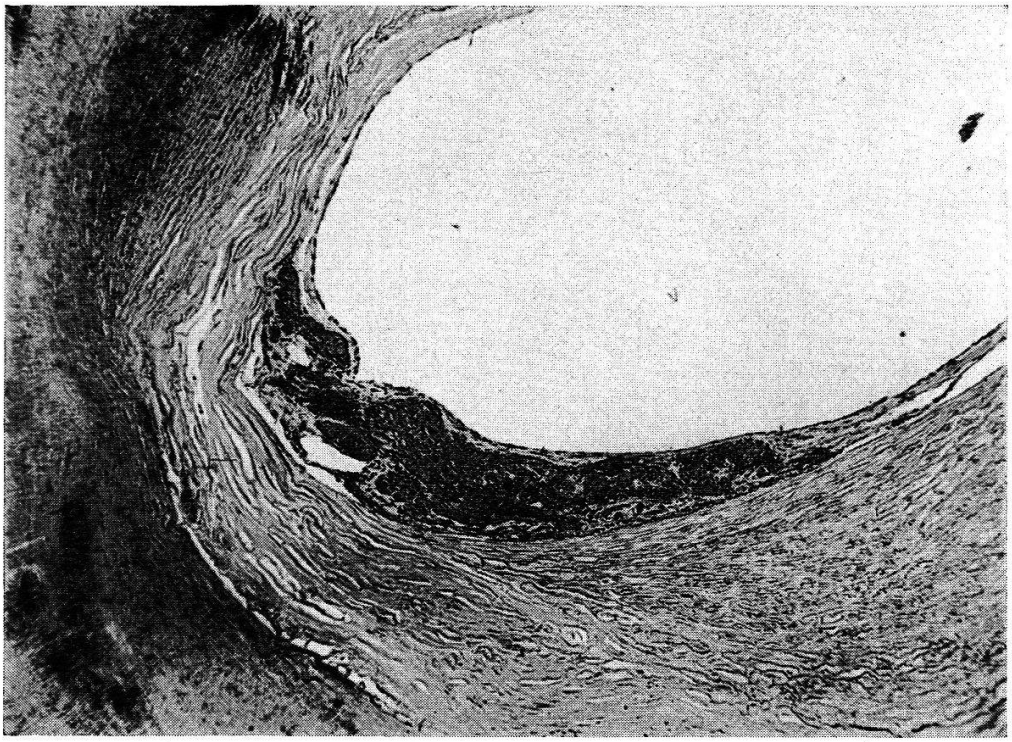

Fig. 7.

covered with endothelium so that it is incorporated in the intima, with the result that when it is subsequently organised, it forms a fibrous thickening of the vessel wall. Failure to recognise this principle has resulted in mural thrombi being overlooked in the past, or mistaken for atherosclerotic plaques. Since most of them undergo some fatty change, they acquire the characters of atherosclerosis, and there is in fact reason to believe that a considerable proportion of the lesions classified under that heading have been in reality products of thrombosis.

It will be readily appreciated how this finding must alter our views on arterial narrowing. A large thrombus occupying the lumen of an artery must inevitably reduce the blood flow, and although it may subsequently be incorporated in the vessel wall, it must still occupy much the same space and reduce the lumen. Fortunately most mural thrombi are relatively small, and do not cause any appreciable obstruction. Their effects are more in the direction of dilatation, since they give rise to fibrous thickenings which, although not necessarily very large, tend to reduce the elasticity of the vessel walls. Such thrombi commonly recur, one on top of another, giving rise to progressive thickenings and ultimately converting the arteries into dilated, almost rigid tubes.

Thus, on the question of arterial narrowing the focus of interest shifts from the somewhat vague general problem of atherosclerosis to the specific one of thrombosis. But this is only a small advance towards the

solution of the problem, for there is still much to be learned about the pathology of arterial thrombosis. We know that an important factor is degeneration of the vessel walls, but this is by no means the sole factor concerned. All of us who have reached middle life have fatty changes in our arteries, and most of us have had mural thrombosis in our coronary arteries from time to time, but that does not mean that we are in imminent danger of sudden death. Mural thrombosis is obviously the natural process by which erosions of the vascular intima are repaired, and so long as it is kept within safe limits, it is probably a beneficial one. It is only when unduly large thrombi form that we are in danger, and what we now have to try and discover are the factors which limit thrombosis and keep it under control. When we have elucidated these we may be provided with a means of rendering atherosclerosis the relatively trivial condition it was thought to be fifty years ago.

Summary

If by atherosclerosis we mean that condition which leads to narrowing of the arteries and impairment of the circulation, then it is not justifiable to assume that disturbances of the fat metabolism are the cause. The process which causes narrowing is not fatty change but thrombosis. When a mural thrombus forms in an artery it becomes organised and converted into a fibrous thickening of the intima, and for a time at least, it reduces the lumen. Thrombosis does not necessarily depend on fatty change in the arteries, nor is there any reason to assume that it depends on general disturbances of the fat metabolism. Most of the fatty changes in atherosclerosis are the result, rather than the cause of thrombosis.

Zusammenfassung

Wenn wir unter Atherosklerose jenen Zustand verstehen, in dem sich eine Verengung der Arterien und eine Schädigung des Kreislaufes entwickeln, so ist es nicht gerechtfertigt, anzunehmen, daß die Ursache in den Störungen des Fettstoffwechsels liege. Der Vorgang, der die Verengung verursacht, ist nicht in der Änderung des Fettstoffwechsels, sondern in der Thrombose zu suchen. Wenn sich in einer Arterie ein Wandthrombus bildet, so wird er organisiert und in eine fibröse Verdickung der Intima umgewandelt und während einer gewissen Zeit zum mindesten verengt er das Gefäßlumen. Die Thrombose ist nicht unbedingt von der Gegenwart von histologisch nachweisbarem Fett in der Arterie abhängig, noch besteht irgend ein Grund anzunehmen, daß sie mit allgemeinen Störungen des Fettstoffwechsels im Zusammenhang stehe. Histo-

logisch nachweisbares Fett in der Arterie ist eher die Folge als die Ursache der Thrombose.

Résumé

Si nous comprenons par athérosclérose un état qui mène à un rétrécissement des artères et à des troubles circulatoires, il n'est pas justifiable d'admettre que ces troubles soient causés par le métabolisme lipidique. Ce n'est pas à l'altération des graisses qu'est dû ce changement, mais à la thrombose.

Le thrombus mural qui se développe dans une artère est organisé et devient un épaississement fibreux de l'intima; pendant un certain temps au moins, il réduit le calibre de l'artère. La thrombose ne dépend pas de l'altération graisseuse dans les artères et il n'existe pas de raisons d'admettre qu'elle dépende de troubles généraux du métabolisme lipidique. La plupart des altérations graisseuses dans l'athérosclérose sont le résultat de la thrombose plutôt que sa cause.