SPECIAL ARTICLE

Compensatory Adjustments in the Structure of Coronary Arteries of the Heart with Stenotic Atherosclerosis

By N. N. ANITSCHKOW, K. G. WOLKOFF, E. E. KIKAION, AND K. M. POZHARISSKI

POSITIVE correlation between the degree of coronary atherosclerosis and severity of resulting secondary lesions (cardiosclerosis, myocardial infarction) is far from the rule. It is also known that even marked stenotic coronary atherosclerosis rarely may fail to produce the changes characteristic of cardiosclerosis or infarction. Moreover, the site of occlusion of a coronary arterial branch by an atherosclerotic plaque may not correspond to the location of infarction. Finally, clinical and postmortem data show that occasionally even occlusion of a main coronary arterial trunk may be unaccompanied by severe disorders of coronary circulation.

Discrepancy between occlusive coronary atherosclerosis and myocardial changes occurs because gradual development of stenotic coronary atherosclerosis is accompanied by a series of compensating adjustments, tending to maintain a more or less effective level of blood supply to cardiac muscle. This study was designed to elucidate the significance of these adjustments through investigation of coronary atherosclerosis (occlusive forms in particular) at different stages of its progression. The degree of narrowing of the arterial bed was determined quantitatively in each case, as well as the severity of the resulting sclerotic myocardial changes; their occurrence and extent were regarded as evidence for insufficiently of coronary circulation. The study was based on an examination of 262 hearts with coronary atherosclerosis from patients 30 to 80 years of age; in 74 of these cases, atherosclerotic changes in the arteries supplying the cardiac conduction system were especially studied.

A special technic was devised to allow examination of the coronary vessels in a state approximating conditions of their filling during life. The principal feature of the technic consisted in dissection of the heart after fixation of the whole coronary arterial system by means of continuous perfusion of these vessels with 10 per cent formol over a 12- to 18-hour period, injection pressure being maintained at about minimal diastolic arterial pressure. This procedure largely succeeded in counteracting postmortem contraction and collapse of the arteries that usually result in deformation of the vessel wall and distortion of its lumen. Fixation of the arteries was followed by their injection with an opaque mixture, suggested by Tolgksaia, of lead carbonate suspended in 5-per cent gelatin, or with colored gelatin.

Then, the subepicardial branches of coronary arteries and their anastomoses were dissected carefully, a binocular lens being used for the smaller branches. The whole length of successfully dissected subepicardial branches was then cut into 0.5- to 0.4-cm. segments. From each of these segments, frozen sections were prepared, stained with Sudan III-hematoxylin, and projected on a sheet of paper, with a camera. Outlines of the arterial lumen in each section, as well as the outline of intima with any atherosclerotic plaques, were

From the Department of Morbid Anatomy, Institute of Experimental Medicine, Leningrad, USSR.
traced on the paper. Finally, the cross-sectional area of the arterial lumen was determined planimetrically and expressed as percentage of the cross-sectional area of the arterial lumen in the same region of the artery, free from any atherosclerotic thickening; the inner elastic membrane was arbitrarily assumed to represent the luminal boundary. In this manner, the degree of luminal reduction in the main coronary arterial trunks and their branches could be evaluated objectively and fairly precisely (fig. 1).

To obtain a more adequate estimate of the influence of narrowing of the coronary arteries on the development of sclerotic myocardial changes, a quantitative method for assay was adapted from that originally suggested for the thyroid gland by Uotilo and Kannas.8

By these procedures, the degree of coronary artery stenosis could be correlated with the extent of sclerotic changes in cardiac muscle. The latter did not occur unless narrowing of coronary artery lumen by atherosclerotic plaques at certain sites amounted to about 70 per cent. This relation demonstrates the high capacity of myocardium to tolerate, without morphologic evidence of pronounced impairment, considerable reduction of its blood supply, provided there is an opportunity for development of a number of compensating adjustments. The main compensatory adjustments accompanying stenotic atherosclerosis assume the patterns of hypertrophy, anastomosis, plaque displacement, recanalization, and atheroma destruction.

**Arterial Hypertrophy**

With gradual narrowing of some of the larger coronary arterial branches by atherosclerotic plaques, hypertrophy develops in other unaffected or but slightly affected branches, thereby becoming responsible, to some extent, for blood supply to the respective myocardial area.
When narrowing mainly affects the anterior descending branch of the left coronary artery, hypertrophy may be seen to involve the diagonal artery, arteries of the sharp and obtuse borders of the heart, the posterior descending arteries, and branches of the affected anterior descending artery originating proximal to the site of maximal obstruction. Narrowing of the right coronary artery is compensated by excessive development of the left circumflex coronary artery, of the anterior descending artery, and of its divisions branching over the anterior surface of the right ventricle. After occlusion or narrowing of the right coronary artery distal to the origin of the artery supplying the sharp border, this branch becomes greatly hypertrophied. With narrowing of the anterior descending and right coronary arteries, hypertrophy also involves the perforating branches that penetrate the interventricular septum and supply the cardiac conducting system. In these cases hypertrophy may also be noted in accessory arteries of the conduction system, originating from proximal parts of the diagonal artery or from the anterior right ventricular artery.4 5 Hypertrophied branches tend to assume the appearance of large arterial vessels with thickened wall and wide lumen; they frequently follow a sinuous course, their lumen occasionally attaining the size of main coronary arterial trunks.

Anastomosis

Collateral blood supply is of primary importance among the compensatory adjustments to stenotic coronary atherosclerosis: gradual narrowing of main coronary arteries by atherosclerotic plaques promotes the development of arterial intracoronary and intercoronary anastomoses (fig. 2), capable of compensating to a certain degree for insufficiency of coronary circulation.6-10

A technic combining angioroentgenography with anatomic dissection was applied to our studies of vascular collateral channels within the coronary arterial system, particularly to arteries supplying the cardiac conduction system. It was not deemed satisfactory to rely on roentgenography alone,11 as had been practiced by a number of investigators, since arterial anastomoses could not be distinguished from overlapping shadows cast by coronary arterial branches. Even stereoroentgenography fails to provide adequate evidence of the presence of arterial anastomoses.10 12 Furthermore, angiographic evidence could not be expected to demonstrate with sufficient accuracy the degree of luminal narrowing by atherosclerotic plaques in coronary arteries as one of the main factors in the development of arterial anastomoses.

Dissection served to reveal the larger subepicardial anastomoses, while angiography proved particularly effective to delineate the smaller intramuscular anastomoses.

Larger subepicardial anastomoses were found within the coronary arterial system in 80 per cent of the cases of stenotic coronary atherosclerosis. As a rule, development of intercoronary anastomoses progresses with the degree of arterial stenosis.

Thus, among 11 cases from our series where coronary atherosclerosis was absent or minimal, subepicardial anastomoses liable to dissection could only be revealed in four hearts.

Of 33 cases of advanced coronary atherosclerosis in subjects belonging to similar age groups subepicardial anastomoses were present in 26 hearts. Moreover, the anastomotic channels were of a larger caliber and more numerous in these hearts than when they occurred in the absence of marked coronary atherosclerosis. Up to 16 to 20 subepicardial anastomoses were found in hearts with severe coronary atherosclerosis.

Intramuscular anastomoses were not so rare in cases with slight, if any, coronary atherosclerosis. These anastomoses, however, were never found to have attained any considerable size in such cases.

On the other hand, in hearts with advanced stenotic coronary atherosclerosis, intramuscular anastomoses proved to be much larger, so that they could actually be dissected in a number of cases. The presence or absence of infarction was not found to influence development of anastomoses, contrary to the suggestion made by Spain et al.13

Distribution of larger arterial anastomoses
was closely correlated with the location and stage of development of atherosclerotic plaques. Thus, occlusion at the proximal end of the descending branch of the left coronary artery was accompanied by the formation of large anastomoses between its branches originating distally to the site of occlusion, and the following branches of the right coronary artery: anterior right ventricular, marginal, and the posterior descending artery. In addition, anastomoses were frequently seen with branches of the left circumflex artery. Proximal occlusion of the right coronary artery was followed by anastomoses between its distal end and branches from the anterior descending and left circumflex arteries. In general, depending on location of narrowing or occlusion of a major coronary artery, blood supply to any particular myocardial area through collateral vessels was often found to depend on other branches of the coronary system. In the majority of cases subepicardial anastomoses were located on the anterior wall of the right ventricle, or about the cardiac apex, as well as over anterior or posterior walls of both atria.

It seems evident that, for the establishment of collateral circulation, a factor of great importance is the time necessary for the formation and opening of intercoronary anastomoses. Indeed, it is known that gradual narrowing of the lumen of coronary arteries by atherosclerotic plaques is often tolerated better than sudden thrombotic occlusion of a single coronary artery.

Coronary insufficiency is usually preceded
by a long period of gradually developing atherosclerosis, with slow narrowing of the coronary arterial lumen. It is evidently within this period that intracoronary and intercoronary anastomoses form, so that considerable readjustment may frequently be found to have taken place in the coronary arterial system.

Development of collateral circulation is also accompanied by marked increase in numbers of intramuscular anastomoses, as is clearly seen in angiographic studies. These anastomoses have been revealed in various myocardial regions, but they occur regularly in boundary zones, supplied by both coronary arteries. Irrespective of the type of blood supply to the heart, the most common site of intramuscular anastomoses proves to be the anterior wall of the right ventricle. Here anastomoses are formed between lateral branches of the anterior descending artery and branches of the right coronary artery (anterior right ventricular artery and artery of the acute margin), as well as the accessory artery. Intramuscular anastomoses over the posterior cardiac wall have been found to depend on the type of cardiac circulation; in the right coronary type, more commonly found in our material, anastomoses were located in the posterior left ventricular wall; with the left coronary type, they were within the posterior right ventricular wall, while with the balanced type of circulation, anastomoses occurred about the posterior longitudinal sulcus.

Important intramuscular anastomoses were observed particularly frequently within the interventricular septum, where most of the cardiac conduction system is known to be located.\textsuperscript{14,15} Within the interventricular septum, anastomoses are formed between perforating branches of anterior and posterior descending arteries (figs. 3 and 4). In some cases, the interventricular septum had been penetrated also by branches of the diagonal anterior right ventricular, and accessory arteries, which had formed anastomoses with the perforating branches. The total number of anastomoses within the interventricular septum that could be traced with adequate pre-
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Provide a partial explanation of the variable degree and clinical course of coronary insufficiency in different patients.

In compensation for stenotic coronary atherosclerosis, a role may also be played by small paravascular arteries and short or "direct" anastomoses, as well as by extracardiac anastomoses.

Extension of the paravascular arterial bed occurs through the formation of numerous fine arterial vessels with interconnecting anastomoses, situated in paravascular tissue along the coronary arteries (fig. 5). Of particular importance in compensating for impaired circulation at the site of the conduction system are arterial branches from right and left coronary arteries, located over the walls of the coronary sinus, that form anastomotic connections. In stenotic coronary atherosclerosis, the caliber of these interarterial anastomoses grows, resulting in wider connections between the distal ends of right and left coronary arteries, where branches supplying the conduction system originate (fig. 6).

Figure 5

cision in the angiograms reached 20 to 25 in occasional cases, but was usually five or 10. The diameter of intramuscular anastomoses varied between 0.1 and 0.5 mm. In a few cases the larger intramuscular anastomoses in the intraventricular septum were 1 mm. in diameter and were dissectible. These were instances in which the proximal anterior descending artery was the site of an old occlusion.

Considerable individual variations were observed in the degree of development both of larger subepicardial and smaller intramuscular anastomoses accompanying stenotic coronary atherosclerosis; in all probability this may pro-
Short, or “direct,” anastomoses form the shortest bypass, bridging proximal and distal sections of an occluded artery (fig. 7). The short anastomoses arise from excessive dilatation of vasa vasorum where the lumen of a coronary artery has been occluded. Occasionally, direct anastomoses assume an odd appearance of interwoven loops. The occurrence of these short anastomoses seems to represent a later event, since they are never observed unless other compensatory adjustments have been well established.

Branches of coronary arteries may have anastomotic connections with pericardial arteries, or with vasa vasorum of large arterial trunks originating from the heart. In several cases these formed anastomoses with atrial branches of coronary arteries including that of the Keith-Flack node; these connections could be of compensatory importance for the atrial circulation and consequently for the atrial conduction system.

Outward Displacement of Plaques

Stenotic atherosclerosis of coronary arteries is also accompanied by certain local changes in their walls, frequently tending to acquire some compensatory significance for maintaining circulation to particular myocardial zones. Thus, development of large fibrotic atherosclerotic plaques in coronary arteries is known to be accompanied as a rule by gradual atrophy of their media, occasionally resulting in its total disappearance. At the same time, the arterial wall with its plaques may be seen to bulge outward; as a result, narrowing of the arterial lumen proves to be less pronounced than might be expected. Atrophy of the medial coat resulting in widening of the arterial lumen at sites of large, closely set, or confluent plaques, has frequently been observed to occur over considerable lengths of the main coronary trunks, as well as in arteries supplying the cardiac conduction system. Consequently, in some cases the significance of these changes may not be restricted to their local effects, since they prove to be of more general importance for improving blood supply to cardiac muscle and to the conduction system in stenotic coronary atherosclerosis.

Recanalization of Thrombi

A factor of considerable importance in compensating for stenotic coronary atherosclerosis is the wide recanalization, frequently found in occluding thrombi with their organization. In a considerable number of cases (12 per cent of our series), the connective tissue, by which the thrombus is being replaced, acquires the appearance of an exceedingly thin partition between two wide channels of vascularized thrombus (fig. 8). Restitution of impaired circulation is effected through these channels, running along the longitudinal axis of coronary arteries.\textsuperscript{16, 17}
Destruction of Atheroma

A certain compensatory role may also be played in stenotic coronary atherosclerosis by some secondary changes, affecting the atherosclerotic plaques and resulting in expansion of the constricted arterial lumen. Dystrophic changes, commonly found to affect surface layers of the plaques, are sometimes apt to loosen their fibrillar structure, so that blood from the arterial lumen penetrates the plaque tissue. Occasionally, this may result in separation and removal of dystrophied tissue, atheromatous mass, and lipid macrophages, the thickness of plaques being reduced and the arterial lumen becoming somewhat enlarged locally.18–20

Thus, it is evident that within the coronary system progressive narrowing of the arterial lumen by atherosclerotic plaques is associated with a variety of compensatory adjustments that favor maintenance of myocardial blood supply at a more adequate level. Some of these adjustments, such as fully developed collateral arteries, are important for adequacy of blood supply to the myocardium as a whole; other structures depicted above (wide channels within organized thrombi, “direct” short anastomoses, and others) are of more local importance in compensating for impaired myocardial circulation.

It should be emphasized, however, that with progression of atherosclerotic lesions in coronary arteries, the process involves arteries where the larger anastomoses originate, as well as the anastomoses proper, so that these may ultimately become insufficient. Then, symptoms of coronary failure may ensue, although anatomic examination reveals fully developed collateral channels. Likewise, progressive deposition of lipids in the walls of the wide channels formed in recanalized coronary arterial thrombi may often be accompanied by secondary thrombosis and failure of the restored circulation.

It may be concluded that the enforcement of measures designed to check the progression of atherosclerotic changes in the coronary arterial system is all the more important, since it may be effective in preventing propagation of these changes to the collateral arterial system and promote the maintenance of its compensatory function.

Summary

Adjustments within the coronary arterial system that compensate for stenotic atherosclerosis include hypertrophy of larger coronary arterial branches unaffected by atherosclerosis that undertake supply of blood to an anemic myocardial area; development of collateral circulation; extension of the “paravalv al” bed; formation of short anastomoses; and wide recanalization of thrombi.

A combination of special technics devised for this investigation included fixation of coronary arteries with formal under pressure approximating the level of diastolic blood pressure, followed by their injection with an opaque mixture or colored gelatin; angiographic examination and dissection; and microscopic examination of numerous cross sections prepared from the whole length of major trunks and their branches. The size of atherosclerotic plaques and degree of luminal narrowing were then determined planimetrically, as a percentage of the original lumen.

These studies yielded objective evidence for assessing the influence exerted by varying degrees of luminal narrowing on blood supply to myocardium as well as on development of intercoronary anastomoses, and their compensatory significance. The principal conditions bringing about insufficiency of compensatory adjustments have also been considered: progression of coronary atherosclerosis involving arterial anastomoses in the process; successive deposition of lipids over the walls of wide channels through organized thrombi, resulting in their occlusion due to secondary thrombosis; and individually inadequate development of compensatory adjustments.

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Scepticism and New Ideas

It is sometimes taken as a matter of course that scepticism is the very highest flower of the scientific spirit. The thesis might be admitted to have an aspect of truth if it did not so often cover a mere automatic means of protecting ourselves against the painful eruption of new ideas.—The Collected Papers of Wilfred Trotter, F.R.S. London, Oxford University Press, 1946, p. 123.
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