Revascularization of the Heart

Histologic Changes after Arterialization of the Coronary Sinus

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A free graft of vein was placed between the aorta and coronary sinus. Three weeks later the sinus was partially occluded at its ostium in the right auricle. Blood from the aorta was made available to the myocardium by way of the venous system. After these procedures were done a histologic study of the venous and arterial channels was carried out. The coronary sinus and its tributaries showed hyperplasia of the intima. The anterior cardiac veins showed dilatation with little or no hyperplasia of intima. None of the veins became occluded. Complete occlusion of major coronary arteries was done. These arteries distal to the occlusion showed medial sclerosis and atrophy. They did not show thrombosis. The myocardium distal to an occluded artery showed many vascular channels.

An operation was developed in this laboratory which made an additional source of aortic blood available to the myocardium. This operation is described on page 801, in this issue.

It was shown by experiment that this operation protected the heart against occlusion of a major coronary artery. In view of the fact that this operation appeared to have therapeutic possibilities for patients with coronary artery disease, this study on the anatomy of the vascular system was carried out. The specimens used in this study were those upon which Hahn and Beck carried out multiple ligation of major coronary arteries.

Method of Study

This report was based upon a study of 37 specimens. A variety of procedures was carried out on the dogs from which these specimens were obtained. The two stage operation was done with an interval of three weeks between the placing of the graft and the partial occlusion of the sinus at its ostium in the right auricle. One or more major coronary arteries were ligated subsequently. Figure 1 shows the various areas from which sections were made. The sections were stained by hematoxylin and eosin and also by the trichrome and van Gieson-Weigert method. The following protocol illustrates the sequence of events in producing one of the specimens for study. (1) A free vein graft was introduced between aorta and coronary sinus; (2) three weeks later the coronary sinus was occluded at its ostium to a diameter of 3 mm.; (3) coronary arteries were ligated at intervals of three weeks to include (a) complete ligation of descending ramus and septal artery, (b) complete ligation of right coronary artery and (c) partial occlusion of circumflex ramus to a lumen of 1 mm. In this experiment the graft was patent for eight months; the coronary sinus was partially occluded for seven months, the descending ramus and septal arteries were completely occluded for six months, the right coronary artery was completely occluded for five and one-half months and the circumflex ramus was partially occluded for five months. Extensive occlusion of coronary arteries similar to that accomplished in this experiment were obtained in other experiments.

Results

The Graft

The appearance of the graft was similar in each specimen. The original vein had undergone marked alterations so that it was difficult to identify intima, media and adventitia (fig. 2, A and B). The graft was a tube of fibrous tissue lined by a smooth endothelium. The media and adventitia were composed of collagenous and coarse elastic fibers. The intima consisted of normal endothelial lining beneath which were elastic fibers and areolar connective tissue. The vasa vasorum of the graft showed marked intimal hyperplasia together with a development of elastic and connective tissue cells.

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Grossly the graft was a strong structure capable of withstanding high pressures. It usually dilated about one-fourth of its normal diameter but dilatation did not always occur. In several instances the dilatation of the graft might be described as slightly aneurysmal, but there was no evidence to indicate that dilatation was progressive with time. There was no evidence to indicate that a vein graft was not satisfactory and that an arterial graft should be used instead of a vein graft.

The Coronary Vessels

Arteries. Sections were taken in areas A, B, C, D, S, and CV of figure 1. In general an artery that had been ligated showed atrophy of the various components of the arterial wall distal to the ligature (fig. 3). The adventitia consisted of connective tissue and coarse elastic fibers. The elastica externa was usually present but was always broken up by penetrating collagenous fibers. The muscle and elastic fibers of the media were infiltrated by fibrous connective tissue. The internal elastic membrane was well developed. The intima was reduced to a thin endothelial layer of cells. The lumen of these arteries remained patent even though the main artery was totally occluded for a period of six months. Patency was observed throughout the arterial system down to the smallest arterioles. The degree of medial sclerosis of arteries was greatest in the larger arteries and least in the smaller arteries.

Veins. The coronary sinus was dilated in almost all specimens. The sinus is shown in figure 4. The intima was thin and consisted of a layer of endothelium and some connective tissue. The media and adventitia consisted of sclerotic collagenous material and coarse elastic fibers. Muscle fibers could not be recognized in the media. This appearance of the sinus was similar to the appearance of the graft.

The veins draining into the coronary sinus presented a different appearance. Marked hyperplasia of the intima was present in these tributaries (fig. 2C). This appeared to be a hyperplasia of connective and elastic tissue elements. In the larger veins a definite medial layer was present and the muscle fibers were dissociated by infiltrating bands of collagenous fibers which appeared to penetrate into the intima. The adventitia contained an abnormal amount of collagenous tissue with elastic fibers.

An artery and vein of approximately equal size are shown in figure 2D. In this illustration it was readily possible to recognize the intimal hyperplasia of the vein. The appearance of the vein was much like that of an artery and the appearance of the artery was much like that of a vein.

The anterior cardiac veins drained independently into the right auricle. These veins were not exposed to similar degrees of stasis and pressure. Communications between these two systems of veins may develop, but as a
rule the anterior cardiac veins did not become an important run-off for blood from the graft system. The anterior cardiac veins showed only some dilatation of the normal wall without showing any of the intimal hyperplasia of the coronary sinus system. The intima was a thin layer of endothelium (fig. 2E). The external elastic membrane was thin and the adventitia was composed of collagenous fibers.

Sections taken from the interventricular septum showed structures comparable to those found elsewhere. Hyperplasia of intima was present in some of the veins and simple dilatation was found in others.

Thrombosis was not found in any of the veins in this study of 37 specimens. This negative finding applied to all veins; the sinus system and its tributaries and also the anterior cardiac veins and their tributaries.

Myocardium

The specimens showed that it was possible to ligate one or more major coronary arteries with the production of little or no gross evidence of infarction. Under the microscope, however, areas of fibrosis were always found in the myocardium that had been supplied by the artery which was occluded even though the specimen did not show an infarct or areas of fibrosis to the naked eye. In some specimens there was no noticeable atrophy of the ventricular wall and grossly the muscle appeared to be normal.

In those specimens in which a definite infarct was present the infarcted area appeared to show an unusual degree of vascularity (fig. 2F). Many vessels were interposed in a mesh of fibrous scar and in such scars there were no muscle fibers regardless of the degree of vascularity. In these scars it was almost impossible to distinguish between arterioles and hyperplastic venules. In our opinion most of these vessels were venules with a marked degree of intimal hyperplasia. In the periphery of an infarct dilated venules engorged with red blood cells were consistently observed.

The arterioles of the myocardium were normal in all sections (fig. 5). The small arteries or arterioles showed none of the medial sclerosis observed in large arteries. The small venules did show changes similar to those shown by the larger veins. If the venules were connected to the coronary sinus system they showed intimal hypertrophy, whereas, if the venules were connected to the anterior cardiac vein system they showed dilatation or normal structure.

Arterialization of the Sinus, Complete Sinus Ligation, without Coronary Artery Occlusion

In specimens from dogs in which this procedure had been carried out, the degree of intimal hyperplasia of the veins was more pronounced than in the specimens already described. The condensation of elastic fibers was more pronounced. Complete thrombosis of many of the veins was found. These observa-

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**FIG. 2. A.** Transverse section of wall of graft eight months after placement. Note the condensation of collagenous and coarse circular elastic fibers marking the original adventitial and medial structures. An endothelial membrane resting upon a thin layer of connective tissue elements probably represents the original intima. In addition, note the remarkable intimal hyperplasia of the vasa vasorum. Van Gieson-Weigert stain.

**B.** Transverse section of graft with greater magnification. Van Gieson-Weigert.

**C.** Transverse section of tributary sinus vein. There is a striking hyperplasia of the intima consisting predominantly of connective and elastic tissue elements. The media is dissociated by infiltrating bands of collagenous fibers which seemingly penetrate into the basal layer of the intima. Van Gieson-Weigert stain.

**D.** Transverse section of arteriole and venule of left ventricle. Note the striking difference in thickness of the walls of the vessels. The venule again presents the characteristic intimal hyperplasia. Triehrome stain.

**E.** Transverse section of anterior cardiac vein and accompanying artery. The artery had been ligated proximally. The vein shows rather marked thinning of all layers. Note the medial sclerosis of the artery. Van Gieson-Weigert stain.

**F.** Transverse section of myocardium showing an infarct. Note the abundance of small vessels in the sclerotic muscle tissue. 125 X. Van Gieson-Weigert.

(The use of color in this illustration is made possible by a grant from Winthrop-Stearns, Inc., to the publication fund of the American Heart Association.)
Figure 2. Legend on facing page.
tions confirmed those reported by McAllister, Leinhninger and Beck. Marked intimal hyperplasia of veins with secondary thrombosis was found in those specimens in which the sinus ostium was completely occluded but in which none of the coronary arteries were oc-

ccluded. It appeared that circulation could not be maintained in this system. The circulation was “locked,” so to speak. Blood could not escape into the auricle by way of a completely occluded sinus ostium and it could not go in a retrograde direction through the myocardium because the coronary arteries were patent and

a normal arterial pressure level was maintained on the arterial side of the capillary bed. The anterior cardiac veins did not develop into an adequate run-off. The blood had no place to go and it would appear that movement of blood is necessary for a blood vessel to maintain itself as a vessel. This type of vascular system could not maintain itself as an open functional system. It was given an extensive trial over a period of several years in this laboratory before it was abandoned.

**Fig. 3.** Transverse section of artery five months after proximal ligation. Rather extensive sclerosis of the medial layer is present. The intima is reduced to an endothelium. Van Gieson-Weigert stain.

**Fig. 4.** Transverse section of the coronary sinus eight months after placement of graft. The sinus is dilated. The intima is represented by an endothelium with a small band of connective tissue. There is sclerosis of the subintimal layers. 175 X. Van Gieson-Weigert stain.

**Arterialization of the Coronary Sinus without Occlusion of the Sinus Ostium and without Occlusion of Coronary Arteries.**

In this type of experiment blood flowed from aorta, through graft, into sinus and into right auricle. In these specimens in which the coronary arteries were normal there probably was no retrograde flow into myocardium. The mean pressure in that portion of the sinus between the graft and sinus ostium measured 18 to 22 mm. Hg. The venous channels from these specimens showed some slight dilatation but none of them showed intimal hyperplasia.

**Specimens Showing Thrombosis of Graft and Sinus.** In these experiments there was no flow through the graft and into the sinus. These specimens were similar to normal hearts in which the sinus was completely occluded by a ligature. In those specimens with thrombus
formation the veins proximal to the thrombus were dilated without showing intimal thickening. In some of these specimens the tributaries to the coronary sinus showed thrombus formation. After ligation of the coronary sinus the pressure in the sinus system rose to aortic levels and the pressure remained elevated after the ligation was done.\(^2\)

**Discussion**

Definite alterations in structure were observed in the coronary sinus and its tributaries after arterial blood was delivered into the sinus and the site of exit of the blood into the auricle was partially occluded. The principal structural alteration was intimal hyperplasia, occurring as early as six weeks after the graft was placed and the sinus was partially occluded. In these experiments the intimal hyperplasia did not produce occlusion of the veins of the coronary sinus system. The anterior cardiac veins were almost always dilated or normal. Rarely was any thickening of intima found in the vessels of this system. In those areas where the two systems came together, veins with intimal hyperplasia and normal veins were observed in the same section. This was found in sections taken from the region of the anterior interventricular sulcus, the interventricular septum and the posterior aspect of the left ventricle.

Definite alterations in structure were also observed in arteries distal to the point of arterial occlusion. This structural alteration consisted primarily of atrophy of the media. The artery distal to the ligature remained patent and patency of a vessel suggested function. The patent artery with proximal occlusion no doubt carried blood. If the artery were severed blood emerged from the cut end.

Comment might be made concerning the cause of the intimal hyperplasia in veins as described in this paper. If the hyperplasia were due to pressure alone, one would expect that hyperplasia would have been found in those specimens in which the sinus had been occluded by a ligature or by thrombosis. Hyperplasia of intima was not found in those specimens. A possible factor in the production of hyperplasia was pulsatile pressure. Could pulsatile pressure as contrasted to a more or less constant static pressure produce these changes? Could alterations in oxygen and carbon dioxide content of the blood in the venous system produce such alterations? An answer to these questions cannot be given.

It was interesting that the vasa vasorum of the vein graft showed intimal hyperplasia whereas the graft itself did not show this alteration in structure.

Several comments can be made concerning the changes in the myocardium supplied by a major coronary artery that had been previously occluded. In the area supplied by the occluded artery there appeared to be an increased number of veins filled with blood. Between these veins were areas of scar which suggested that oxygen exchange requiring the thin walls of capillaries was not adequate to preserve the viability of muscle fibers.

**Conclusions**

1. Arterialization of the coronary sinus system, with partial ligation of the sinus at its ostium, produced marked alterations in structure of the sinus and its tributaries. This alteration was primarily fibroelastic proliferation of the intima. This alteration in structure was observed after six weeks and it did not proceed to complete occlusion of veins.

2. Major coronary arteries underwent structural alterations after they were occluded by ligature at the origin of the artery. Distally the arterial wall showed atrophy with sclerosis of the media.

3. The anterior cardiac veins showed little or no structural change.

**References**


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