Demonstration of Muscle Sphincters as a Capillary Component in the Human Heart

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The capillary network in the ventricular myocardium in man consists of 2 sphincter-type capillaries (the metarteriole and the precapillary) and a nonmuscular capillary, the classic or true capillary. The muscular components of the metarterioles and of the precapillaries are innervated by nerve fibers of which the terminal structure ends as a knotted fibrillar process near the muscle nucleus. The sphincter capillary and its nerve constitute a functional unit. These structures are encountered in the myocardium of man more frequently than elsewhere. In man these functional units conceivably may play a much more prominent role than heretofore realized in the dynamics of cardiac vascularization.

Attention has been focused on coronary circulation for several decades and, although the general paths of circulation have been adequately established, knowledge concerning the specific details of capillary circulation and types of vessels in the human heart still leaves much to be desired. Wearn's investigation of the coronary capillaries was of a quantitative nature in which he attempted to determine the relative number of these structures in the normal heart as opposed to the number in the abnormal failing heart.

Studies of capillary vessels in fixed preparations and in vivo have revealed that this system is not composed solely of one type. Although capillary variants have been demonstrated in a variety of organs, their location and distribution appear to be correlated with their functional activity. The structural pattern of the capillary system in mesenteric capillary circulation, in the pulps of human teeth, and in the dog's heart consists of a thoroughfare channel that is subordinate to the metarteriole. The latter may communicate with either a precapillary or a true capillary. Arteriovenous anastomoses have been observed to join arterioles or metarterioles with venules.

If the capillary variants that have been observed in the dog's heart could also be demonstrated in the myocardium of man, the dynamics of coronary circulation in the normal and diseased states might be better understood. It is the purpose of this paper to discuss the capillary circulation of the human heart from a point of view heretofore not considered.

Material and Methods

Hearts were obtained at autopsy within approximately 1 hour after death to reduce the possibility of postmortem changes. Tissues were fixed in 5, 5, 8, and 10 per cent aqueous solutions of formalin successively for 3 hours each. The tissues were kept in 10 per cent formalin for an additional 48 hours; then they were washed in running tap water, dehydrated by the usual alcohol series, cleared in xylene, and embedded. The sections were cut 5 μ thick and were arranged serially on coded slides. The Lillie-Pasternack method was used to stain the muscle components of the tissue and on alternate slides the Bodian method was employed to demonstrate nerve endings. Trials with fixation in only 10 per cent formalin demonstrated appreciable tissue distortions, which were not found when gradual fixation was employed. Sections of hearts kept in 0.9 per cent saline solution for intervals of 3 hours or more before fixation in 10 per cent formalin demonstrated postmortem changes that progressed rapidly and proportionally with time after the initial period of 3 hours.

Results

The larger arteries that are found superficially on the myocardium Anastomose freely with some of the daughter vessels invading the substance of the heart tissue. These vessels that enter the substance of the myocard-
diurn carry with them a rather dense areolar connective tissue in which are located the accompanying veins and nerves. Ganglonic masses are observed in this dense connective tissue of the ventricular myocardium. As the arteries travel through the tissue and bifurcate, they decrease in diameter; simultaneously the connective tissue in which they travel becomes progressively less dense. The rapidity with which the caliber becomes lessened varies with the different daughter vessels and their ultimate function. In those vessels that act primarily to transport blood through the tissues, the diameters decrease gradually; in those that vascularize the adjacent area, the diameters are reduced with great rapidity and they terminate in a capillary network.

The arterioles are characterized by an intima, which consists of an endothelial lining and a thin delicate subendothelium with an internal elastic membrane rarely in evidence. The media consists of a continuous layer of muscle generally 1 cell in thickness (fig. 1). The adventitia of these vessels is composed of a looser type of areolar connective tissue. When the size of a terminal arteriole is reached, the characteristics of the media begin to change. The continuous layer of muscle, so characteristic of the media of arterioles and larger vessels, becomes discontinuous. With this loss of continuity of the muscular coat, these vessels can no longer be considered arterioles but metarterioles (figs. 2 to 4). The sphincters associated with the metarterioles are in the form of minute circumferentially arranged muscle bands composed of 1, 2, or 3 cells, which function as a unit. These are usually found in pairs (rarely more than 3) in that portion of the metarteriole which communicates with the parent arteriole. However, as the distance from the parent arteriole is increased, not only are the sphincters reduced in numbers, but the distance between sphincters is increased (fig. 3). Although the sphincter unit, which is made up of a greater number of muscle cells, is generally located closer to the parent vessel, this need not always be the case (fig. 4). Metarterioles are observed in which a unit of as many as 3 muscle cells is found between individual muscle units.

The precapillaries found in the human heart may arise as a bifurcation either of a metarteriole or of an arteriole. At the segmental area of attachment with the parent vessel, the precapillary possesses muscle cells, herein termed the precapillary sphincter (fig. 5). The number of muscle cells comprising the sphincter in this type of capillary varies again from 1 to 3. The portion of the precapillary distal to the sphincter is indistinguishable from a true capillary, since its sole composition is endothelial.

The sphincters that are found in the metarterioles or the precapillaries are identical in position and in their anatomic features with the muscle cells, which comprise the media of the larger vessels (arteries or veins).

Arteriovenous anastomoses are observed in the ventricular myocardium (fig. 6). These vessels, which act as shunts bypassing all or some of the capillary circulation, are herein demonstrated to connect arterioles with venules or metarterioles with venules. The walls of these vessels may vary in their degree of musculature depending upon whether the parent vessel is an arteriole or a metarteriole. The segment of the arteriovenous anastomosis communicating with an arteriole is considerably more muscular than a segment of comparable location attached to a metarteriole. The portion of the arteriovenous anastomosis, intervening between the points of attachment from artery to vein, decreases in its musculature as the distance from the parent vessel is increased. This reduction may range from an occasional individual muscle to total absence.

The true capillaries found in the human heart consist of an endothelial tube completely devoid of muscular components. Although these vessels are generally oriented parallel to the long axis of the cardiac fibers, some capillaries are noted to run obliquely or less often at right angles to the myocardial muscle fibers.

The capillaries anastomose so profusely among the cardiac fibers that an individual fiber may have several true capillaries asso-
Fig. 1. Arteriole of ventricular myocardium. Note continuous muscle layer. M, muscle nucleus; L, lumen of vessel; E, endothelial nucleus. Romanowsky, 5 μ, X 400.

Fig. 2. Metarteriole of ventricular myocardium in connective-tissue septa (C.T.S.). M, muscle nucleus; E, endothelial nucleus. Romanowsky, 5 μ, X 140.

Fig. 3. Metarteriole at right angle to muscle fibers of ventricular myocardium. L, lumen of the vessel; containing E, erythrocytes; M, nucleus of muscle sphincter; and E, endothelial nucleus. Romanowsky, 5 μ, X 900.

Fig. 4. Metarteriole of ventricular myocardium showing 3 muscle cells making up the sphincter. M, muscle nuclei; L, lumen of the vessel; surrounded by, E, endothelial cells. Romanowsky, 5 μ, X 400.

Fig. 5. Precapillary branching from metarteriole. Precapillary sphincter consisting of 2 muscle cells, M. Note smaller metarteriole with endothelial nucleus, E, bulging into lumen containing erythrocytes, R.

Fig. 6. Arteriovenous anastomosis. Note that segment of vessel distal to vein is more muscular, as evidenced by muscle nuclei, M. Romanowsky, 5 μ, X 140.

Associated with it. Although branching of the capillaries into 2 daughter vessels is the general rule, trifurcation is not uncommon.

Nerve fibers accompanying the vessels of all calibers are herein demonstrated. The larger nerve trunks travel with the larger vessels in the areolar connective-tissue septa of the heart. The branching of the larger nerve trunks is associated with the partitioning process of the connective tissue that invades
the myocardium. The smaller nerve trunks that result from progressive subdivisions run in close proximity to the capillary system. At intervals, a nerve fiber which remains proximally attached to the parent fiber is extruded. This daughter fiber travels to the muscle sphincter of the metarteriole or precapillary with which it is associated or it may be associated with an adjacent vessel. Prior to intimate association with the muscle cell, the nerve fiber becomes splayed. The fibrillar process thus formed surrounds the muscle cell, so that the knotted ends terminate in the region of the nucleus (fig. 7). Although nerve fibers travel along with true capillaries, no association between the endothelial cells and these fibers is observed (fig. 8).

The sphincters of the metarterioles and precapillaries are found in both the relaxed and the contracted conditions. In the relaxed state, the muscle nuclei are ovoid and somewhat elongated when viewed from the surface. This condition is reflected in the underlying endothelial cell and the lumen of the vessel. The nucleus of the endothelial cell is greatly elongated and appears laterally compressed (fig. 4). The lumen of the muscular capillary appears to be normal in that it is symmetrically round (no inward bulging of the endothelial nuclei).

In the contracted condition, the muscle nuclei of the sphinietered capillaries appear broadly ovoid (surface view). The underlying endothelial cells are altered in diameter, their nuclei become rounded to the point that they protrude into the lumen, which has become constricted at this point. The degree of luminal constriction is contingent upon the intensity of contraction. The endothelial cells between sputinaters in the metarterioles and the endothelial cells immediately distal to the precapillary sphincters appear to be identical with the endothelium underlying the sphincters in the relaxed condition. In the contracted condition of the sphincter, however, the endothelium underlying the sphincter and that portion between sphincters appear to be different. The endothelium un-
Discussion

The anatomic structure of the larger arterioles in the myocardium was observed to be more or less consistent with that found in other parts of the body except that an internal elastic membrane is rarely seen. The primary function of this membrane is to give support and strength to the walls of the vessel. In the myocardium of man, and especially in the ventricular myocardium, the walls of these vessels are greatly reinforced by the surrounding muscle tissue. It is not inconceivable that the internal elastic membrane of arterioles in this part of the heart should be at best very poorly developed or even totally wanting.

With the demonstration of the capillary variants in the pulps of human teeth^7,8 in the myocardium of the dog^4 and with the command of the contractibility of these structures by various chemical and physical means,^7,8 interest was aroused in a similar capillary network in the human heart. Unless the tissue is obtained immediately after death and is fixed gradually, postmortem changes in the appearance of the capillaries and nerve fibers are effected. Rapid fixation results in tissue distortion which renders the demonstration of these structures extremely difficult if not impossible.^4

The sphincters of the metarteriole and precapillary are identical in structure with their counterpart in the myocardium of the dog. These are also identical with the muscle cells that are associated with the other vessels (arteries and veins) of the body except for those associated with the human dental pulp. The nuclei of the muscular components of all vessels of the radicular and coronal pulps are characterized by chromatin material that appears finer and consequently stains more hypochromatically than these structures in other vessels of the body.^3

Although there appears to be no qualitative difference between the capillary sphincters in the myocardium of dog and of man, one conspicuous observation was made: the frequency with which the metarterioles, precapillaries, and the arteriovenous anastomoses are encountered in the ventricular tissue of man greatly exceed that found in the dog. Furthermore, while most of the capillary variants in the myocardium of dogs are located between the cardiac muscle fibers, in man, these structures are not restricted in their location but are found in the looser connective tissue septa as well. Finally, while the true capillaries in the dog are characterized by dichotomous branching resulting in 2 daughter capillaries of equal diameter, in man trifurcation as well as bifurcation of these vessels is present.

The metarterioles and precapillaries in the myocardium of man were observed in the constricted and in the dilated conditions; these are correlated with their association with nerve endings. There has been some controversy about the precise ramification of autonomic efferent fibers associated with blood vessels, heart, and other visceral structures. Some investigators postulate that the end structures of these nerves terminate in the nuclear region of the muscle cell; others report that the nerve-end apparatus, which may be in the form of bulbs, loops, or free endings, terminates either intercellularly or intracellularly; still others maintain that the beaded fibrillar end-process of the nerves terminate as synecytially arranged plexi enveloping individual muscle cells. Our results,^3,4 corroborate those of the other investigators who have reported the knotted fibrillar processes. Furthermore, evidence supporting the existence of a terminal reticulum was not obtained.
The true capillary, which is solely endothelial in nature and hence is completely wanting in muscle cells, has not been demonstrated to have associated with it the knotted fibrillar processes characteristic of the sphincters of the metarterioles and the precapillaries.\textsuperscript{4, 8} It is quite possible that, where nerve-end apparatus has been reported associated with endothelial cells,\textsuperscript{10} the vessels in question were not true capillaries but sphinctered capillaries.

Capillary occlusion effected by the endothelial cells, as reported by Midsuno\textsuperscript{11} and by Sanders et al.\textsuperscript{12} was not interpreted by Chambers and Zweifach\textsuperscript{2} and by Kahn and Pollak\textsuperscript{13} to result from the intrinsic action of the endothelial cell but from the contraction of the sphincters of the metarterioles and the precapillaries. Our studies tend to substantiate the interpretation of Chambers and Kahn and their associates, for no evidence of capillary constriction was observed in those vessels of the dental pulp,\textsuperscript{4, 8} nor in the myocardium of dogs,\textsuperscript{7} which are wanting in muscular components. This condition is also found to be characteristic of those portions of the muscular capillaries intervening between sphincters.

Qualitative differences in the capillary components on the one hand and the density of vessels in the myocardium on the other, would strongly suggest that cardiovascular dynamics play a far more important role in the functional processes of this organ than has been realized. Chambers and Zweifach\textsuperscript{2} were able to produce changes in the diameter of the vessels when epinephrine and histamine solutions were dropped on the omentum of the dog and rat. Provenza and Biddington\textsuperscript{8} effected marked vasodilatation and vasoconstriction of the sphinctered capillaries of the radicular and coronal pulps of man when nitroglycerin and epinephrine, respectively, were topically applied. Identical results were produced with the intracardiac administration of drugs.\textsuperscript{4, 7} The pharmacologic control of the circulation through the vessels of the capillary system emphasizes the importance of the capillary system in considerations of treatment of cardiovascular diseases.

**Summary**

Sphincter capillaries are components of the capillary bed in the ventricular myocardium of man. The ventricular myocardium is vascularized by a capillary bed consisting of 3 types of vessels. The metarteriole is a vessel of the same caliber as the true capillary. It is differentiated from the latter in that at varying intervals 1 or several muscle cells make up a sphincter unit. Although the larger sphincter units are found more proximally located to the parent vessels, this condition need not be true for all metarterioles. The precapillary is the same anatomically as the true capillary except that at the segmental area of an attachment with the parent vessel (metarteriole or arteriole) a sphincter consisting of 1 to 3 muscle cells is found. The true capillary consists of a simple endothelial tube.

Arteriovenous anastomoses are found in the ventricular myocardium of man. These are vessels that act as shunts, bypassing some or all of the capillary types. The arteriovenous anastomosis may connect an artery with a vein or a metarteriole with a vein. The anatomic distinction between parent origin (artery or metarteriole) is made on the basis of the degree of musculature present in the wall of the arteriovenous anastomosis.

The sphincter and its nerve-end apparatus constitute a functional unit. Nerve fibers are located in close proximity to the capillary types. At varying intervals, daughter nerve fibers divorce themselves from the parent trunk and travel to the muscle sphincter of the metarteriole or precapillary with which it is associated or to adjacent vessels. These fibers terminate as fibrillar processes in the nuclear region of the cell. True capillaries have not been demonstrated to have nerve-end apparatus associated with them.

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SUMMARIO IN INTERLINGUA

Capillares con sphincteres es componentes del vasculatura capillar in le myocardio ventricular del homine. Le myocardio ventricular es alimentate per un vasculatura capillar que consiste de 3 typos de vasos. Le metarteriola es un vaso del mesme calibre como le ver capillares. Illo se distingue per le presentia, a varie intervallas, de mechanismos sphincteric consistente de 1 o plure cellulhas muscular. Ben que le plus grande mechanismos sphincteric se trova generalmente in sitos plus proxe al vaso parente, iste condition non prevale necessariare in omne metarteriolas. Le precapillares es anatomicamente le mesmo como le ver capillares, excepte que in le area segmental del attachamento al vaso parente (que pote esser un metarteriola o un arteriola) un sphincter se trova que consiste de 1 a 3 cellulhas muscular. Le ver capillares consiste de simple tubos endothelial.

Anastomoses arterio-venose se trova in le myocardio ventricular del homine. Istos es vasos que age como shunts saltante plures o omnes del typos capillar. Le anastomoses arterio-venose pote connectar un arteria con un vena o un metarteriola con un vena. Le differentiation anatomic secundo le vaso parente—arteria o metarteriola—se face secundo le grado de musculatura presente in le pariete del anastomosis arterio-venose.

Le sphinctere e su apparato de termino nerval constitue un unitate functional. Fibras nerval de ordine filial se distacha a varie intervallas ab le trunco parente e viagia al sphincter muscular del metarteriola o del precapillar con que illos es associate o a un vaso adjacent. Iste fibras se termina como processos fibrillar in le region nuclear del cellula. In ver capillares, nulle associate presentia de apparato de termino nerval ha unquam essite demonstrate.

REFERENCES

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