CLOSURE OF THE DUCTUS ARTERIOSUS AND ITS BEARING ON ARTERIO-SCLEROSIS

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THERE have been very many views expounded on the process and nature of the closing of the ductus arteriosus, and yet, up to the present time, there is not one theory that has been universally accepted. Most of the expressions of opinion were made previous to 1883, when Thoma was led to believe that the fibrous closure of this vessel played a great part in the production of arteriosclerosis in later life. As this view has of late years been discredited, the attention of investigators has been taken away from the study of the ductus arteriosus, and very little new work has appeared on the subject in recent years.

Next to the importance which Thoma ascribed to the ductus arteriosus in its relation to arteriosclerosis is the non-closure of the duct in certain individuals leading to permanent circulatory defect with sequelæ. Of cases of this nature there are a considerable number reported in the literature, and many of them have formed the basis for the study of the functions of the ductus arteriosus.

I was led to the study of the ductus arteriosus and the nature of its closing by a conviction of the importance of the study of the physiological function and the mechanics of different vessels in the body. I would emphasize my belief that the diseased processes in different arteries is dependent, to a very large extent, on the nature of their walls. We must abandon the old conception that the arterial system is of like structure in all its parts. It represents in truth a common trunk, the aorta, onto which there are engrafted branches of various kinds, each of which has work of special nature to perform.

The functions of the arteries of the uterus, where there is a periodic congestion, throwing a greater work on the media, differ from those of the kidney, where the supply is fairly uniform, and adaptability of the arterial wall is of less importance.

The ductus arteriosus has structurally no homologous vessel in the body, and it is this histological difference, together with peculiar conditions of the blood pressure at birth, which lead to the closure of its lumen.

Haller looked on the closure of the ductus arteriosus as the outcome of a peculiar coagulation of blood substances. Kilian (1826) was the first to call attention to the part played by the expansion of the lungs in the closure of the ductus, pointing out that there is a greater demand by the lungs on the pulmonary system, thus diminishing the quantity of blood passing through the ductus arteriosus.

Among the rather unique explanations for the closure of the ductus, is that given by Chevers. He believed that the recurrent laryngeal nerve, which, on the left side, loops around the ductus arteriosus, has the effect of cutting off this vessel at the beginning of respirations. King held that the expansion of the left bronchus after birth compressed the ductus and also rendered the communication with the aorta less direct, thus inducing the closure of this vessel. Rokitansky and also Meyer believed that the closure of the ductus was consequent to the change in the course of the vessel.

The literature contained many references to cases in which there was a persistent ductus or aneurysm of the ductus, or thrombosis of the ductus. In most instances the patient was but a few months or years old, but in others the condition was present in adult life. The most frequent cause of patent ductus arteriosus, in young children, is partial atelectasis of the lungs, while in the rarer cases, and those of adult life, possess some anomaly of the pulmonary artery or the aorta. Virchow and Rauchfuss point out that a persistent ductus arteriosus in children is most often correlated with marasmus. This will be understood later when I point out that the proper closing of the ductus arteriosus requires the full expansion of the lungs, a condition not properly attained in marantic children.

In adults, Gerhardt has met with cases of patent ductus arteriosus,

and found the most constant clinical symptoms to be (*a*) hypertrophy and dilatation of the right heart, and (*b*) a loud systolic murmur over the second left intercostal space. Hochhaus had a case which gave these signs and at autopsy the diagnosis of patent ductus arteriosus was verified, there being also a constriction of the aorta immediately above the ductus arteriosus.

To the many theories enunciated by other authors, Strassmann adds another. The relative pressures in the aorta and pulmonary artery become reversed immediately after the lungs are inflated. Then the blood-flow, instead of passing from the pulmonary artery to the aorta, attempts to pass in the reverse direction. However, as the relative pressure increases in the aorta, the upper and angular lip of the mouth of the ductus becomes pressed inward upon itself, and thus occludes the lumen. Strassmann claims to have demonstrated this valvular action of the aortic opening in the dead newborn child. He found that no fluid entered the ductus arteriosus when the injection was made into the aorta, and when the pressure was kept below 100 mm. of mercury.

Kiwisch gives a very comprehensive description of the circulatory changes occurring after birth. During the process of the expansion of the lungs, not only is the air but also the blood is made to enter this potential tissue. The supplying of the pulmonary radicles with larger quantities of blood necessarily utilizes some of the fluid formerly passing by way of the ductus arteriosus. Kiwisch believed that the nervous control played an important part in the active contraction of the ductus arteriosus, while a compensatory relaxation occurred in the vessels of the lungs, thus allowing freer access of blood into them. The final closure takes place, as Rokitansky also described it, by a proliferation of the tissues of the intima, without the intervention of a thrombus. Rokitansky also demonstrated that the occlusion of the ductus was not necessarily a simultaneous process throughout the vessel, but that different points of the vessel often became more contracted, and were earlier occluded than others. Such a condition in the vessel would give the appearance of aneurysm formation with thrombus production.

Langer was the first to note the microscopic appearance of the

ductus arteriosus as it was closing. The vessel showed active proliferation of the cells of the intima, so that the vessel wall became thicker than the aorta or the pulmonary artery. This thickening of the wall encroached upon the lumen of the vessel, and eventually completely blocked it. Walkhoff, too, noted that the normal histological structure of the ductus arteriosus differed considerably from either that of the aorta or the pulmonary artery. Principally was this noted in the intima and media. In the former, the tissue is much looser and is devoid of elastic fibers, while the media lacks the parallel bands of elastic fibers which lie toward the muscle layers. There are, however, according to him, fine fibers of elastic tissue present, but in such small quantity as to be of little importance. In the media, too, there is a considerable quantity of connective tissue present about the elastic fibrils. These, he considers, may be the cells which lay down the elastic fibers. The closure of the ductus, he believes, is due mainly to histological changes in the wall of the vessel, supplemented by thrombus formation and displacement of the thoracic organs. He lays some stress on the altered position of the heart, which is so acted upon by the recently dilated lungs as to bring about a stretching and more acute arching of the ductus arteriosus. He believes, too, that there is increased pressure in the lesser (pulmonary) circulation during the first two or three days of life. The aortic arch, too, is assumed to alter its position, which, together with the displacement, brought about by the inflated lungs, produces an actual kinking in the ductus. The pulmonary orifice of the ductus is placed at a more decided right angle to the trunk of the pulmonary artery, and apposition of its walls is brought about by the downward pull exerted upon it by the fixed pericardial attachment. Structural changes begin in the wall of the vessel by the second day, where longitudinal layers of tissue (muscle?) are found in the media. The intima, too, undergoes rapid cell proliferation.

In 1871, Schulze made a very complete study of the ductus arteriosus and its mode in closing. He pointed out, first, that blood-vessels became obliterated, either as a consequence of lowered blood pressure, or stagnation of its fluid contents. The latter

process brought about thrombus formation, while in the former the contractile muscular walls of the vessel firmly closed down on the lumen. This can, however, occur only to a certain extent in most vessels, as they possess elastic rings, which in themselves can cause a distended vessel to return to its ordinary lumen, yet cannot bring about contractions in that vessel wall beyond this. Muscular fibers are the only tissue elements present, endowed with the property of active shortening. When, therefore, Schulze says that both a drop in the blood pressure and stagnation of the blood result in the same vessel, the factors for the obliteration of such a vessel are then complete. This condition occurs at a certain period in the ductus arteriosus. Complete stasis of the blood current is present, then, when the lowered pressure in the pulmonary artery equals that in the aorta, and this period exists, not only for hours, but for days, until the enlarging and hypertrophying left heart gradually increases the pressure in the aorta much above that of the pulmonary artery. Schulze pointed out that while this obliteration of the lumen may be one coming on rapidly after birth and with the onset of respirations, the complete closure of the ductus by fibrosis is a matter of weeks. This view of Schulze is strongly attacked by Schanz, who could not conceive how there might ever come a time when both pulmonary and aortic pressures were equal, and, even granting this, how the circulation in the ductus arteriosus was brought to a standstill. I shall not discuss Schanz's attack on the mechanical theory of the closure of the ductus arteriosus at this juncture.

Schanz, however, brought forward another view. He described at length the relative positions of the thoracic organs, before and after respiration had commenced in the child. He also determined the various fixed points of the vessels and heart, and how these were affected in respiration. The thorax of a child who has not breathed is small, the diaphragm rises very high and the heart lies in a more horizontal position than the adult. The aortic arch, too, is more transverse, though firmly fixed to the spinal column. Opposite to this fixed point the ductus arteriosus opens into the aorta. At its other extremity are the sources of the pulmonary arteries, and at the point where these are given off, the pericardial sac is firmly

attached to the base of the vessels. This pericardial sac, he points out, is adherent to the diaphragm, and through the anterior mediastinum to the sternum. Schanz finds that after respirations have commenced, the relative positions of the vessels to the intrathoracic organs is considerably altered. Particularly does he find that the direction of the ductus arteriosus, in its relation to the pulmonary orifice of the heart, is changed, and this, he holds, is the result of the firm attachment of the heart through the pericardium to the diaphragm and sternum. With the expansion of the lungs the diaphragm is drawn downward and the sternum rises and increases its distance forward from the vertebral column. In these new positions the heart is pulled upon so as to become more vertical, altering its relation to the ductus arteriosus. Not alone is the relative position of the ductus arteriosus disturbed, but this vessel also experiences an active stretching during expansion of the chest.

In considering the above opinions, one is struck with the many sides there are to the question of the closure of the ductus arteriosus, and to seriously weigh the theories expounded by Thoma, the bearing upon what we may term the mechanics of arteriosclerosis makes a study of the mechanics, and the histological structure of this part of the circulation essential.

Briefly, the fetal circulation differs from that of adult life in having the blood entering the right auricle divided into two streams. The greater part of the aërated blood coming from the placenta passes from the inferior vena cava directly through the foramen ovale to the left heart, and is supplied to the head and upper extremities. The venous blood returning from these parts enters the right auricle by the superior vena cava, and with an admixture of inferior caval blood, which is aërated, passes to the right ventricle, from which a meagre supply goes through the pulmonary system, while the greater part passes by way of the ductus arteriosus to the aorta and supplies the abdomen, the lower extremities and the placenta. During this stage, the right heart, the trunk of the pulmonary artery and the ductus arteriosus form the most conspicuous part of the circulation in the thorax. The ductus arteriosus is in a direct line with the pulmonary trunk, is the direct continuation of the same, and is of

almost equal size, while it is of greater diameter than the descending arch of the aorta. A distinct narrowing of the aortic arch is to be observed just above the entrance of the ductus into it. This constriction of the aorta serves, to some extent, to prevent a back flow of blood coming from the high-pressured ductus into the arch of the aorta. This lessened caliber of the aorta, above the point of junction, is, it will be seen, merely the expression of the fact that below the point of junction the vessel is fitted to convey an increased amount of blood, that, namely, reaching it from the ductus arteriosus along with that conveyed through the aortic arch, or, conversely, it is an indication that the blood entering from the ductus is not distributed in both an upward and a downward direction, but presses only downward.

It thus becomes evident that the greater part of the work of the circulatory system, during fetal life, is thrown upon the right heart. This fact is borne out by the relative increased size and strength of the right heart over the left, as is seen at fetal autopsy. In newborn children we are accustomed to see the right ventricle almost double the size of the left, and this can only be accounted for by the greater amount of work this organ has to do.

With this more powerful organ the blood pressure in the right heart must necessarily exceed that on the left side. Likewise, the blood pressure in the pulmonary artery, and in the ductus arteriosus, is greater than that in the aorta, thus causing the blood to flow from the pulmonary system to the aorta. Relatively, therefore, the blood pressure during fetal life and before the lungs have become expanded is high in the ductus, and at least of such force to overcome the pressure in the aortic system. In adult life the condition of affairs is reversed, so that the aortic pressure then far exceeds that of the pulmonary system.

The change of the relative pressure from that, as it is found in fetal life, to the condition as we see it in the adult, is not a sudden or instantaneous one, and as Schultz has pointed out there must be a time when the blood pressures in the pulmonary artery and the aorta are equal, and an equilibrium is established between the two systems. This we shall subsequently study in greater detail.

The histological structure of the ductus arteriosus is also deserving of note, particularly as its make-up is rather unique. It is striking how the histological descriptions of the different authors have varied; this discrepancy in the histological finding is in the main due to the different stages of collapse at which the vessel was examined. It is well known to us all what a different picture is obtained from a vein in the state of collapse and one distended. The former gives one the impression of a diseased vessel with thickened walls. The thickening is only apparent and not real, due to the packing together of a given mass of tissue into a smaller space. Thus, too, the structure of the ductus arteriosus appears different, depending on whether the vessel is examined in the collapsed or dilated state.

The ductus is lined by endothelium which is placed on an appreciable layer of connective tissue. This connective tissue seems fairly loose, and comes into prominence when the vessel is collapsed, when it appears loose and swollen. In the dilated vessel, this connective-tissue layer is stretched out and is very thin. Beneath this layer is a much interrupted internal elastic lamina. This membrane is not continuous, but is made up of many irregular strands which overlap each other when contracted. The internal elastic lamina does not form a conspicuous tissue as in vessels of the muscular type, but may consist of several thin lamellæ instead of one heavy one. Beyond this lies the media, made up almost entirely of muscle tissue, but having a fine network of elastic fibers intertwining the muscle bundles and linking them together. The musculature of the media differs from that of other arteries in possessing no regular arrangement. The circular muscle bundles are in excess of the longitudinal, and the latter have no fixed position in the middle coat. Longitudinal muscle cells are met within all parts of the media, and the circular fibers are not so regularly disposed of as in other arteries. One is impressed with the relative abundance of muscle tissue in the wall of the vessel. The adventitia does not seem to differ from that of other vessels.

Thus the structure of the ductus arteriosus differs from that of either the pulmonary artery or the aorta. In each of the latter the media is strengthened by heavy bands of elastic fibers which

pass circularly about the vessel. These, as has also been noted by Walkhoff, Langer, and Thoma, are wanting in the ductus arteriosus except for the irregularly disposed fine fibers. This loss in strength by the lack of elastic tissue is more than compensated in the increased amount of muscle fibers.

Involuntary muscle fibers, such as are present in the ductus arteriosus, must be considered as tissue with potential energy. These muscle fibers are constantly on the stretch, while the vessel possesses its normal lumen. With each pulsation the muscle fibers give, and then contract again as the blood pressure is lowered, and it is the function of these fibers to contract to their limit when the pressure is lowered within the lumen of the vessel.

Further, the ductus arteriosus is provided with an accessory bundle of muscle fibers at each extremity. This muscle bundle is circularly disposed and occupies a position superficial to and within the tissue of the media. This ring or layer belongs to the intima, and to this extent may be compared with Jores' musculo-elastic layer. It strengthens the joint between the ductus and each of the main arteries. The peculiarity of this tissue is, that the fibers in it are regularly disposed in a circular manner, and that this mass transgresses the confines of the media; but as it merges with the aorta the fibers are seen to take a very superficial position and to form part of the musculo-elastic layer. This layer was observed and described by Thoma; to Jores we owe the recent and fuller description of the same. It has been shown more recently that the mouths of all branches of vessels are strengthened by a small, angular mass of tissue, whose purpose it is to give a firmer welding at a point of weakening in the main artery.

With the beginning of respirations at birth, a considerable change takes place within the thorax. The respiratory movements of the chest increase its internal capacity, and this is further increased by the descent of the diaphragm. Expiration again tends to diminish the thoracic cavities, but after respirations have once properly begun the chest never again recedes to the small and unexpanded state found in fetal life.

The expansion of the chest brings with it changes in the internal

organs, and amongst these the closure of the ductus arteriosus. It is conceded by all that the ductus arteriosus changes the size of its lumen very rapidly after respirations have begun, and although its lumen is not completely obliterated, for days or weeks later, the duct is practically functionless after the first hour or so of birth.

As the lungs fill with air, they occupy a different position from the atelectatic fetal organs. The lungs rise from the position they occupied against the vertebral column and the angles of the ribs, to a position nearer the centre of the thoracic cavity, so that the hilus is raised closer toward the sternum. This change in position has an effect, no doubt, on the relative positions of the other organs, but I cannot hold that it plays such an important role as is credited to it by Schanz and others. When they say that the altered position of the thoracic organs tends to produce a tugging on the ductus arteriosus to such an extent as to obliterate its lumen, they are discounting the force required to produce such a change in as large a vessel as the ductus arteriosus. I have attempted in the newborn to alter the lumen of the ductus by tugging at the pericardial sac at the root of the pulmonary artery, and found I could produce but little change in the diameter of the vessel. To reduce the lumen of the ductus, even in the slightest, necessitates such force as will appreciably lengthen the vessel. Such a stretched vessel does not simulate the closed or closing ductus. The closing ductus not only decreases the size of its lumen, but also actually shortens in the length.

Although the position of the organs is to some extent altered in the chest cavity, it is evident that this is not important. The difference in the direction of the ductus arteriosus before and after expansion of the lungs is noticeable, and yet in mechanics without bearing. My observations convince me that the arch of the ductus arteriosus is rather straightened, and the alteration in the direction of the ductus to the pulmonary artery is very slight. As adult life is reached these relationships are, of course, much altered, but at the crucial time, when the ductus is becoming obliterated, there is no sufficient alteration or kinking in the blood current from the pulmonary artery to the ductus, to account for the phenomenon of closure.

The closure of the ductus, I believe, depends mainly on two factors: (1) The reduction in the blood pressure, and (2) the muscular contraction of its walls.

Not alone does the expansion of the chest favor the access of air to the lungs, but the way is opened for a more ready flow of blood through the pulmonary system. This increased amount of blood is sent to each lung by its respective pulmonary artery, which becomes twice or three times the size it was in fetal life. To call on the main pulmonary trunk for this extra amount of blood, necessarily reduces the pressure within it to a very considerable degree; in fact, to such an extent that it can no longer overcome the tonic contractile force of the ductus arteriosus. That the muscular contraction of the ductus plays a part in the closure of the vessel is seen in the longitudinal folds into which the vessel is thrown; folds which represent the compressed intima and subendothelial connective tissue. Occasionally transverse folds are also noted, due to the very active shortening of the vessel by the longitudinal muscle fibers.

I have had the opportunity of studying at postmortem the circulatory system and ductus arteriosus in a great number of infants, varying in age from the newborn to those four months old. The patency of the ductus arteriosus was determined by injecting a colored fluid into the left carotid artery, and allowing this under slight pressure to find its way through the patent arteries. Usually the abdominal aorta was ligated to prevent unnecessary waste of fluid. I have never been able to verify Strassmann's observations that the upper lip of the opening of the ductus arteriosus into the aorta acted like a valve, which prevented the aortic blood from passing back into the pulmonary artery. At all times when the ductus arteriosus was unobliterated by new-formed or forming fibrous tissue, the colored fluid found its way into it for some distance, sufficient to stain it. Occasionally one does meet with the ductus, three or four days, or more, after birth, which has its lumen obliterated, but through which a probe can still be forced. The narrowness of the lumen is due entirely to the contraction of the vessel walls, and it is but seldom that the lumen contains blood clot. Only in those cases in which the muscle bundles, at both or either extremity,

contract more rapidly or contract against a blood pressure which still keeps the middle portion of the ductus arteriosus patent, do we find blood imprisoned in the middle part of the ductus.

It is the relative abundance of muscle cells in the ductus, as compared with the elastic tissue, that permits of the active contraction in its walls. This power of contraction is exceptional, compared with the aorta or the peripheral arteries. In each of the latter there is a definite and maximum amount of contraction to which the vessel can be subjected, while on the other hand the musculature of the ductus arteriosus may completely obliterate its lumen by its contraction.

The fall of the blood pressure, in the right heart and pulmonary system, to that degree which allows closure of the ductus arteriosus, immediately sends more blood around to the left heart and aortic system. This throws more work on the left heart, but still this organ cannot raise the blood pressure in the descending aorta sufficiently to reinstate the lumen of the ductus from the side of the aorta. The left ventricle gradually gains power until the blood pressure in the aorta reaches and exceeds that which had previously existed in the pulmonary artery. But in the meantime the contracted ductus arteriosus is undergoing histological changes. The endothelial lining of the ductus is shelled off during the firm contraction of the lumen. Cellular debris and some leukocytes occupy the central core and in a short time cellular proliferation becomes active, mainly from the subendothelial layer of connective tissue. This fibrous tissue soon forms a felted network throughout the former lumen of the vessel, where the endothelium has been lost, and obliterates it.

The media of the collapsed ductus arteriosus, in the newborn child, shows the same tangled appearance of its muscle cells as does the contracted ductus in an infant several days old. In the newborn child that has not breathed, there is contractile power left in the muscle cells of the ductus which acts after the circulation has ceased. The histological picture of such a vessel does not differ from the active contraction of the muscle cells of the ductus taking place during life.

The cases of patent ductus arteriosus are, I believe, the result of imperfect expansion of the lungs. In these cases the blood pressure

has never been lowered in the pulmonary system to the point which allowed the walls of the ductus to overcome it. In consequence of this the flow of blood through the ductus is constant, and the current is from right to left; that is, from pulmonary artery to aorta. This condition is permanent in those cases in which the expansion of the lungs is gradual and a matter of months and years. The right heart remains persistently larger than the left, and the blood pressure, in consequence, is likewise continually higher in the pulmonary system. From the lessened work that is thrown on the left ventricle it remains small, and the ascending aorta and the arch never develop to the size that is attained in the normal adult with the closed ductus.

There are other series of cases in which the ductus remains permanently patent, such as congenital narrowing of the pulmonary orifice, and stricture of the descending aorta, but these need not be discussed here.

In speaking of the closure of the ductus arteriosus, Thoma referred to it as a process of contraction without further explanation of its nature. He did, however, describe at some length the processes which he believed were associated with this phenomenon. He placed great stress on the fact that connective tissue was present underneath the endothelium in the "Nabelblutbahn," while in the remaining arterial systems none was present in early life. The proliferation of this connective tissue after birth became more marked, and was accounted for by the lessened b'ood content in the circulation of the "Nabelblutbahn."

Thoma found that the intima of the ductus arteriosus and the umbilical arteries contained relatively large quantities of connective tissue during fetal life. This connective tissue served the purpose not only of obliterating the lumen of these arteries after they had contracted, but also of sending a fibrous-tissue layer into the intima of the vessels with which they were connected, and in which an altered condition of blood relationship was to be found.

Thoma believed that he could follow the development and spread of the connective tissue in the system of arteries, lying between the ductus arteriosus and umbilical vessels, from the fibrous-tissue layer in the intima of these arteries, respectively. He studied a series of

arteries taken from fetal life to the age of twenty-one, and found that the connective tissue developed in the intima of the aorta by the growing downward from the ductus arteriosus and upward from the hypogastric vessels. These two layers advanced along the aorta until they met and formed one continuous tissue. Such a uniform and prominent layer he found in no other system of vessels. This development of connective tissue begins immediately after birth and continues into adolescence. Thoma considered that the thickening of the subendothelial layer of fibrous tissue was compensatory, in nature, and due to lessened blood flow.

His view, today, is quite untenable. We do not doubt that there is a disproportion of the fluid blood to the vessel walls in the arterial system, but we cannot believe that this is entirely confined to one district. Moreover, a disproportion between an elastic system of tubes and its contents is only too readily compensated by the contraction of the walls, to say nothing of secretion or excretion of fluid taking place when necessary to alter the contents quantitatively.

This conception of the natural thickening of the intima, in arteries brought about by reduced blood flow, underlies Thoma's principles on arteriosclerosis. Where, in the infant, an entire system of vessels undergoes intimal thickening normally, in the adult, localized areas in the intimaa take on this change pathologically. In most cases Thoma believed the media was primarily at fault, leading to a slight dilatation. This dilatation immediately gave the essential factors of disproportion, leading to compensatory hypertrophy of the intima.

I have attempted to follow Thoma's studies on arteriosclerosis with the microscope. The changes which he found in the "Nabelblutbahn" as the outcome of the closure of the ductus arteriosus were not evident. It is true that the arteries vary considerably in the amount of connective tissue present in the subendothelial layer, and also in the definiteness of the internal elastic lamina. But this variation is to be noted before birth, and I could never convince myself that in the aorta there were any tissue changes as a result of alteration in the fetal circulation. More particularly the development of the subendothelial layer does not proceed or extend from the fibrous-tissue layer of the ductus arteriosus.

Thoma's localization of the connective tissue in the thoracic aorta below the ductus arteriosus, and in the abdominal aorta, would, according to his dictum, place the frequency of arteriosclerosis in this region away above that in the ascending limb and arch of the aorta. Such a relationship, however, does not exist. One of the commonest sites of change of the intima in the aorta is in the convexity of the arch immediately opposite the origin of the vessels of the neck, and above the entrance of the ductus arteriosus. In this region, the aortic wall is thrown into folds which fibrose and frequently undergo fatty and calcareous degeneration.

There is occasionally a small sclerotic patch at the site of the opening of the ductus arteriosus into the aorta. This plaque represents the remains of the fibrosis which closed off the ductus arteriosus, and is only visible as a pucker in the wall, 2.5 mm. in diameter. I have never been able to trace any spreading fibrosis from this centre, and I do not believe that this plaque plays any role in the production of arteriosclerotic changes, or leads to any weakening of the vessel wall.

The musculo-elastic layer of the intima is a rather uncertain layer as regards the aorta in general. Its presence is fairly uniform at the mouths of the arteries where it spreads over the inner wall of the aorta as a flat disk. The peculiarity, however, exists that the muscle fibers in it are, to a great extent, derived from those in the media of the smaller artery. This layer spreads out for some distance in the deep layer of the intima so that a plaque of tissue exists here, which is not found in other sites. As this layer is common to the insertions of all the larger vessels, no significance can be attached to its presence at the opening of the ductus.

I would, therefore, be unwilling to grant that the closing of the ductus arteriosus throws any light upon the origin of arteriosclerosis that from my observations the obliteration of the ductus arteriosus results as a fibrosis subsequent to a contraction of the vessel walls. This contraction is dependent on two main factors: (1) An exceptionally muscular vessel wall acting on (2) a diminished blood pressure.

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