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SOME POINTS RESPECTING THE LOCALIZATION OF SYPHILIS ON THE AORTA

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Ever since Vesalius first described internal aneurysm, referring particularly to aneurysms of the thorax, numerous observations have been made upon the manner of origin and the seat of aneurysm upon the aorta. For many years statistics have been collected indicating the frequency with which aneurysms are found upon different arteries, in a hope that the anatomical distribution of these lesions would give some clue for their occurrence. Although Pare observed that internal aneurysm was not uncommonly associated with the pox, irrefutable evidence of the importance of this disease for the development of aneurysm was not established until 1875 when Francis Welch, in his study of syphilis occurring in the army, described a specific type of reaction in the aorta resulting from lues. For a time following the observations of Welch little support was given to his statement but during the last few decades the truth of his findings has been confirmed by many authors by different methods of analysis. The earlier studies dealt with the naked-eye appearance of the aorta which, when it was involved in syphilitic disease, showed characters quite distinctive and different from those seen in arteriosclerosis. Then, too, the microscope assisted in defining a type of lesion peculiar to syphilis and distinguishable from other diseases of the arteries. True gummata were also occasionally found, leaving no doubt as to the nature of the process acting upon the arterial wall and eventually bringing about such weakening as to permit of aneurysm. The final demon-

stration of the spirochete in a variety of arterial affections removed all question concerning the localization of the virus of syphilis in the tissues of the aorta and other vessels.

At first sight it would appear that the problem of syphilis and the arteries has been completely unfolded in the progressive steps illustrated in the many studies since the days of Pare. Most of the work has been developed in logical sequence from the early and rather gross observations to the minutiæ of histology and bacteriology. We recognize fully the clinical importance of syphilis as a systemic disease and have many means for the diagnosis of its presence and for the discovery of its relatively early localization upon the arteries. We are, furthermore, aware that the localization of syphilis upon the vessels occurs with greater frequency in certain arteries, the aorta and cerebral vessels, than in others, as well as that the infection occurs in certain regions of these arteries with greater frequency than elsewhere. The predilection of the syphilitic virus for localizing in distinct districts in the aorta has always received much comment. It is true not only that aneurysm of syphilitic origin locates most commonly on the first part of the aorta but also that syphilitic aortitis in the earliest stages of its development is seen with equal frequency on this portion of the vessel. The mechanical theory of aneurysm which placed greater stress for the production of aneurysm upon the effect of high blood-pressure or, as others would have it, upon the effect of the velocity of currents, than upon the disease in the wall of the artery, had for a time enticed our attention into channels of thought and theory no longer tenable with the newer studies. Granted, of course, that two factors must be available for the development of aneurysm, first the weakening of the vessel wall and second the presence of a blood-pressure (normal, subnormal or excessive), we must not lose sight of the fact that for the development of true aneurysm, the presence of a localized weakening of the artery is of first importance. It is only a weakened vessel which can develop aneurysm; hence, appreciating that the spirochete of syphilis is the most common damaging agent of the aortic wall, the important point occupying our attention is, why should it localize with such great frequency in isolated segments of the aorta? There is nothing in the character of the tissue of the

aorta which could lead us to believe that the chemical characters of particular portions offer a better nidus for the infection, nor is there anything in respect to the microörganism whereby preference would be shown in localizing in one or other portion of the vessel.

The common localization of syphilitic arteritis upon the ascending aorta with the transverse and descending thoracic aorta following next in frequency is now well known. The aortitis beginning in the first portion of the aorta usually localizes at a point just above the aortic ring and then spreads with considerable rapidity along the arch of the aorta for variable distances. The lesion also makes its way in the opposite direction, so that the tissues at the aortic orifice, particularly the valve leaflets, become more or less involved. The spread toward the heart, however, progresses more slowly and we have several examples where, although there was clinical evidence of incompetency of the aortic valve, this was due not to disease upon the aortic valves but to a stretching of the aortic ring. In these instances the syphilitic disease of the aorta stopped fairly abruptly at the upper margin of the sinuses of Valsalva and did not produce any lesion in the aortic tissues contained within the heart. An interesting feature of the syphilitic process of the aorta is the sharp line of demarcation which separates the diseased area from the healthy. This boundary marks the advancing border of the syphilitic process extending to occupy new tissue. The involved aortic wall with its marked thickening, corrugation and scarring is also in sharp contrast to the aorta in other portions. This contrast is decided whether the non-syphilitic areas show scleroses of other kinds or not. The syphilitic process does not come to occupy any particular face in the circumference of the aorta and thus does not show a characteristic distribution like the nodular endarteritis which is so commonly observed in the vicinity of the mouths of the intercostals and at the entrance of the ductus arteriosus. The syphilitic process almost always surrounds the lumen, though, as we have pointed out before, the intensity of the involvement at particular points differs in the individual cases.

Another peculiar feature of syphilis of the aorta is the infrequency with which two foci develop concurrently upon separate portions of the aorta. Occasionally, a dual localization is found to

have occurred, one in the thoracic portion and the other in the abdominal. Less frequently two separate foci occur within the thorax itself; and for the moment I do not recollect ever having seen such a condition recorded. At first sight it might suggest itself that, because aneurysm is sometimes encountered with multiple sacs, one, it may be, situated upon the ascending aorta, a second upon the transverse, and a third upon the descending thoracic, we are dealing in such an instance with separate localizations of the syphilitic virus. Careful examination of these specimens demonstrates that the syphilitic process is diffusely disseminated over the entire thoracic aorta and that the aneurysms have individually developed at situations where local damage has advanced more than in the remaining portions of the arterial wall. That individual and isolated infection may occur in different portions of the aorta is not to be denied, but where this takes place within the thorax, the lesions in their early stages progress with such rapidity that they fuse at their borders and can no longer be distinguished as separate occurrences. The occasional double localization upon the aorta is seen where a specific infection has involved the first portion of the thoracic aorta while a second attack has occurred in the abdominal aorta, usually in the vicinity of the celiac axis. Under such circumstances a portion of aorta free from luetic change intervenes between the two foci. It is possible that a relationship between the two lesions may exist but up to the present it has not been demonstrated. Broadly speaking, however, the syphilitic attack upon the arterial wall differs very materially in its distribution from that of ordinary arteriosclerosis and endarteritis. The syphilitic lesion may occur simply as a patch of greater or less extent, the progress of which is dependent upon the lateral spread from that patch as well as upon the intensity with which the arterial wall is affected by the disease. On the other hand, the more common arteriosclerotic affections are not so constant as to the particular portion of the aorta in which they locate and for them it is the rule to appear at multiple sites with lesions which are quite distinct and unrelated.

Our attention has been attracted, both from postmortem studies and experiment, to the part played by the lymphatics in disseminat-

ing syphilitic and other infections along the course of various arteries. We have found that the lymphatic channels of the outer wall of the aorta form a fairly intricate system which communicates with neighboring lymph glands. This system of channels may be demonstrated by injection experiments whereby the interlacing communications stand out quite prominently. From these injection experiments it would appear that the most profuse system of channels is found in those positions of the aortic wall which lie in closest relation to the neighboring lymph glands, while as a greater distance is interposed between the lymph gland and the area provided a smaller number of lymphatic vessels is to be demonstrated. This is particularly evident in the descending thoracic aorta where a portion of the aortic wall is free and unattached, whereas its posterior and lateral portion lying close to the vertebral column is in close proximity to the lymph glands of this region.

If we follow the aorta from its beginning we find that its first portion lying within the pericardial sac appears to have lymphatic channels in common with the pericardium as it is reflected over it. Macroscopic lymph glands have not been demonstrated between the pericardium and the aortic wall. Directly over the pericardial sac where it is reflected from the aorta to become the parietal pericardium, and lying along the left lateral border of the ascending aorta, are a group of lymph glands which communicate with other glands in the anterior mediastinum and which, furthermore, supply this portion of the aorta. In this region the anterior and left border of the aorta appears to have a richer supply of lymphatic vessels than the right border. About the arch of the aorta there are a number of lymphatic groups, each of which has abundant communication with the aortic wall. The ascending arch has lymphatic connections particularly with glands in the anterior mediastinum, while the transverse arch has a drainage both to the mediastinal glands and to those about the right border of the trachea. The descending arch receives lymphatics from the glands along the left border of the trachea as well as from the glands at its bifurcation. As we pass to the descending thoracic aorta we find a variable number of lymph nodes lying along the border of the aorta and particularly on the right side. The lymph channels from these

nodes form a plexus about the exit of the intercostal arteries and advance in single lines around the anterior and free portion of the aortic wall. In the abdominal aorta an intricate plexus of lymph channels is found in the region of the celiac axis which supplies fairly uniformly the aorta in its entire circumference. In the lower portion the aorta receives a rich supply of lymphatics from the retroperitoneal lymph glands which lie along each border of the aorta. These lymphatic channels of the aortic wall lie for the most part in the adventitia, in close relation to and following the course of the fine nutrient vessels which are found in this structure. As the denser portion of the aortic wall is approached the lymphatic vessels become fewer in number and extend only as very fine structures into the adventitia as it adjoins the media. The one feature that is striking is that the lymphatic supply of the aortic wall is not uniformly disposed. In certain portions a much richer supply of lymph vessels can be demonstrated. These ramify in an arborescent or stellate manner, leaving other portions of the aortic wall with a more meager distribution.

To determine the part played by the lymphatics in conveying infection about the arterial walls, bacteria were inoculated into the loose tissue of the mediastinum of rabbits. The organisms used were varieties of streptococci, chiefly of the viridans group. In these experiments it was found that the microörganisms after setting up a localized reaction at the point of inoculation migrated in various directions, most rapidly along the flow of the lymph to the neighboring glands. Gradually, however, the dissemination was of a retrograde character, whereby the microörganisms followed the lymphatics into the various tissues in the vicinity. Thus, the infection was found to follow the fine channels passing about the aorta as well as the structures at the hilus of the lungs. In the rabbit, however, the lymphatics are not nearly so numerous about the aorta as they are in man. The small-sized aorta in these animals is poorly supplied by vasa vasorum which penetrate to the media, but the adventitial vessels are well marked. Yet the results of the experiments were sufficiently clear to indicate a distribution of the infection by way of the lymphatics to the large vascular trunks of the thorax.

A similar but clearer evidence of the lymphatic distribution of infection was obtained in man. It was found that in the severe cases of pneumonia coming to autopsy, an almost constant infection of the glands of the anterior mediastinum was to be noted. Under these conditions the lymphatics stand out prominently, the glands are swollen and succulent, and great chains of them can be traced along the trachea and its bifurcation, as well as below the arch of the aorta. The tissues are usually loose and edematous, and if the autopsy has been held shortly after death, the subject is a favorable one for demonstrating by the injection method the course of the lymphatics. But more than this, the infecting agent, the pneumococcus, may be isolated from the tissues along the course of the lymphatics and even up to and in the tissues of the outer portion of the aortic wall. Such infections in the aortic wall have previously been demonstrated by Andrewes, and are in accord with our own previous studies in which inflammatory reactions have been observed to follow the course of the nutrient vessels in typhoid fever, acute rheumatic fever, pneumonia and sepsis. In other words, those inflammatory reactions which we have described as types of acute non-suppurative mesarteritis are the result of infection by various bacteria localizing upon the aortic wall by way of the lymphatics.

Further examples illustrating the progress of a bacterial virus along the periarterial lymphatics, are readily at hand. The importance of these perivascular channels is also illustrated in the spread of the infection in periarteritis nodosa where it may be shown that the involvement of an artery results from the passage of the infection along the lymphatics to the ramifications of that particular artery. We were able to observe this in two cases in which the hepatic artery with its branches was the seat of an acute progressive inflammatory lesion. In a like manner, one can readily follow the perivascular migration of infection in the arteries of the meninges. Here it will be found that the infecting agent and the inflammatory exudate progress along the course of the meningeal arteries as they lie embedded in tissue and that this reaction in the lymph spaces precedes the appearance of the exudate in the larger spaces or caverns of the meningeal folds. Likewise and of better illustration is the similar reaction which follows the course of the nutrient vessels

passing from the meninges into the brain substance. Similarly the importance of the lymphatic channels, particularly of those surrounding the nutrient vessels of tissues, may be cited in reference to the myocardium and kidney. These are of course common observations, but for the most part we have not been recognizing their importance from the view-point of the further dissemination of the virus nor from the stand-point that when the infectious agent is in such close proximity to arteries of various sizes, actual infection of the arterial wall is liable to occur.

If we again revert to our problem respecting the localization of infection in the aortic wall, we must emphasize these three anatomical conditions: (1) as we have pointed out that there are certain regions along the course of the aorta in which the arrangement of the lymphatic channels is more complex and their number far greater than in other portions; (2) that the aortic wall itself is richly supplied with nutrient vessels, the vasa vasorum, each of which has a liberal lymphatic drainage following its course; and (3) that these lymphatics are in direct association with the larger lymphatic system which surrounds the aorta as a whole and which has two large drainage beds, one in the thorax and one in the abdomen. It is in relation to these drainage beds that the syphilitic virus comes to be distributed to particular segments of the aorta.

The route followed by an infection and the advance of the reaction from one tissue to another can be followed much more readily when the invasion is due to bacteria causing acute responses, than when the reactions are more chronic and come under observation only in the later stages of the lesions. This is particularly true in the case of syphilis, in which we rarely recognize the earliest metastatic lesions. Syphilis of the aorta has rarely been observed at a time before the typical changes of the inner or intimal surface are quite distinct. Under these conditions we must appreciate that the syphilitic process of the vessel wall is quite late and advanced, while many of the reactions involving different structures in the infection have been obliterated by the secondary fibrosis. Nevertheless, with some care the track of the reactions may still be followed both within the vessel wall and in the surrounding tissue. In a few cases we attempted to follow the relation of the inflamma-

tory process as it made its way along the vasa vasorum from the periarterial structures to the vessel wall proper. Under these conditions it was not difficult to demonstrate a chronic mediastinitis which, though of very irregular distribution, nevertheless had a distinct course along lymphatic channels to and from the mediastinal lymph glands. These inflammatory processes appeared mild in degree and would not have attracted attention save that in following the channels more closely it was found that periodic exacerbations occurred along their tracks A varying amount of fibrosis was the outcome of the reaction. Where the more aggravated response led to local cellular infiltration occasional true gummata appeared. It was, however, quite unusual to find marked gummatous destruction of the mediastinal tissues; in fact we have observed this in only one instance. The lymph glands themselves may respond in the earlier stages of the disease by hyperplasia but we have found it unusual for these glands to enlarge to such a degree that they would clinically or even pathologically attract attention. During the subsequent process of the syphilitic infection the diffuse fibrosis that is observed in the mediastinum also occupies in some degree the lymph nodes.

By thus localizing in the mediastinum, the syphilitic virus has an opportunity of attacking to greater or less degree the important visceral contents of this division of the thorax. The most accessible and important structure is the aorta. The heart itself is peculiarly isolated so that, although it has an extensive lymphatic drainage, it has no dominant compensatory lymphatics advancing upon it from the parietal pericardium. The only region in which accessory lymphatics become available is at the base where the parietal pericardium is reflected directly upon the great vessels. The trachea and large bronchi, which lie in close relation to the lymphatic system of the mediastinum, show a considerable immunity to the localization of the syphilitic virus. The ascending limb and arch of the aorta, on the other hand, are themselves surrounded by a network of lymphatic and bloodvessels and present a vulnerable tissue for the spirochete. Thus with the localization of the syphilitic virus in the rich lymphatic bed of the thorax, it becomes almost certain that the infection will also involve the tissues of the aorta.

The close relation between the luetic inflammatory processes of the mediastinum and those of the aortic wall is also shown in the late fibroses which lead to such unusual thickening of the arterial coat and which, furthermore, bind the aorta firmly in its mediastinal bed. The thickening of the aortic wall, when involved in syphilis, is the result of a connective-tissue overgrowth in part situated in the intima and media but for the most part lying in the adventitia and binding this structure to the neighboring periarterial tissues. Syphilitic aortitis has always an associated syphilitic periarteritis. As previously stated, we do not often have the opportunity of tracing the early inflammatory responses which communicate between the mediastinum and the aortic wall, but there is always the evidence in the late cases of reparative fibrosis which distorts the vascular structures. Of course in the presence of aneurysm, one must be guarded in distinguishing the fibrosis which has resulted from the syphilitic virus from that which has resulted secondarily to the presence of aneurysm from mechanical irritation.

Though we feel confident of the important part played by the lymphatic system of the thorax in localizing syphilis to distinct portions of the arterial wall, it is not clear as yet why and in what manner the virus finds its way to this particular region of the body. By analogy and in comparison with certain other infections, it is probable that the systemic distribution of the spirochete is accomplished by the blood stream. As with other infections, certain tissues and structures are more receptive for the metastatic infection than others. In some instances the localization of the infection may be associated with trauma, but this can hardly be a factor within the chest. Up to the present time animal experimentation has given no clue suggesting the reason for the thoracic metastasis in man. It is probable that the selection of the mediastinum by this infection is bound up with the question of the biological properties of the microörganism and the favorable conditions presented by particular tissues for its growth.