ARTERIAL LESIONS ASSOCIATED WITH RHEUMATIC FEVER.

By OSKAR KLOTZ.

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By Oskar Klotz.

From the Pathological Laboratories, University of Pittsburgh, Pittsburgh, Pa.

(Plates XXIII.–XXIV.)

As our attention has been more and more centred upon the etiological factors associated with arterial diseases, we have had a better opportunity of studying each type in turn and of observing the various grades of intensity in which the particular process may occur. It is only by studying each process accurately that its importance in relation to the general subject of arterio-sclerosis can be determined. A number of such specific processes have received adequate attention, so that to-day we are familiar with at least the main points concerning them. Syphilis of the arteries has been well studied, and the effects of overstrain upon the arterial wall is well known in connection with particular systems. Moreover, we are familiar with the effect of occasional bacterial invasions upon the vessel wall, but the different results that may be induced by the same organism distributed in various parts of the body are not well determined.

Repeated suggestions of the harmful effect of certain bacteria upon the arterial wall have been made by clinicians, and these have, to a certain extent, been verified in animal experimentation.

The clinical evidence of arterial changes, though, in itself, indicative of pathological processes, gives no clue as to the actual lesion that has occurred in the artery. Furthermore, the mode of invasion, as well as the progress of the disease in the tissues of the artery, cannot be followed by the clinical evidence alone. On the other hand, it is difficult to correlate the pathological findings of arterial disease, with the actual factor causing it, if the pathological examination is not accompanied by a study of the disease in life, as well as a study of the agents which have been active in its production.

The association of rheumatism with diseases of the vascular system has been emphasised mainly by French authors. Rheumatic phlebitis, although rare, has been discussed in the works of Bouillaud (1840 [27]),

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Trousseau (1828 [28]), Legroux (1884 [29]), Lemaire (1864 [30]), Boinet (1899 [3]), Vaquez (1905 [26]), Achard (1900 [31]), and others, while inflammatory conditions of the arteries associated with rheumatism have been observed and reported upon by Leger (1877 [16]), Hanot (1896 [12]), Besson (1900 [2]), and others. Of these reports, however, only two (Leger and Hanot) have been amplified by autopsy.

Some have been insistent that a definite disease with clinical symptoms occurred in the aorta of patients suffering from acute rheumatism. Although they were agreed that the process was of an inflammatory nature, there was some discussion concerning the process by which the inflammation reached the vessel wall. Some claimed that the infection proceeded continuously from the affected aortic valves along the surface of the aorta. Others, however, indicated that such a process was not the common one, in that the abdominal aorta was not infrequently involved, and never showed a continuous intimal infection.

There has been considerable doubt as to the presence of inflammation of the peripheral arteries in which the *materies morbi* of rheumatism was the etiological factor. Some of this doubt has arisen because the majority of observations have been made clinically, and it has been contended that by this means alone it is impossible to differentiate the inflammatory condition from embolism and other processes. Quenille (1906 [22]) reports upon rheumatic arteritis, and indicates that others, Lemaire (1864 [18]), Fernet (1865 [7]), Lécorché (1869 [15]), and Lemoine (1869 [19]), have made similar observations. These reports, however, mainly clinical, deal with the acute stage of the process when the individual offers symptoms pointing to lesions of the arteries. On the other hand, Géneau de Mussy (1892 [11]) believes that many of the thickenings encountered in the arteries in later life are the result of rheumatic conditions following upon one or more acute attacks accompanied by fever. He reports the case of a young man, æt. 23, who for a month had articular rheumatism with endo- and pericarditis, and later developed thickening of the peripheral arteries.

Rheumatic arteritis appears in two clinical forms. On the one hand, it is a simple inflammation surrounding the artery and accompanied by localised pain and throbbing along its course. On the other hand, an inflammatory process begins from within, and an obliterating arteritis, which is also accompanied by localised pain, gives evidence of permanent obstruction of the vessel. These types differ, in that the former shows the inflammatory condition to be in the media and the outer coat, while the latter is a condition of primary endarteritis, associated with thrombosis or embolism.

Foajole (1866 [8]) reported this condition in a young girl, æt. 15, who in the course of acute articular rheumatism with endocarditis experienced a violent pain in the side of the neck. The author observed the increased volume of the right carotid as well as a gradual hardening of its walls. After a few days the pain disappeared, but returned after a fortnight. Besson reported the case of a man, æt. 23, who two years previously had an attack of acute articular rheumatism with heart disease. The patient indicated the region of the left subclavian where a definite throbbing, synchronous with the heart beat, could be observed. Later the condition resembled an aneurysm of the axillary artery.

Conti (1905 [5]) reported a similar case in a young man, æt. 17. He showed symptoms of thoracic and abdominal aortitis, as well as an arteritis of the left carotid. Barié ([2]) reported the case of a man, æt. 20, who during the course of a rather mild acute articular rheumatism developed a progressive pain in the right arm, which, at the same time, became swollen, heavy and throbbing. The vessel of the arm was thickened and on pressure caused pain. Gradually the right pulse became less, but under salicylates the condition improved.

In many instances it is difficult to rule out the diagnosis of embolism. Legroux (1884 [17]) reports the case of a girl, who at the age of 12 had her first attack of acute rheumatic fever. During convalescence she suddenly experienced a numbness in the left arm and forearm with a complete loss of function of this member. The pulse could not be felt. He concluded that an embolus had occluded the left brachial artery, which was very painful. In this case the acute rheumatic fever seems to have initiated the processes in the heart, which was followed by the occlusion of the left axillary artery by an infected embolus, giving rise to a localised arteritis and ending in aneurysm.

Roche and Burnand (1908 [24]) report the case of a man, æt. 30, who had long suffered from rheumatism. His first attack had occurred seventeen years previously, and since then he had suffered recurrent attacks, in each of which the heart was more or less involved. Recently, his heart failed to compensate for the severe lesions of the mitral and aortic valves. When seen by the authors, he was cyanosed and showed œdema of the lower extremities. He had continuous fever of moderate degree. After some weeks his temperature suddenly went up, and he complained of pain in the left arm, which continued to increase. In three days the radial pulse disappeared. Gradually a very small radial pulse was again obtained. After some weeks a mass appeared close to the upper humerus which was quite painful to the touch. Some time later the right arm became involved so that the radial pulse disappeared.

These authors believed that the clinical cases of rheumatic arteritis must be classified by analogy, comparing the clinical manifestations with the findings reported at autopsy. Leger and Hanot have described rheumatic aortitis, while Rabé ([23]) has studied rheumatic disease in the coronary artery. The latter described two principal lesions, one consisting of a proliferating endarteritis, the other of a diffuse mesarteritis. It is probable that the other peripheral arteries react in a manner similar to but milder than that in the coronary arteries.

The importance of the relation of such medial disease to aneurysm is also evident, and it must be recognised that the mesarteritis occurring in rheumatism may, at times, be so severe that various forms of ectases and sacculations may occur. In fact, in the reports of Feytaud (1906 [9]) we have evidence that an aneurysm developed in the aorta in consequence of a rheumatic infection. It would appear that aneurysms of the peripheral vessels are less frequent. Nevertheless, such have also been reported by Legroux (1884 [17]), Roger and Gouget (1907 [25]), as well as by Schmey (1905 [33]). Similarly Routier (1905 [34]) reported a case of acute aneurysm of the posterior tibial artery developing in the course of rheumatism.

The close relationship of peri-arteritis nodosa, with its aneurysms, and acute rheumatic fever, has also been suggested. It would appear that a fair number of these cases are associated with attacks of acute rheumatic fever. Thus, in general, one must consider acute rheumatic fever as a factor in the production of arterio-sclerosis, as well as of aneurysm.

In German and English literature less importance has been laid upon the association of acute rheumatic fever with arterial disease. Nevertheless, if we carefully study the reports of acute mycotic aneurysms such as have been described by Osler (1909 [22]), Eppinger (1887 [6]), McCrae (1905 [21]), and others, we find that not a few are the sequel of rheumatism, particularly where the disease had endocardial manifestations. The importance of acute vegetative valvular disease, affecting the mitral or the aortic cusps, in relation to an arterial involvement is particularly interesting.

Clinically this relation of rheumatism to heart lesions and the arteries has been studied by Feytaud (1906 [9]). He had the opportunity of studying five cases, but had no opportunity of making an autopsy on either of the two fatal cases. These cases described by Feytaud were clinically demonstrated to have developed aneurysms, and the very interesting feature concerning them is that the aneurysm in each case developed in the first part of the aorta. All of his cases occurred in children varying in age from 12 to 16 years. In one of them the aneurysm had ruptured.

There is, therefore, considerable evidence forthcoming indicating that acute rheumatic fever has a direct relation to arterial diseases.

On a previous occasion (1912 [13]) we have pointed out how commonly the effect of acute rheumatism is to be observed in the arterial tree. In this communication it was shown that the results of acute rheumatic fever may be distinguished in the arterial wall during the primary acute attack, the recurrent acute attack, as well as in the chronic stage of the disease. It was also indicated that each of these stages could be recognised with fair accuracy by the character of the inflammatory reaction present in the arterial wall. Thus we might say that the arterial lesion simulates in many respects the inflammatory manifestations present in the myocardium. We were impressed with the fact that certain portions of the arterial system are as frequently attacked in rheumatism as in the musculature of the heart.

In our first report we presented the results of three cases of acute rheumatic fever (first attack), four cases of recurrent rheumatic fever, and eight cases of chronic rheumatism. Since this report, we have further followed the pathological lesions occurring in new cases of rheumatic fever, particularly observing the character of the lesions in those dying during the first attack of this disease. Our findings in these latter cases is similar to that previously reported. We have found, however, that the type of inflammatory exudate is not as constant in character as was originally observed.

The lesion is essentially an inflammatory one which is present in the adventitia and media of the arteries. The intima is not disturbed, save as a late secondary reaction over the inflamed media. The inflammatory exudate is mainly distributed about the vasa vasorum of

the adventitia and follows the fine nutrient vessels lying in the outer portion of the media. This reaction is accompanied by a destruction of the neighbouring muscle cells and elastic fibres. The extent of this destruction is dependent upon the intensity of the reaction (Plate XXIV. Figs. 3 and 4).

This very feature, the intensity of the reaction, we have found to vary quite widely, and thus too, as we have indicated above, does the character of the inflammatory exudate differ. In our early cases where the reaction was moderate the exudate consisted mainly of lymphocytes and plasma cells. Latterly, we have found, and particularly in association with a case presenting an aneurysm, that polymorpho-nuclear leucocytes may also be present in large numbers in reaction. The presence of fibrin in the uncomplicated lesions we have not observed.

Another point upon which we must lay some stress has repeatedly presented itself in our studies. This is, that the point of predilection in acute arteritis, associated with acute rheumatic fever, is the ascending limb of the aorta. Though we have observed inflammatory reactions in other portions of the aorta and a few instances about some of its branches, these results were inconstant.

We have previously suggested the similarity of these lesions to those found in the early stages of syphilitic aortitis, and the obvious suggestion that these diseases might run a fairly similar course presented itself. One very decided difference, however, must be recognised between the syphilitic disease of the aorta and that of rheumatic origin. In the former, the process about the vasa vasorum when once begun is progressive, so that the media becomes more and more involved in its neighbouring parts. It would appear that in syphilis the disease rarely comes to a standstill, at least in as far as the recognised and studied cases indicate. It may be that with the newer treatments this view must be modified. In rheumatic disease of the aorta the process usually comes to an end spontaneously, but always predisposes the involved areas to recurrent attacks.

Recently Fukushi (1913 [10]) has described what he believes to be a characteristic lesion for syphilis in the aorta. Not only does the inflammatory reaction occur mainly in the adventitia and the media, but the cells of the exudate consist mainly of plasma cells and lymphocytes. This author has been so impressed by the abundance of plasma cells in the syphilitic lesions of the aorta that he believes their presence is indicative of the specific nature of the infection. Although the actual number of plasma cells has not drawn our particular attention, we have always observed their presence in the arterial lesions associated with acute rheumatism, and we are not inclined to believe that these cells serve the diagnostic purposes suggested by Fukushi.

The fibroses which are present in the adventitia as well as the

media of the aorta in elderly individuals are not uncommonly the late effects of acute rheumatic fever, and if we compare the findings of Koester (1875 [14]) and his pupils in arteriosclerosis with these observations, one is struck with the similarity of the processes described. Koester paid little attention to the etiological factor which induced the inflammatory reaction of the media which he viewed as being so important in subsequently leading to intimal thickening. We believe with Koester that, in as far as the inflammatory processes of the media associated with rheumatism are concerned, the intimal thickening is secondary.

Although it is the tendency for the inflammatory lesions of acute rheumatic fever to heal in a process of fibrosis, yet in a number of cases the arterial lesion is distinctly progressive, the destructive changes being so rapid that repair is impossible. In these instances the process developing in the outer portion of the artery continues to bring about destruction of the fixed local tissues until the strength of the vessel wall is greatly impaired. In these instances the inflammatory reaction spreads from its primary location about the vasa vasorum until several of the involved areas coalesce. The degree of inflammation being more acute, causes a more rapid melting down of the tissues. Aneurysm with or without rupture is the end result.

Such a case beginning in acute rheumatic fever with cardiac involvement and ending in a saccular aneurysm of the ascending aorta has come to our notice. We have given rather extended notes upon this case in order that we may offer convincing proof of the intimate relation of acute rheumatic fever to severe arterial disease.

We are much indebted to Dr. O. M. Edwards for the clinical history of this case.

Clinical History:—The patient was a boy, æt. 6 years, who had been quite robust, although he had had measles, chicken-pox, and whooping-cough. Six and a half months ago (September 1911) he became ill with symptoms simulating typhoid. His temperature, varying from normal to 104° F., continued, along with some indefinite muscular pains, and pains in the joints. Early in December he had some severe pains in the region of the heart and his joints, the elbows being particularly painful.

When admitted to the hospital on 1st March 1912, the child was suffering from severe precordial distress, pains in the joints, and choreiform attacks. The child was so restless that to examine him was very difficult. The heart was enlarged, the right border extending 1½ inches to the right of the sternum. At the apex both heart sounds were distinct, but over the pulmonary area a systolic murmur obscured both sounds. Over the aortic cartilage a loud systolic murmur was heard, but the second sound was not distinguished. Pulse, 140; hæmoglobin, 45 per cent.; leucocytes, 18,000. The urine contained albumin and granular casts.

For the next few days the child was very fretful and complained of severe pains in the joints and about the heart. The systolic murmur of the heart could be followed from the aortic cartilage along the great vessels of the neck. A blood culture showed a pure growth of a streptococcus growing in short chains. This organism was not studied on differential media.

Four days after admission the child died.

Autopsy.—At autopsy the chief findings were associated with the circulatory system. No important changes were found in the other organs, save the presence of infarcts in the spleen, and both kidneys. These infarcts were recent as well as old, in the latter some fibrosis was evident.

The heart was relatively large. The muscular walls were fairly firm. The left heart occupied much the greater part of the whole organ, and the apex consisted of the tip of the left ventricle. The apex was somewhat rounded; in fact, the whole was globular. The pericardial surface was for the most part quite smooth, but at the base, and particularly over the auricles and around the great vessels, there was a fine granular exudate of fairly recent lymph. At the base of the organ a portion of the pericardial sac was found adherent to the first part of the aorta. On the external surface the vessels of the heart appeared normal.

The right heart appeared quite healthy. There was but little blood within its chambers, and the tricuspid and pulmonary valves were without change. The musculature of the right auricle was rather pale but not thickened.

The left heart appeared out of proportion in size with the right side. The auricle was not enlarged, although the endocardial lining of its cavity appeared white and thickened. The left ventricle was large. The musculature was thick, and measured from 1 to 1·75 cm. The cavity itself was also large. The musculature of the left ventricle was pale and rather streaked. Some of these streaks showed fine lines of congestion or hæmorrhage. The mitral valve was of usual size. The cusps were a little œdematous along the free edge and both showed some granular vegetations. The mural cusp showed evidence of previous inflammatory processes in the presence of some erosion and fibrous thickening. The recent vegetations consisted of granular fibrinous deposit which could easily be removed.

The aortic ring showed extensive change. The normal architecture of the valve was entirely lost. Of the valve leaflets, only one could be distinguished. The area previously occupied by the other two cusps was filled in by massive fibrinous deposit, which distorted the aortic opening and almost occluded it. The deposit of this inflammatory exudate was accompanied by erosion of the surrounding tissue, including some of the mural endocardium just below the aortic ring at the base of the mitral valve. The exudate was confined to a strip of tissue about half a centimetre in width directly over the aortic valves. The openings of the coronary arteries were to a certain extent encroached upon by the vegetations on the valves. Immediately above the sinuses of Valsalva there was a portion of the base of the aorta which was quite free from acute disease.

The aorta presented a most remarkable condition. In the ascending limb, and situated upon the posterior surface but projecting slightly to the right, was a bulging mass the size of a pigeon's egg, measuring 2·5 × 2 × 1·5 cm. (Plate XXIII. Fig. 1). When viewed from without, this mass was found to lie within the pericardium, but to it the parietal pericardium was found to be adherent. The mass projected as a mushroom-shaped tumour, and was quite injected on its outer surface, so that its boundaries were easily distinguished. Immediately beyond the point of attachment of this mass to the aorta the tissues were quite pale. When viewed from within, it was seen that the projecting mass was due to a circumscribed bulging outwards of the aortic wall. The aorta was involved in this dilatation by about two-thirds of its circumference. The transverse portion of the arch of the aorta was not involved. The saccular dilation began suddenly on all sides, and its cavity contained a considerable amount of fibrin deposit, which had a rough and nodular appearance. At the lower margin of the saccular dilatation the intima of the vessel showed some pearly thickening. The remaining part of the aorta and the large systematic vessels appeared to be quite free from macroscopic change.

Bacteriology.—At the autopsy a culture was taken from the blood and the

spleen, and in each instance a streptococcus growing in short chains was isolated. The individual organisms commonly arranged themselves in pairs.

Heart.—Sections were made from the various parts of the heart muscle. It was found that irregularly distributed through the musculature and more particularly through the walls of the left ventricle there were aggregations of inflammatory exudate consisting of polynuclear leucocytes, lymphocytes, and plasma cells. These inflammatory infiltrations were most evident in the regions of the small nutrient vessels of the heart muscle. In the vicinity of these reactions the heart muscle showed evidence of degeneration, and at times considerable areas of heart muscle consisted of indefinite wavy fibrils which had lost their staining qualities. In places these areas of degeneration showed some replacement by connective tissues. Fragmentation of the nuclei of the muscle cells was commonly observed in the areas where degeneration was progressing. In the vicinity of the areas of degeneration the muscle nuclei yet remaining appeared much larger than elsewhere.

Aorta.—Sections of the ascending branch of the aorta taken a short distance from the aneurysm showed a healthy character to the intima as well as in the media (Plate XXIV. Fig. 2). There was, however, observed in the tissues of the media an occasional inflammatory infiltration around the vasa vasorum of the outer third of the vessel. This exudate consisted mainly of lymphocytes. In the vicinity of this infiltration some disturbance of the muscular and elastic tissue elements of the media was observed. The adventitia of the ascending limb of the aorta showed quite an extensive inflammatory infiltration around the vasa vasorum of all sizes. In some places this infiltration was composed for the most part of leucocytes, in other places lymphocytes and plasma cells were predominant. Although the infiltrations were quite extensive, no destruction of tissue was observed in the adventitia. There was no evidence of anything simulating abscess formation. In some of the small vessels of the adventitia proliferative changes could be seen in the intima. Occasionally a few fibrin threads were present in the vicinity of the inflammatory reactions.

Sections obtained in closer proximity to the aneurysm of the aorta showed characters similar to the above, but of greater intensity. The infiltration about the vasa vasorum in the adventitia was more marked, and the inflammatory reaction extended more deeply into the aortic wall along the paths of the nutrient vessels. A greater number of leucocytes were present in the exudate in the media, and about these reactions the vessel suffered severely. The muscular elements were destroyed and their place was taken by a granular débris. The elastic tissue elements were swollen and distorted, so that they no longer retained their parallel arrangement. The inflammatory exudate led to the production of wide spaces between the altered elastic fibres. The greater amount of change was in the outer third of the aorta, but inflammatory products were also present in the inner part of the walls. Close to the aneurysm the entire wall of the aorta was seen to be infiltrated with polynuclear leucocytes. The leucocytes followed the spaces between the elastic laminæ and gradually displaced the muscle elements. In places the elastic fibres were also destroyed so that only fragments of them remained. At the mouth of the aneurysm it was seen that the intima and the greater part of the media had been destroyed and these coats came to a sudden end. The outer portion of the media was everted and dragged along with the adventitia, which formed the saccular pocket of the aneurysm. The wall of the aneurysm was formed by the adventitia with a narrow margin of the media, and was reinforced on the outside by the adherent portion of the pericardium. The sac of the aneurysm contained an adherent fibrinous clot in which numerous leucocytes were found. The greater number of leucocytes were found upon the surface of the adherent blood masses within the aneurysm.

Here and there along the wall there was some attempt at organisation of

the inflammatory exudate. There was no evidence of abscess formation in any part of the tissue. On the surface of the intima, close to the aneurysm, there was some adherent blood-clot. The intima appeared slightly œdematous and thickened beneath this attached clot.

Bacteria were demonstrated in the tissues showing the acute inflammatory reaction. These were of the nature of Gram-positive cocci, appearing singly, sometimes in pairs, and rarely in short chains.

The above case is clearly one of an acute saccular aneurysm, occurring at an unusually early age (6 years). The clinical course of this disease was that of acute rheumatism in which the heart had suffered severe valvular disease. The inflammatory process in the aorta simulated in every respect the lesions as we had described them for acute rheumatic fever in a previous article. In this case, however, the destructive feature and the acuteness of the process in the arterial wall was much greater than any we had previously observed.

The development of aneurysm in acute rheumatic fever simulates the process in syphilis in as far as the inflammatory invasion begins in the adventitia and the vasa vasorum of the media. Syphilis was not to be thought of in this case, in that the arterial process was too rapid in its development. The inflammatory exudate was, in part, of a polymorpho-nuclear character, and there was no evidence of fibrosis in the vicinity of the damaged areas in the artery. Moreover, the secondary intimal reaction with its nodular thickenings as it occurs in syphilis was not present, and a type of streptococcus was demonstrated in the affected tissues.

When it is appreciated that acute rheumatic fever attacks the arterial system as an inflammatory process of varying degree, one may readily understand the finding of arterial damage of all grades of intensity. It is probably more common to meet with the more simple inflammatory processes than the more intense ones, which act so severely upon the artery as actually to weaken its walls. Nevertheless, it is more than probable that the subsequent fibrosis plays some part in bringing about the progressive changes in later life.

The repeated observation that systematic bacterial invasion is prone to attack the ascending limb of the aorta still remains without adequate explanation. It has repeatedly been impressed upon us that when the bacteria themselves are making inroads on the vascular tissues, they do this by attacking them by the way of the vasa vasorum. It is only when bacteria are carried in larger emboli or are caught in thrombotic masses that they attack an artery from the surface of its lumen. Moreover, it is much more common to observe this bacterial invasion in the ascending aorta, than it is in any other portion of the arterial system. In confirmation of this we need only refer to the processes induced by syphilis (Heller, 1903 [35]) (Chiari, 1903 [4]), influenza (Marmorstein, 1908 [20]), rheumatism (Feytaud, 1906 [9]), typhoid and streptococcal septicæmia.

It is possible that in a number of cases the ascending aorta may

become involved in an inflammatory process by the direct extension of the disease from the aortic valves upon the surface of the aorta. This mode has been suggested for a number of cases of acute mycotic aneurysm, in which acute valvular disease was present in the heart. This primary invasion of the lining membrane of the aorta was suggested by the continuous layer of exudate from the involved aortic valve to the aneurysm. In not a few cases, however, as well as our own, there was a strip of healthy aorta lying between the valvular disease and the aortic aneurysm. From the presence of the great damage in the external zone of the aorta, as well as the constant finding of inflammatory foci of lesser degree in the outer part of this vessel, we feel convinced that these aneurysms have their beginning in the progressive destruction in the outer portion of the arterial wall.

In conclusion, it is important that greater attention be given to the various types of acute aneurysms and their relations to acute rheumatic fever; and, further, that the almost constant presence of some inflammatory reaction in the ascending limb of the aorta be recognised as an associated condition in this disease.

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DESCRIPTION OF PLATES XXIII.–XXIV.

Plate XXIII.

Fig. 1.—Acute mycotic aneurysm of ascending aorta in a boy of six years, suffering from acute rheumatic fever.

Plate XXIV.

Fig. 2.—Section of the aorta at the border of the aneurysm (Fig. 1), showing the acute mesaortitis and periarteritis with rupture of the inner arterial walls.

Fig. 3.—Acute rheumatic mesaortitis and periarteritis. (Boy æt. 14 with acute rheumatic fever.)

Fig. 4.—Acute rheumatic mesaortitis and periarteritis. (Boy æt. 17 with recurrent rheumatic fever.)

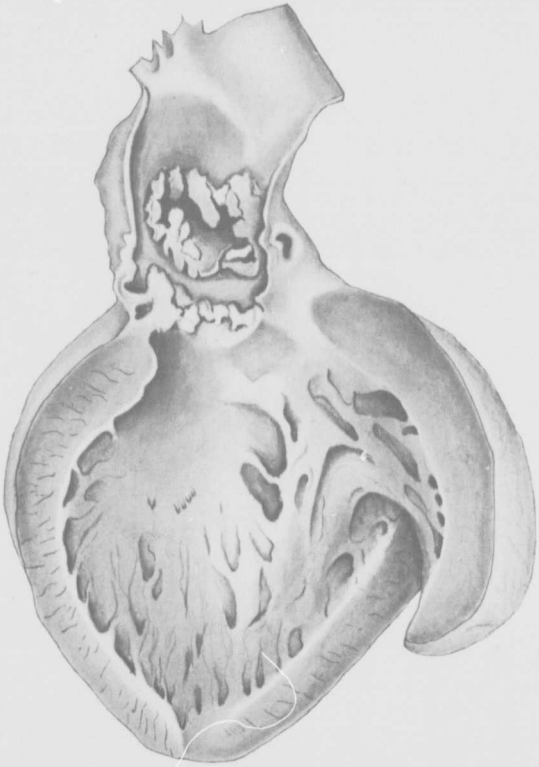

FIG. 1.

FIG. 2.

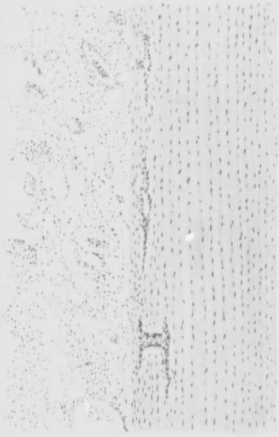

FIG. 3.

FIG. 4.