

in veterinary journals, but we have been unable to obtain these publications.

Marek describes the condition as a neuritis of the cauda equina.

The clinical condition in our patients seems to have been quite similar to that described in the horse, and the findings at operation were very like those found at the postmortem examination in the animals.

We have, therefore, been forced to the suggestion that our cases and perhaps some of those in the literature with like histories are examples of a true toxic neuritis of the caudal nerve roots. The probable existence in man of such a disease has been contended by several writers (Balint and Benedikt,⁶ L. R. Muller⁷ Raymond⁸), and has been produced experimentally by Orr and Rows⁹ who repeatedly have shown toxins to be capable of travelling from the sciatic and other nerves to the posterior root ganglia, along the spinal roots, and upward in the cord.

In their animals the signs of inflammatory reaction and of degeneration in the cord were inversely as the distance from the toxic focus, and were the result in each case of an infection of the lymphogenous paths.

It is our belief that our cases are examples of a morbid process akin to that produced experimentally by others, and it is our hope that in the future the study of other cases may make more plain the nature of the infection or toxemia and the possibility of its cure.

PRIMARY TISSUE LESIONS IN THE HEART PRODUCED BY SPIROCHETE PALLIDA.¹

By ALDRED SCOTT WARTHIN, PH.D., M.D.,

PROFESSOR OF PATHOLOGY IN THE UNIVERSITY OF MICHIGAN, ANN ARBOR, MICHIGAN.

(From the Pathological Laboratory, Ann Arbor, Michigan.)

ALL recent statistics show a marked increase in the occurrence of cardiac disease, and various theories have been advanced to explain this increase. Alcoholism, nicotinism, nervous strain, overeating and drinking, intestinal intoxications, chronic infections, etc., have been given as the factors responsible for the myocardial affections that are seen with an apparently increasing frequency,

⁶ Deutsch. Zeit. f. Nervenheilkunde, xxx, 1.

⁷ Ibid., xix and xxi.

⁸ Nouvelle Iconographie de la Salpêtrière, 1895.

⁹ Jour. Ment. Sci., London, 1910, lvi, 86-89; Rev. Neur. and Psych., 1912, x, 405-438.

¹ Presented before the Section of General Pathology, International Congress of Medicine, London, August, 1913.

but there is little unanimity of opinion as to the relative importance of these etiological agents. That syphilis plays an important role in the production of cardiac disease has long been suspected, and statements to this effect occur in the majority of text-books, usually unsupported by any pathological evidence. The truth of the matter is, that before the discovery of the *Spirochete pallida* as the etiological agent of syphilis, the pathologist himself recognized but few lesions of the heart as essentially pathognostic of syphilis. As to the significance of the gumma, he had no doubts; but gummas of the heart are relatively rare, hence his actual proof of cardiac syphilis became restricted to those instances in which the gumma was present. The frequent association of forms of chronic myocarditis, fibroid heart, anemic infarction of the myocardium and coronary sclerosis, with other pathological evidences of syphilis elsewhere in the body, such as tabes, paresis, gumma of the brain or liver, aortic aneurysm, bone lesions, orchitis fibrosa, etc., has given the pathologist a strong leaning to the view that the heart is one of the most frequently affected organs in syphilis. In my own experience this has been the case, and I consider the most frequent pathognostic lesion-complex of syphilis to be that shown by the heart, aorta, and the orchitis fibrosa syphilitica of the testes. To these, a fourth lesion could be added as next in constancy of occurrence, the presence in the adrenals of small areas of plasma-cell infiltration.

That these lesions are actually syphilitic could only be assumed upon the strength of circumstantial evidence before the demonstration of the *Spirochete pallida* gave us a positive finding by which the diagnosis of syphilis could be made absolute. The whole pathology of syphilis must then be worked over from the standpoint of this new criterion, and this is particularly true of the affections of the heart long supposed to be syphilitic, but which from their nature could not be positively determined to be so. From this point of view I have been for several years engaged in a study of cardiac syphilis based upon the occurrence of the *Spirochete pallida* in the tissues of the heart, and the results of this study, insofar as the primary tissue lesions of the heart muscle are concerned, I wish to give here in a condensed form.

The material studied consists of two hundred hearts, fifty of congenital syphilis and one hundred and fifty of acquired syphilis. They represent all ages and all stages of the disease; the congenital cases are mostly newborn and young children, the acquired cases mostly adults in middle life with a history of old infection. The number of active secondary stage cases in the adult is small, but sufficient to trace the development of the lesions through successive stages. The Levaditi method in its original form has been used chiefly in this work, as it still remains the most satisfactory method for the demonstration of the spirochete in sections. For the study

of the tissue changes themselves the ordinary staining methods have been employed, with resort to special stains for special purposes, whenever this was considered necessary to determine the nature of the lesion. As a result of this study the primary lesions of cardiac syphilis may be described as follows:

PARENCHYMATOUS. *Localizations of Spirochetes in the Myocardium without Recognizable Tissue Lesions.* Large colonies of spirochetes may be found in the myocardium, either in the tissue spaces of certain muscle areas, or about the bloodvessels, without any changes in the neighboring heart muscle that can be recognized by any of the technical methods employed at the present time. The muscle stains as well as normal heart muscle; it contains no vacuoles or granules, and presents all the appearances of normal muscle. The spirochetes lie in the intermuscular spaces, often in great numbers. Sometimes they appear within the muscle substance, as shown in cross-sections, but this is not common. Such findings are most frequent in congenital syphilis, but such collections of spirochetes without recognizable myocardial changes are found also in acquired syphilis, particularly in active secondary stages or early tertiary.

Pale Degeneration of the Heart Muscle in Association with Spirochete Pallida. One of the earliest recognizable changes in the heart muscle in areas containing spirochetes is the loss of color in the muscle fiber and its failure to take eosin in the normal way. Compared with normal areas, such affected muscle appears light and clear, with a loss of its striations, and shows vacuolated or light-staining nuclei. In the severe grades of this change the muscle passes so insensibly into the connective tissue that it is difficult to separate the two, so closely do they come to resemble each other in ordinary stained sections. Vacuoles may or may not be present in these fibers. The appearance of the fiber is not wholly like that of Zenker's necrosis, as it is less waxy or hyaline, appearing "washed-out." The fibers are also smaller than normal. This form of degeneration may occur as a purely parenchymatous change, but is most commonly associated with interstitial changes, particularly with the mucoid edema so frequently seen in congenital cases. This change is probably to be interpreted as being of the nature of a serous atrophy or liquefaction necrosis, but there is never any fraying-out of the cell protoplasm as in ordinary liquefaction necrosis.

Fatty Degeneration. A marked fatty degeneration of the cardiac muscle is often the only tissue lesion associated with the presence of the spirochete colonies in the myocardium. It occurs as a focal change, visible to the naked eye as yellowish pin-head spots, but often larger. Microscopically, the fibers are atrophic and filled with large droplets of fat, the droplets, as a rule, being larger than those commonly seen in fatty degeneration of the heart

muscle in such conditions as anemia, phosphorus poisoning, etc. Usually two or three large vacuoles replace the cytoplasm. This fatty degeneration of the fibers occurs also in the muscle surrounding the areas of interstitial infiltration and proliferation. In these areas of fatty degeneration, fewer spirochetes are usually found than in the focal areas of fatty degeneration unaccompanied by interstitial changes. In the case of severe vascular and perivascular infiltration and proliferation, irregular areas of fatty degeneration occur along the affected areas, but this is probably a secondary change to the circulatory disturbance. In the focal areas without other changes than the mere presence of the spirochetes, the occurrence of the fatty change must be explained as due to the presence of the organism, the latter probably robbing the tissues of their oxygen and food supply. Following the focal fatty degeneration, there may occur later a deposit of lime salts, so that focal areas of calcification can be produced by syphilis, and their occurrence in the myocardium should lead to a suspicion of this infection.

Simple Atrophy. Colonies of spirochetes can sometimes be located by the presence of focal areas of simple atrophy, the muscle showing no other change than a marked reduction in size. The interstitial substance may or may not be increased or show proliferation, and the pale degeneration and fatty degeneration may be associated with the atrophy.

Necrosis. In virulent cases of congenital syphilis in which the tissues of the body show enormous numbers of spirochetes, yellowish or light-colored areas may be found in the myocardium as well as in other parts of the body. These areas rarely exceed 5 mm. in diameter, and are usually much smaller. In the heart the muscle in these areas appears as fine fibrillæ without nuclei, or is entirely absent, its place being taken by a collection of lymphocytes, plasma cells, and fibroblastic cells. Around the borders fibers showing transition stages of liquefaction necrosis are seen, and the surrounding tissue appears as in a chronic edema, the tissue elements being pushed apart and the spaces filled with a fine albuminous precipitate, a mucoid substance and cells. With the specific mucin dyes, as kresyl violet, reactions for mucin are almost always obtained in these areas of liquefaction necrosis. Such changes are absolutely independent of any vascular changes, and are wholly the result of the spirochetes that lie packed in great numbers in these necrotic areas.

INTERSTITIAL CHANGES. *Edema.* In syphilitic hearts, particularly in congenital syphilis, pale areas, moist and translucent, may be seen even with the naked eye, or the entire heart wall may be very pale, translucent, and moist. On microscopic examination the pale foci are found to be areas in which the changes are wholly suggestive of edema. The muscle fibers are pushed apart, the reticulum is fibrillated and contains fine granules, and the number of wandering

cells is more or less increased. The presence of fat vacuoles in the muscle fibers adds to the general picture of a severe local edema, so that the average observer would pass it as an edema. But the Levaditi preparations show these apparently edematous areas to be filled with spirochetes, and the mucin tests show frequently the presence of a mucin-like substance, so that the edema is more of the nature of a myxedema. In these areas the spirochetes often appear closely applied to the capillary walls. Some of these areas are relatively poor in cells, but the majority show a fibroblastic proliferation, large, pale, epithelioid cells occurring, their cell bodies lightly staining, and their whole appearance washed out. Mononuclear white cells, plasma cells, and lymphocytes are present in varying numbers; and every transition exists between these pale, non-cellular, watery areas and those containing many cells.

Interstitial Proliferation. This may occur as the first recognizable tissue lesion, but usually after it has reached a certain point the parenchyma shows degenerative changes also. In the heart the proliferation appears to be always primarily vascular or perivascular, the endothelial cells of the capillaries proliferating and forming rods and groups of pale epithelioid cells, the capillary becoming thicker and thicker as the mass of cells in its walls increases. Now capillaries are produced and the area may come to be highly vascularized, but the new vessels are quickly obliterated by the proliferation of the wall. In the larger vessels, particularly in the arterioles, the proliferation is almost wholly perivascular and the spirochetes are found in great numbers in the perivascular lymphatics. Later these areas may become fibroid, and every possible transition stage is found between the focal edemas, and the areas of proliferation that may be interpreted as non-caseating gummas when sharply localized. In the congenital syphilis cases caseation of these areas must be very rare, as we have never found it. Such areas of proliferation without caseation exist also in acquired syphilis.

Myxoma-like Areas. A striking finding in the hearts of congenital syphilis is the occurrence of round, translucent areas that microscopically suggest myxomas and have been mistaken for such. With ordinary stains, hematoxylin and eosin, they appear as sharply circumscribed, spherical areas in which the heart muscle fibers have practically disappeared, only a few atrophic fibrillæ being left. A gelatinous tissue containing branching epithelioid cells and lymphocytes forms the main part of the area and new capillaries occur in it. Mucin tests show the presence of a large amount of mucin, so that the resemblance to a myxoma is greater still in preparations stained in this manner. Levaditi preparations show the presence of spirochetes in varying numbers in these areas, although the number is usually not so great as in the focal fatty areas and edemas. It is probable that the infection is a less viru-

lent and more sharply localized one. These areas may be regarded as young or undifferentiated gummas, myxogumma, without fibroid change or caseation, the tissue remaining in a fibroblastic semigelatinous state. The infiltration of lymphocytes and plasma cells is often very slight, so that this adds to the deceptive appearance of this formation, and if the Levaditi method for the demonstration of spirochetes were not carried out, the true nature of the process would not be detected.

CONCLUSIONS. These studies of cardiac syphilis would show that the primary lesions produced by the *Spirochete pallida* may be either parenchymatous or interstitial. The parenchymatous lesions are a peculiar pale degeneration, fatty degeneration, simple atrophy and necrosis; the interstitial lesions are the occurrence of a peculiar form of edema (myxedema), vascular and perivascular infiltration, and localized myxoma-like formations. The parenchymatous changes may occur absolutely independently of the interstitial, and the latter may be found with no associated changes in the neighboring heart muscle. The more marked the interstitial changes the more likely are parenchymatous changes to be associated with them, but the most marked parenchymatous lesions may occur without any interstitial changes. The purely parenchymatous lesions are found especially in virulent congenital and active secondary and early tertiary syphilis; in milder and older infections the interstitial changes, particularly the localized vascular and perivascular proliferations, predominate. The myxoma-like formations resembling undifferentiated gummas also occur in more localized and milder infections.

It is also of great importance to know that the heart is so frequently the seat of spirochete localization. The cardiac localization of spirochetes we have found to be more common than the hepatic. Spirochetes may be found in great numbers in the heart when no others can be found elsewhere in the body. In such cases the cardiac muscle may also show no lesions that, according to the older knowledge, would be classed as syphilitic, indeed, no organ or tissue may show any histological signs of syphilis even when the organisms are present in great numbers. That syphilis can produce purely parenchymatous lesions primarily in the myocardium opens up greatly the possibilities of this infection as a factor in the increasing myocardial affections of unknown origin. To what extent the *Spirochete pallida* is the etiological agent in these conditions cannot be estimated with certainty at the present time, but my own experience would make me believe that syphilis, both congenital and acquired, is the most important etiological factor in the production of cardiac disease, both myocardial and endocardial.