

reactions, and much of the response is spent in the tissue surrounding the small vessels coursing through the cortex. To a certain extent, however, intimal reactions are also found. The latter, however, arise somewhat later in the course of the kidney disease, so that examples are not difficult to demonstrate in which intimal sclerosis is wanting while a non-suppurative inflammation is active about the vessel. Later, however, the picture is reversed and the intimal sclerosis attracts our eye. This is now the stage when appearances suggest that a close relation of cause and effect exists between the intimal arteriosclerosis and the renal fibrosis.

The intimal disease of the arteries most commonly met with in the late stages of chronic interstitial nephritis consists of a chronic endarteritis with deep, fatty change. The presence of a true hyperplasia of the musculo-elastic layer with secondary degeneration of the inner muscle bundle has never been met with by us, nor have its advocates ever clearly demonstrated its presence. The finding of splitting of the internal elastic lamina is now found to have no specific bearing on the problem of arteriosclerosis. McMeaus (of our laboratory) has shown that such splitting is the common occurrence during inflammatory reactions of the intima.

Granted, therefore, that the early reactions which lead to the granular contracted kidney, simultaneously involve portions of the kidney parenchyma and its arteries, it is often extremely difficult to distinguish in the late stages of the disease exactly how much of the scar tissue has resulted through inflammation or as replacement fibrosis following arteriosclerotic atrophy. We should, however, continue to distinguish clearly the arteriosclerotic kidney of Ziegler from the granular interstitial nephritis, the former giving rise to true atrophic processes in the parenchyma with replacement fibrosis, the latter having an inflammatory basis for the development of connective tissue variously distributed about the important structures of the organ.

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## CERTAIN SYPHILITIC AFFECTIONS OF THE HEART AND AORTA.<sup>1</sup>

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A VARIETY of morbid states of the heart and bloodvessels, all serious in nature, may develop during an attack of unquestioned syphilis. While the writer would not go so far as to say, with

<sup>1</sup> Read at a stated meeting of the College of Physicians of Philadelphia, June 2, 1915.

some recent investigators, that syphilis is the principal factor in the production of heart disease, it can at least be safely assumed that rheumatism and syphilis head the list as causes of organic injury to this organ. The advent of the Wassermann reaction has shown, in a convincing manner, that the role of syphilis as an etiological factor in diseases of the cardiovascular system had previously been underestimated. It is frequently the earliest clue to lues, especially in females, who, in many cases at least, know nothing of syphilitic infection, while in other instances a Wassermann reaction will, as has been well said, "unlock the tongue."

The cardiac lesions caused by the *Spirocheta pallida* are usually considered as belonging to the tertian stage of syphilis, but recent investigators have shown that they may develop soon after primary infection. Grassman<sup>2</sup> and later Brooks<sup>3</sup> and others have expressed the opinion that damage of a serious character may appear as early as the forepart of the second stage. The fact should not be lost sight of that both aortic and cardiac syphilis may be the result of hereditary lues. It is definitely known that the *Spirocheta pallida* has a selective action for the heart. As stated elsewhere, "of all the viscera the heart is among the earliest to become involved in this disease." The importance of recognizing the cardiac element at the earliest possible moment is further shown by the fact that involvement of this organ may develop soon after the primary infection without symptoms which attract attention until months or even years later.

The claim made by Landois, Citron,<sup>4</sup> Hausmann, Sears,<sup>5</sup> and others that lues may affect the heart alone is both interesting and important. In two infants who died, one at three months of inanition and the other at eight days of asphyxia, Warthin and Snyder found the *Spirocheta pallida* in the heart muscle, while neither histological lesions nor spirochetes were found elsewhere.

Among the commonest cardiovascular conditions due to syphilis are myocarditis, aortic regurgitation, angina pectoris, and meso-aortitis, often resulting in aneurysm.

**MESAORTITIS.** Since mesaortitis, with or without coronary changes, is commonly the primary complaint in cases in which, as frequently occurs, two or more of the affections named above are found in association, it will be considered first in this paper. That this condition is due in many cases at least to syphilis has been demonstrated both by postmortem evidence and the results of carefully conducted therapeutic observations. In 1910 Longscope<sup>6</sup> pointed out that a peculiar type of arteriosclerosis (mesaortitis)

<sup>2</sup> Deutsch. Arch. f. klin. Med., 1909, lxxvii, 455; 1901, lxxviii, 58 and 264.

<sup>3</sup> AMER. JOUR. MED. SCI., October, 1913, p. 513.

<sup>4</sup> Berl. klin. Woch., 1908, xl, 2142.

<sup>5</sup> Archives of Diagnosis, January, 1913, p. 62.

<sup>6</sup> Jour. Amer. Med. Assoc., January 8, 1910, p. 118.

was frequently associated with aortic incompetency due to chronic aortic endocarditis. For example, in a series of thirty-seven autopsies showing mesaortitis a chronic aortic endocarditis occurred thirteen times, or in 35.1 per cent. Again, in 21 cases of chronic aortic endocarditis unassociated with lesions of any other valves occurring in connection with mesaortitis it was found that the lesions varied somewhat in extent in the individual instances, "but were always confined and often sharply localized to the arch of the aorta."

Of the 21 cases of aortic insufficiency associated with mesaortitis, 11 gave a definite history of either syphilitic infection or syphilitic lesion (gummata).

Harlow Brooks,<sup>7</sup> who made an anatomical study of the heart and aorta in fifty consecutive autopsies, found that 66 per cent., "including well and incompletely treated instances, died as a result of or with serious circulatory disease apparently of specific origin." Of these the myocardium was seriously involved in 44 cases, the coronaries in relatively greater degree than the general arterial system.

That this mesaortitis is of specific nature, with definite characteristics, is shown by the fact that the spirochetes have been found by Schmol and Wright in the lesions, the latter being able to demonstrate these organisms, often in enormous numbers, in all of five cases. Says Osler: "Microscopically the most important changes are found in the media and adventitia: (a) perivascular infiltration of the vasavascularum; (b) small-celled infiltration in areas of the media, with (c) splitting, separation, and destruction of elastic fibers and the muscle cells. The process is largely a productive mesaortitis, and so marked may be the foci in the adventitia and media that they look like miliary gummata, and, in fact, were so described as far back as 1877 by Laveran and by Heiberg."

**ANEURYSM.** The intimate connection between lues and aneurysm was well known to the older writers—to Pari, Larcisi, and Morgagni; but it has been specially emphasized by many modern writers, among whom the names of Osler, Heller, Koster, Chiari, Benda, and Klotz are conspicuous.

The belief that in persons under forty-five years of age syphilis plays the overshadowing role as an essential factor in causing aneurysm is confirmed by practically all of the more recent writers. On the other hand it may not be wholly gratuitous to caution the medical profession, as Hausmann has done, against regarding every case of aneurysm, even in syphilitic subjects, as due to lues.

Two additional facts may aid materially in distinguishing the etiological variety of aneurysm under discussion, namely, that the root of the aorta, *i. e.*, the ascending portion of the arch, is the usual seat of luetic aneurysms, and that they are frequently multiple.

Statistical evidence is not wanting to strengthen the view that syphilis is the most potent etiological factor in the production of aortic aneurysm. Cunston<sup>8</sup> quotes Rasch, of Copenhagen, who found twenty-eight aortic aneurysms in a series of 3165 autopsies. In 16 cases, or 57 per cent., syphilis was positively known to exist, while in 7 others, or 25 per cent., syphilis could be taken for granted in all probability. Etienne in a total of 240 cases of aneurysm found syphilis to be the cause in 166 cases, or 69 per cent. These figures have been amply confirmed by the following, among other percentages: Malnsten, 80; Heller, 85; Hampeln, 82; Pansini, 65.

My own collective investigations yielded a totality of 621 cases, of which number 363, or 58.5 per cent. were of luetic origin. In view of the fact that some of these cases had not been submitted to the Wassermann test, this percentage is too low. Among eight instances included in the above figures occurring in the Medico-Chirurgical Hospital, six were caused by lues.

A full discussion of the diagnosis of syphilitic thoracic aneurysm is not within the scope of this paper, but I desire to lay particular stress on a single fact bearing on this phase of the subject, namely, that a positive Wassermann reaction without confirmatory historical or clinical evidence (*e. g.*, age of the patient, site of the tumor-like protrusion, history of specific infection, etc.) does not warrant an assured diagnosis of lues.

**AORTIC INCOMPETENCY.** Syphilis is now generally regarded as an essential factor in the causation of aortic incompetency, more particularly in cases which develop before the forty-fifth year of life. The chronic aortic endocarditis is commonly associated with mesaortitis, as before stated, affecting the root of the aorta, and, indeed, may be the result of direct involvement of the segments in such cases. It is worthy of note that this etiological variety of aortic incompetency is often met with unassociated with widespread arteriosclerotic changes. In this connection it should be stated that a pure mitral lesion is seldom produced by lues, but a combined aortic and mitral lesion is commonly caused by syphilis.

There is a consensus of opinion to the effect that the most important etiological factor in the production of aortic incompetency is luetic infection. This view is amply supported by statistical observations. Thus Longcope<sup>9</sup> in a series of thirty-seven autopsies showing mesaortitis found thirteen instances of chronic aortic endocarditis (35.1 per cent.). Aguin, of 21 cases of aortic insufficiency, 11 either gave a definite history of syphilis or syphilitic lesions were discovered at autopsy. Citron obtained a positive Wassermann reaction in 10 out of 16 cases of this cardiac lesion, or in 62.6 per cent. Fiessenger<sup>10</sup> obtained a history of syphilis in 28 out of 37 cases of

<sup>8</sup> Archives of Diagnosis, January, 1913, vi, 25.

<sup>9</sup> Loc. cit.

<sup>10</sup> Bull. de l'Académie de Médecine, October 10, 1911.

aortic insufficiency. Collins and Sachs<sup>11</sup> found a positive Wassermann reaction in 10 out of 13 instances of aortic valvular disease. Babeock<sup>12</sup> records 16 cases of aortic regurgitation, of which 11 were submitted to a Wassermann test with a positive reaction in all of the cases.

My own collective investigations into the question of the frequent association of aortic insufficiency and syphilis embrace a total of 219 cases inclusive of the figures cited above. Of these 133, or 60.7 per cent., were clearly due to lues. In a considerable number of the cases of aortic incompetency no reference to the Wassermann test was noted. Obviously then the above figures underestimate the true role of syphilis in the production of this condition.

Severe pains may attend an invasion of the valve segments often accompanied by angina pectoris from implication of the coronaries in early cases developing more or less acutely. If the specific character of the cause be overlooked an inappropriate or the usual routine treatment of chronic valvulitis be adopted these cases may reach an early fatal termination. On the other hand, intensive antisyphilitic treatment may, if instituted early, bring about marked improvement, and the cases progress as aortic incompetency due to other causes.

While a certain diagnosis of syphilitic valvulitis affecting the aortic segments can not be made without a clear history of either specific infection or a positive Wassermann reaction, supported by confirmatory evidence, yet in the absence of rheumatism, gout, lead, alcoholism, pyogenic infection, or a predisposing occupation such cases should be labelled suspects and given the benefit of vigorous antisyphilitic treatment. Obviously, in instances belonging to this group the Wassermann test should be carried out, whenever possible, before remedial measures are instituted.

There are a few special physical signs which aid in the establishment of the luetic character of the chronic valvulitis. For example, Sachs<sup>13</sup> points out that "enlargement of the left ventricle is generally not so marked as in other forms of aortic insufficiency, and, therefore, the capillary pulse and double sound over the aortals are not so marked." I have observed the presence of a more decided arrhythmia in cases of aortic incompetency due to syphilis than in those due to other causes.

The early recognition of the true nature of the lesion becomes a matter of much practical importance, to the end that the ravages of this disease may be, to a great extent at least, obviated by suitable treatment. In this connection it should be pointed out that congenital cases of this affection may be due to hereditary lues.

<sup>11</sup> AMER. JOUR. MED. SCI., September, 1909, p. 314.

<sup>12</sup> LANCET-CLINIC, August 15, 1912.

<sup>13</sup> ARCHIVES OF DIAGNOSIS, January, 1913, p. 62.

In cases in which the history is obscure too much stress can not be placed on the value of the Wassermann reaction as a means by which to determine the etiological variety in question. As in the case of aneurysm, so in aortic incompetency, a positive reaction alone unsupported by other clinical evidence does not warrant an assured diagnosis of lues, but it renders it highly probable that syphilis exists.

On the other hand it must be recollected that aortic incompetency occurring in a luetic subject may be due to causes other than syphilis, more especially if the valvular lesion develop after middle life. Here it should be noted that the cardiac lesions of syphilis usually appear within two or three years after infection, a fact of considerable diagnostic significance in some cases at least.

**MYOCARDITIS.** As stated above, early involvement of the myocardium is not infrequent in the course of syphilis. Isaac Adler<sup>11</sup> first pointed out that the most important lesion of the heart is one of the myocardium, which lesion is dependent on periarteritis of the coronary vessels. Here it should be well understood that while endarteritis is the frequent important lesion, actual gummata in the myocardium are distinctly infrequent. Warthin<sup>12</sup> has described a syphilitic interstitial myocarditis in the absence of coronary periarteritis, and has demonstrated that the light-staining patches of proliferating stroma represent localized colonies of the spirochetes. Mareek, Simons, Buschke, and Fischer have also demonstrated the spirochetes in the diseased muscle of luetic myocarditis.

The recognition of incipient myocardial involvement is difficult, since the functional derangements thus produced are often slight, or, indeed, the condition may be entirely latent. The onset of the symptoms, if it develop in the secondary stage of syphilis, may be somewhat rapid or even acute. The principal features are arrhythmia, particularly intermittence and tachycardia, and less commonly extrasystoles. Brooks emphasizes among the earliest symptoms "irregularity of action, more marked when strain is added by mild exercises or through nervous apprehension;" he found the same thing true of the tachycardia, which is "incited to a degree by conditions which in the normal would fail to elicit such a response." Grassman writes: "I have studied 288 cases of secondary syphilis, and in 85 per cent. found disturbances of the rate and rhythm of the pulse, while in 40 per cent. accidental murmurs, usually with dilatation, occurred."

Pain is not a prominent feature, as a rule, in the early phases of the disease, although a feeling of thoracic oppression and slight dyspnea may be noted. In rare instances in which extensive

<sup>11</sup> Trans. Assoc. Amer. Phys., May 3, 1895.

<sup>12</sup> AMER. JOUR. MED. SCI., March, 1912.

lesions are present, actual pain with more or less tendency to radiation may be observed. The symptoms enumerated do not differ from those due to the myocarditis of other infections than syphilis, and it has been shown that these indications may all disappear in the course of a few days as the result of energetic antisypilitic treatment—a fact that emphasizes the importance of an early recognition of the condition.

In the tertian and quaternary stages of myocardial syphilis the symptoms and signs do not differ materially from those presented by myocarditis due to other causes. Not a few cases are latent and unsuspected during life, but are discovered if they come to autopsy. Soon or late in some cases dilatation is observed to occur, especially as the result of unworked exercise, and this may be attended with a murmur.

Anginoid pains are not uncommonly present and obliterative endarteritis implicating the coronaries and producing myocarditis may result in attacks of true angina pectoris.

The markedly irregular character of the arrhythmia has been, as stated above, emphasized by Brooks, and his observation has been confirmed by my own experience. The observation first made by Runeberg, namely, tonelessness of the first sound at the apex, has since been confirmed by Callender<sup>16</sup> and others.

It is to be observed that neither a characteristic grouping of features nor a single pathognomonic symptom, unless it be a positive Wassermann reaction, are presented by the condition. As regards the Wassermann test it may be said that although a positive or negative reaction is not an absolute criterion of the presence or absence of a syphilitic infection, Brooks contends that it is better than the 70 per cent. of error based on the history or clinical findings alone.

Certain clinical peculiarities already mentioned may, however, serve to arouse suspicion of syphilis. Of these the tonelessness of the first heart sound and the decidedly irregular, accentuated character of the arrhythmia deserve special mention. Again, the association of phenomena which point to syphilitic involvement of other organs and structures of the body often throw light on the character of any cardiac lesion that may be present. Lastly, all determining causes of myocardial disease other than syphilis should be carefully excluded.

Heart-block is frequently caused by syphilitic lesions of the bundle of His, but this phase of cardiac lesions can not be enlarged upon here. Suffice it to cite the figures of Robinson, who found that among 16 cases of heart-block due to such lesions 6 at least were of syphilitic origin.

**ANGINA PECTORIS.** The writer has collected 270 cases of angina pectoris from the literature, of which only 72, or 26.5 per cent. gave evidence of syphilis. This percentage, however, is much too low, since in 250 of the recorded instances no mention was made of a Wassermann test, sole dependence being placed in the history. The close association of syphilis and angina is amply confirmed by modern authorities. Breitmann,<sup>17</sup> of St. Petersburg, writes: "Every case of angina pectoris during the younger period of life is open to the suspicion of syphilitic origin." R. O. Moon<sup>18</sup> has been much impressed with the great predominance of lues in connection with true angina, and has seldom met with a case since the advent of the Wassermann test which did not give a positive reaction. Saundby<sup>19</sup> states that congenital syphilis as a cause of angina pectoris is not to be overlooked in young patients.

**PROPHYLAXIS.** My discussion of the treatment of cardiovascular syphilis will be, owing to the exigencies of time and space, limited to prophylaxis. Doubtless the incidence of cardiovascular disease would be much lessened by a more systematic and vigorous treatment of luetic infection in general. There is perfect unanimity among syphilographers and clinicians of wide experience regarding the belief that when either syphilis of the myocardium of marked extent or aortic incompetency exists a cure is impossible of attainment.

Physicians should, therefore, feel themselves charged with a serious responsibility on behalf of the victims of luetic infection and carry out the treatment of early syphilis in the wisest manner possible. An added reason for adopting this course lies in the hazard arising from the administration of salvarsan or neosalvarsan in the severer forms of cardiovascular syphilis. It has been found that death, either occurring suddenly or after several days from the use of these agents, is commonly due to myocardial degeneration secondary to coronary lesions.

As stated elsewhere, "A sane view of the prophylaxis of cardiac involvement in this disease demands inclusion of the treatment of its secondary manifestations." It is in this stage that its development may take place, and also that the time of cardiac invasion can be fixed by the appearance of certain clinical features, in some cases at least.

In concluding the writer desires to make grateful acknowledgment of the assistance rendered by Drs. H. Leon Jameson and Andrew A. Anders in the work of searching the literature in connection with these statistical investigations.

<sup>17</sup> Quoted by Bruce, *Lancet*, London, 1911, ii, 69.

<sup>18</sup> *Clin. Jour.*, London, 1912-1913, xli, 353.

<sup>19</sup> *Ibid.*, May 21, 1913.