THE GULSTONIAN LECTURES,
on MALIGNANT ENDOCARDITIS.
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LECTURE III.

Diagnosis.—Few diseases present greater difficulties in the way of diagnosis, difficulties which in many cases are practically insurmountable. It is no disparagement to the many skilled physicians who have put their cases upon record to say that, in fully one-half of them, the diagnosis was made post mortem. In spite, too, of able memoirs in the journals, the disease has not been much known, and it is only of late years that the text-books have contained chapters upon it. The protean character of the malady, the latency of the cardiac symptoms, and the close simulation of other disorders, combine to render the detection peculiarly difficult.

In the group of cardiac cases in which the disease attacks a patient the subject of chronic valvulitis, the matter is usually easy enough. The existence of fever of an irregular type, and the occurrence of embolism, generally, are sufficient to place the case to endocarditis. It must be remembered that simple valvular endocarditis not uncommonly attacks sclerotic valves, and may be accompanied by slight fever. Of course, in chronic heart-disease, irregular pyrexia may arise from other causes—local suppuration, cellulitis, etc.—which must be excluded.

In rheumatic fever, a disease in which the heart is more systematically examined than in any other, if with the occurrence of a murmur the symptoms become aggravated, this is a typical pyemic or pyemic type, the recognition of the complication should be easy. The onset of severe head-symptoms in rheumatism—dullness, with fever and coma—requires to be carefully distinguished. Fortunately, the simple endocarditis common in this disease rarely, as I shall have occasion to show, passes into the grave form.

In pneumonia, a prolongation of the course, with the supervision of typhoid or septic symptoms, should lead to a very careful examination of the heart.

The greatest difficulty is met with in those acute cases resembling the malignant forms of the fevers; here the affection may simulate typhoid, typhus, cerebro-spinal meningitis, or even hemorrhagic small-pox. Even with the detection of a heart-murmur, the judgment may have to be suspended. Shortness of breath and weakness, and the advent of profound blood-poisoning, before the development of any special features upon which a diagnosis could be based.

From typhoid fever, with which the cases are most often confused, the mode of onset, the pyrexia, and the abdominal symptoms, offer the chief points for discrimination. The onset of severe endocarditis is more abrupt, not so often preceded by a period of failing health and progressive weakness. In a large number of cases, cardiac pain or oppression and shortness of breath are mentioned as early symptoms. The fever rarely presents, in the early days of the disease, the regularity of typhoid, and from the outset may be very high. A sudden fall to the normal, or even below, may occur; indeed, irregular pyrexia is one of the most important diagnostic signs. The combination of diarrhea, abdominal distension, and a rose-coloured eruption, points strongly to typhoid fever. The rash, when present, is usually petechial, a rare circumstance in typhoid fever. The development under observation of pronounced murrain, particularly of ascitic and regurgitant, is most suggestive of malignant endocarditis, and the occurrence of emboli would be a positive confirmation. Rigors rarely occur in typhoid fever, while they are common in endocarditis. It is well, however, to bear in mind that, in many of the most severe cases, death may occur, as in any of the infective disorders, without the development of the special symptoms necessary for a diagnosis.

Many of the cases present the clinical features of pyemia, a condition which may actually exist, dependent upon the ulcerative lesions on the valves; and here the diagnosis lies between an ordinary septic infection from a wound, or auto-infection from a primary endocardial inflammation.

It is interesting to note the similarity of those cases of acute endocarditis in which death occurs in a few days, without the development of any other than the valvular lesion, with those instances of rapidly fatal acute peritonitis and necrosis, and also with those cases of meningitis septicus of an acute type.

It seems strange that difficulties should arise in the diagnosis between malaria and malignant endocarditis, but the records of cases plainly show that for weeks or months a condition of intermittent pyrexia may occur, simulating every type of ague. The phenomena in regularity, in order of sequence, and in the accompanying general conditions, may fulfill every condition of a quotidian or tertian intermittent; and the development of cardiac symptoms, with breathing of the rheumatic type, may also indicate the nature of the disease.

Etiology and Pathology.—With a view of obtaining data upon which to base statements regarding the etiological relations of malignant endocarditis, I have gone over the records of 209 cases. As before stated, 37 of those occurred in connection with pyemia, traumatic or puerperal. Doubtless this number could have been very greatly increased had I examined files of special gynecological and surgical journals, but my investigation did not lie so much in these directions. In 45 cases, there was no record of any previous disease which could be taken into account as possibly connected with the endocarditis. In 127 cases, there was a history of past or existing disease with which the cardiac trouble could, with a greater or less degree of probability, be associated.

One or two general considerations may first be mentioned. The period of middle life gives the greatest number of cases. Young children rarely were the victims; there were only 15 cases under 10 years of age, and all males. Many cases over 50. The cases occurring in connection with rheumatism presented an average younger age than the others; there were 36 instances under 20 years of age, out of 61 cases in which this point was mentioned. Of 160 cases (exclusive of traumatic and puerperal), 99 were in males, and 61 in females.

Persons debilitated by exposure or other causes, or addicted to drink, seem particularly liable to be attacked; and in such subjects, during the course of an acute disorder, this complication is much more likely to arise.

As has been already referred to, the existence of sclerotic valvulitis is a very important factor in the etiology of severe endocarditis, a very considerable proportion of the cases occurring in individuals whose valves are thickened and crumpled from chronic inflammation.

The existence of a primary protopathic endocarditis must, I think, be allowed. In 45 cases, no history could be obtained of rheumatism or other affections with which endocarditis is known to be associated. Many of these cases were of the most malignant type; in 10, death took place within a week. A specific statement of the absence of rheumatism was generally given. The onset was usually like that of a specific fever, headache, vomiting, rigor, pyrexia, and often early delirium and unconsciousness. Typhoid or rheumatic type, but, when more prolonged, a pyecnic condition may be the features of these cases. Of such cases, one developed with chronic valvular disease, some while under treatment, others in whom the compensation was complete and the old lesions only detected at the necropsy. In 8 instances, the ulcerative process attacked aortic valve, which was fused, and had undergone the fibroid changes always associated with this malformation.

In 127 of the cases, the endocarditis was associated with other diseases, some of the most important of which we shall now proceed to consider.

Rheumatism.—Since Bouillaud called special attention to the frequency of cardiac complications in this disease, its importance in the etiology of endocarditis has been universally recognised. And, as regards the simple form of endocarditis, the general statements are quite true, but, fortunately, the graver and fatal form is much less common, much less, I think, than is usually supposed. In 53 cases, there was a history of rheumatism, past or present. I included every case in which there had been the record of an attack, recent or remote. In only 24 did the symptoms of severe endocarditis arise during the progress of the acute or sub-acute disease. In 29 cases, there was simply a history of rheumatism, often years before, and no mention of any active process of the disease. These 29 cases were not considered as cases of endocarditis. Dr. Ogilvie called attention to the fact that ulcerative endocarditis occurred very often in persons in whom no rheumatic history could be traced. Of 21 cases which he reported, some of which were probably rheumatic, in only 3 was rheumatism mentioned. In only 3 also of the Montreal cases was there any positive history of rheumatism, either before or during the attacks. The following case, under the care of Dr. Ross, is a good example of the mode of onset.

B. M., aged 22, a healthy girl until three weeks before admission to hospital, on January 4th. At that time she was attacked with
rheumatism of the wrists and ankles, not very severe, and she did not receive any treatment. A week from the beginning of the attack, she began to have chills, two or three a day, and also became feverish. During the next week she became worse, had occasional chills, not delirious; was brought to hospital on the 4th, in a very low state. On the 5th: there was delirium and incoherence. Pulse 100°. Double murmur up and down sterno; joint-troubles not evident. On the 6th, 7th, and 5th, she remained in the same state, no chills; temperature ranged from 100° to 102°. On the 9th, she was more restless. On the 11th a green membrane was noticed on oral faucae. On the 12th, the membrane in the throat had extended, and covered the soft palate. Temperature 103°. On the 15th she died suddenly. The necropsy revealed a large deep ulcer at the aortic ring, mostly destroying one segment, and penetrating deeply between the auricle and the left ventricle. There were small infarcts in the brain, extensive recent diphtheria of faucae.

In a larger number than in any other group, selerotic valves were found, with the existence of which the past rheumatism could, in many instances, be connected. A primary rheumatic endocarditis was recognised by Latham, also by Graves and Stokes, and it is quite possible that some of the cases which I have grouped as protopathic represented instances of the kind in which, if life had been prolonged, joint-troubles might have occurred.

Cases of acute rheumatism sometimes occur in which there may be multiple aillary abscesses (Fleischhauer, Viechow’s Archiv, Band ixii), and a pyenic condition similar to the case just described, but without the presence of endocarditis, cocci have been found in these abscesses, and the cases resemble those rare instances of idiopathic pyemia. It is noteworthy of observation that a skin-eruption was most frequently noted in connection with the rheumatic condition, generally an erythema. In a case narrated (British Medical Journal, 1885, vol ii), it was observed on both face and hands.

The occasional presence of a jaundice rash in rheumatism (Petter, Union Medicale, 1910), and in puerperal fever (Hicks, Obstetrical Society, vol. xii), has long been recognised.

In aches, with which simple endocarditis is so often associated, the malignant form very rarely supervenes.

Pneumonia, as Bouillaud pointed out, is not infrequently complicated with endocarditis, but the important part which it plays in the etiology of the malignant disease has not been generally recognised.

In the cases I have reviewed, it stands at the head of the list of diseases in which secondary endocarditis of a severe nature develops, 54 instances having been noted, rather more than 25 per cent. of the total number of cases. For this I was quite prepared by our Montreal experience, for, in 11 of the 23 cases, the attack was associated with pneumonia. Of the occurrence of acute endocarditis in this disease, the statements are somewhat diverse. Bouillaud thought that, in a third or fourth of the cases in which there was a-sided pneumonia, there was inflammation of the serous membranes of the heart. Grisolle, in his classical work on pneumonia, states, on the contrary, that it is a rare complication, and this would certainly appear to be the conclusion of the Committee for the Collective Investigation of Endocarditis, which report upon 10,000 cases, endocarditis is only once mentioned. My experience at the Montreal General Hospital is very different. I have notes of 103 post mortem cases of lobar pneumonia, and the occurrence of endocarditis is noted in 16 cases, or 15 per cent. Of these cases, 11 were of the malignant form. An analysis of these shows that, in 6, the left lung was involved; in 5, the right; in 4, the upper lobe was affected; in 7, the lower. In 9 of the cases was there pericarditis; in 5 of the 11 cases, there was suppurative cortical meningitis. In the 54 cases which I have reviewed, in 38 the lung affected was mentioned, and in 26 the affection was on the right side, and only 10 on the left; figures which are opposed to the statement of Bouillaud, that it is in left-sided pneumonia that endocardial complication so frequently occurs. In 54 cases with acute pneumonia, meningitis is more frequently mentioned, and, in one instance, the membranes of the spinal cord were also affected. The aortic values seem more often involved than the mitral. In 17 instances, there were old sclerotic changes in the valves.

The clinical features of several cases in which the endocarditis came on during pneumonia have already been given. In many of them, as in the girl, M. D., aged 29, referred to in the second lecture, the patient was light in hospital unconscious, and died with a few days, with symptoms of a grave cerebral disorder, there is a history of ordinary pneumonia, and the case may pursue the usual course, and defervescence take place, when, in a day or so, fever of an irregular type recurs, and typhoid or pyemic symptoms appear. The mortality of cases of this kind is high. In two cases of this kind, the patient succumbed to a lobar pneumonia and endocarditis unconnected with any sepsis. Two of the Montreal cases were of this kind. In three or four cases, there were rheumatic symptoms preceding or accompanying the pneumonia, as in a case of Dr. Musser’s, the remarkable temperature-chart of which is here shown.

Inhabitants were more often attacked than in the other groups. There were 10 individuals over 50 years of age. In the Montreal cases, 3 of the patients had had pneumonia before; in 1 it was the third attack, and in every one of them there was history of either drink-

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hopeful; and it would not be rash to predict that the knowledge twenty-five years hence will be as much in advance of to-day as the information on the subject is of the time when Dr. Kirtes made his memorable investigations. A serious difficulty exists in the circumstance that we have not to deal with a single form of disease—an entity—but with a special condition under which a variety of affections, too, the pathology of which is, in most instances, by no means clear. No one can doubt that the more severe cases of endocarditis present in a typical form all the features of those diseases which we can collectively term rheumatic, and belief in the etiology caused by the absorption of some poison, the development of which in the blood and tissues profusely disturb, and finally annihilate, function.

Briedly stated, the theory of acute endocarditis which at present prevails, and the only one to which I shall refer, is, that it is in all its forms, an essentially mycotic process; the local and constitutional effects being produced by the growth on the valves, and the transfer to distant parts of microbes, which vary in character with the disease in which it develops. This very attractive theory can be adjusted to meet every requirement of the case, though, as yet lacking certain of those substantial data necessary for full acceptence, but which, having been furnished of late years in other diseases, may in due course be in full acceptence.

Let us see, first, what has been done, and the important facts at our disposal seem favourable to this view. The constant presence of micro-organisms seems undoubted; only, in the simple acute form, we need more careful observations with our improved methods. Some good observers have not been able to constitute the verrucose outgrowths (Klebs, Archiv für Exper. Pathologie, Band iv; Köster, Virchow's Archiv, Band lxxiii). The careful study of such a material has not been recommended by Gramm should readily determine this question. A study of the endocarditis of puerperal and traumatic pyemia will be most likely to yield important information, as here the conditions are simpler, and the immediate cause of the outbreak of the disease is more easily determined. The cardiac complication in these cases is only part of a general process, excited by a local lesion, and is entirely secondary and subsidiary. Micrococci arranged in chaflets are constant constituents of the endocarditis, and of the effects of inoculations, and a comparison of these with the phenomena of putrefaction is recommended. In the original lesion, or of the metastatic foot, should yield results of great value in the interpretation of the phenomena of secondary endocarditis.

In rheumatic fever, we are still too far from any accurate knowledge of its intimate pathology to dwell on the possible connection of any organism peculiar to it, and the endocarditis common in its course. Klebs (Archiv für Experiment. Pathologie, Band ix) distinguishes the microbes occurring in rheumatic cases from those of the septic forms. In pneumonia, micrococci undoubtedly abound in the exudation of the air-cells, and their mode of growth in gelatine is peculiar, but the numerous experiments on artificial production are not yet conclusive. The evidence is accumulating which places pneumonia among the infective disorders; and it certainly is a seductive view to take of its pathology to regard the local pulmonary lesion as excited by the growth of micrococci in the air-cells, and the various consequent inflammations, the early and peri-carditis, the pleurisy, the meningitis, the membranous gastritis or colitis, as due to the penetration of the organisms to deeper parts, and their local development under conditions dependent on the state of the tissues. The processes are all of the character described as croupous, and have as common features the presence of micrococci in a coagulable exudation, the absence of pus, however, to settle the identity of the organisms of the air-cells with those of the consequent inflammations; but we may reasonably hope ere long to have some positive data from investigations in this disease, which, more than others, offers favourable opportunities for the solution of these problems.

In diphtheria, as we have seen, myotic endocarditis rarely occurs; and, in the few instances observed in association with scarlatina, varicella, erysipelis, and other affections, we have positive information with regard to the characters of the micro-organisms.

In the way of experimental investigation of the properties of the micrococci, not much has been done of a satisfactory nature. Heiberg (Virchow's Archiv, Band ivi) placed bits of vegetation from a puerperal case beneath the skin and in the peritoneal cavity of a rabbit without effect. Eberth (Ibid., Band ivii), Birch-Hirschfeld (Archiv der Italienischen Medizin, Band xvii), have produced panophthalmitis in the rabbit by inoculating the eye, and I was able to produce well marked mycotic keratitis in the same animals with fresh material from the valves of two cases. H. Young, of Manchester, inoculated rabbits with pus from an abscess in ulcerative endocarditis, and was able to detect micrococci in the blood of the rabbit after death.

No conclusive culture-experiments have yet been made. Grancher (Journal de Médecine de Paris, December 20th, 1884) has cultivated a microbe from the blood, taken during life with all necessary precautions, but apparently not in series, and no inoculations of animals were made. He supposed, "d'avec cette mode on ne peut encore parler, et bien que l'on ait trouvé des cultures sur gelatine, mais on n'a pas noté d'aucuns résultats favorables.

How do the micrococci reach the valves? In cases of puerperal and traumatic pyemia, the external lesion is undoubtedly the source of infection which is conveyed through the venous system; and, in these cases, it will be remembered that the right heart is most often affected. In other instances, where the skin is unbroken, we must suppose them to gain access by the lungs or intestines, most probably by the former; and, in these instances, the left heart is the chief seat of the mycosis. Whether they reach the valve with the general blood-current, as Klebs supposes, or through the coronary arteries, as Czerny supposes, or through the early vegetations in a non-vascular region of the valves, and from the fact already referred to, that colonies of micrococci can be seen directly upon the endocardium, it seems probable that Klebs's view is the correct one. Housting (Arch. de Méd. 1880) has shown that the thickening or the closure of the valves are the usual seat of the process, that the micrococci, circulating with the blood, are here closely pressed into the endothelium by the firm apposition of the flaps. Whether or not in these cases the endocarditis will arise, depends materially on the condition of the valve-tissue. In a case of pneumonia or other disease—such as pyemia—in which we may suppose microbes circulating in the blood, the endothelium of normal valves may be able to resist their invasion, or, even if they lodge and penetrate, the condition may be favourably disposed to its removal.

Are the micrococci in simple endocarditis, as Klebs maintains, or are they a necessary by-product, as J. Goodhart suggests (loc. cit.), in patients with chronic septic valves like walking mushroom-beds, in common times without a flaw, but in periods of epidemics taking in germs by various channels, which fertilize in some cases into ulcerous endocarditis, while, in others, the micrococci multiplying in the blood, and going to the seat of the disease, as if by the good will of the patient, and their toilings and works will be a blessing to the world.

An industrial exhibition for the working classes of East London will be opened by the Princess Louise on May 4th. The exhibition is a philanthropic scheme, and loans of works of art and other objects of interest are invited as well as subscriptions to the prize fund. The secretary is Mr. A. McLagen, 506, Commercial Road East.

The third edition of Dr. W. H. Day's work on Headaches has been translated into the Russian language by Dr. J. J. Truswitz, Surgeon to the Russian Imperial Navy.