attachment, however, was very thin, and as a precaution was sewn over; the hole in the transverse mesocolon was closed. The omentum and the gastro-hepatic omentum were then separated from their attachments to the stomach.

Massage of the Heart.

At this stage the patient suddenly stopped breathing and his heart ceased to beat. His head was lowered and oxygen only was passed down the intratracheal tube under intermittent pressure. The stomach was rapidly separated, between clamps, from the duodenum and thrown over to the left side of the abdomen. The heart was then gently massaged through the diaphragm at the rate of about sixty to the minute, artificial respiration being kept up meanwhile; 10 minims of 1 in 1,000 adrenaline were injected into the heart muscle through the chest wall. Three minutes elapsed before any sign of heart movements was noticed, when a single forcible contraction was felt; this was followed by fibrillary twitchings for about ten seconds, and was then succeeded by a series of regular, rapid, feeble beats until gradually it beat with its normal rhythm, but at rather a rapid rate. Shortly after the heart began to beat the patient commenced to breathe. Hot packs were placed on the chest wall and the operation was proceeded with, a Billroth No. 1 anastomosis being made, after having excised the distal half of the stomach with the gastro-jejunal anastomosis. This operation took forty minutes to complete, the anaesthesia being continued with pure nitrous oxide-oxygen through the tracheal catheter.

In the excised portion of stomach there was no sign of the old gastric ulcer, but there was a small gastro-jejunal ulcer, a third of an inch in diameter, surrounded by an indurated wall, on the left side of the junction.

After-History.

The patient was returned to bed with hot-water bottles and was given rectal injections of saline and glucose. His pulse rate remained very rapid and its volume was very small, but at the end of three hours he showed signs of recovery and became extremely restless. His temperature remained normal, but the respiratory and pulse rates were raised for about ten days. Some suppuration took place in the abdominal wall.

Ten days after the operation he had a severe haematemesis, which was followed by another two days later. He was put on a modified Lennhartz diet. From this time onwards he began to improve and made an uninterrupted recovery. When discharged from the hospital, on November 21st, he was taking a light diet, was free from symptoms, and was putting on weight. He has remained well, without any further symptoms. The wound was healed and the pulse, temperature, and respiratory rates were normal. A barium meal, given just prior to his departure from the hospital, demonstrated that the new channel was working satisfactorily. He saw me on March 17th, 1926, stating that he had no symptoms, was quite fit, and was leaving for Uganda.

There are some points worthy of comment in this case, apart from the recovery of the patient. Up to the moment of his collapse there was no indication that this was about to happen; in fact, only just prior to the moment I had commented to the anaesthetist that he was standing the operation well. In the second place, it is surprising that, in addition to obtaining a recovery of the heart's action, it was possible for me to complete the operation, which took at least another forty minutes. Naturally, the completion of the operation was carried out under a severe stress, and it is my belief that the haematemeses were of the nature of secondary haemorrhages, probably due to faulty technique.

Cases of recovery after massage of the heart are, of course, on record, although in many instances failure occurs; the patients survive the operation, but either never regain consciousness or die of some lung complication. In some cases the abdomen has required to be opened in order to perform necessary manipulations. In this case, however, although some preliminary manœuvres had to be effected, owing to the nature of the operation in hand, in order to reach the diaphragm, very little time was lost before massage was commenced. In addition, it is possible that recovery was naturally aided by the presence of a tracheal catheter in position at the moment of cardiac failure, which permitted the immediate inflation of the lungs with oxygen under pressure; so that while the heart was being massaged the artificial circulation provided sufficient oxygenated blood to the brain to obviate the cerebral anaemia which usually proves fatal in these cases. The production of a pink coloration of the patient's face with each artificial pulsation of the heart was a very noticeable feature. The diaphragm was not incised, but the heart was squeezed by the right hand inserted under the diaphragm while the heart was pressed against the anterior chest wall. So far as could be observed, both before and after the operation there was no heart lesion.

I am indebted to my house-surgeon, Mr. Dodd, and to the anaesthetist, Mr. Hower, for so ably assisting me to bring about the man's recovery.

Lumleian Lectures ON ENDOCARDITIS.

BY
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LECTURE III.*

I PROPOSE now to deal with the anatomical and bacteriological parts of my subject, and then with considerations of diagnosis, pathogenesis, and treatment.

STATE OF THE ENDOCARDIUM BEFORE INFECTION.

The state of the valves prior to the onset of septic endocarditis is an important point. In my original series of 118 *post-mortem* examinations in 150 cases I found evidence of old valve disease in 80 per cent. The figures of other observers approximate very near to this. But it is to be noted that this figure refers to acute and chronic cases when taken together. If we consider acute cases alone the figure is undoubtedly much smaller. If we take the series of cases of ex-soldiers by themselves we find it smaller still. Thus, out of 13 autopsies in this class Starling found scarring from old rheumatic disease in one only. Carey Coombs's experience is much the same. The inclusion of 20 cases of ex-service men explains why, in a second series of 162 cases at St. Bartholomew's Hospital, the figure is only 50 per cent. You, Sir, in the course of the Lumleian Lectures given by you in 1920, stated that, despite the prevalence of sepsis in the wounded during the great war, infective endocarditis was uncommon; that a number of acute and rapidly fatal cases of the disease occurred in men in whom no primary source of infection could be found *post mortem*; and that in these cases the infection had attacked healthy valves. Summing up, therefore, it may be said that in acute cases generally, and in the chronic ex-service cases, there is a notable absence of pre-existing valvular disease; in chronic civilian cases there is a marked preponderance of pre-existing valvular disease. It has perhaps been too readily assumed that the nature of the pre-existing valve damage found at autopsy is generally rheumatic in origin. Care must be taken, as Libman has pointed out, to distinguish the residues of rheumatic infection from the residues of an old septic endocarditis, since it is now known that this latter process may recur after years of apparent freedom from active infection. The patient's history is therefore of great importance in judging the nature of cicatricial and of sclerotic changes in the valves. Since pericarditis is known to be quite rare in chronic septic endocarditis, evidence of this at autopsy is much in favour of old rheumatic infection. The type of myocardial disease, if this be present, may also assist in a correct interpretation of the findings.

Of the valves affected it is again important to distinguish acute from chronic cases, and civilian chronic cases from ex-service chronic cases. In acute cases the incidence of mitral and aortic disease is probably about equal. Of 34 such cases due to *Streptococcus pyogenes* Thayer found the aortic valve involved in 20 cases, the mitral in 26. Gonococcal infection, however, tends to attack the aortic valve by precedence. Thayer's cases, forming the fullest series of which we have details, showed 66 per cent. aortic and only 19 per cent. mitral. There were right heart lesions as often as mitral in this infection. Of 40 cases of pneumococcal endocarditis, Thayer found the aortic cusps involved in 20, the mitral in 13, and the valves on the right side of the heart in 7 only, thus disposing of the fallacy that pneumococcal infection is prone to attack the right heart chiefly. In chronic septic endocarditis, however, there is a preponderance of mitral infections in civilian cases, and a still greater preponderance of aortic cases in ex-soldiers.

MURAL INFECTION.

Mural infection is, I believe, more common than is generally thought. I found instances of this condition in 52 per cent. of 118 *post-mortem* examinations. Thayer's figure is as high as 84 per cent. in chronic cases. Auricular

* Delivered before the Royal College of Physicians, London, on March 30th.

infection is much more common than ventricular. The occurrence of mural endocarditis is usually attributed to the influence of pre-existing scars from old rheumatic disease. The occurrence of mural lesions without valve lesions must be quite rare. I cannot find any case in the literature which is at all comparable with one which I described in my original series, and where, fortunately, a *post-mortem* examination was possible. The disease had lasted for over two years, the type being very chronic, the fever very mild. There was no sign of valvular disease during life. This patient was for some weeks in a sanatorium on account of pyrexia, sweats, and malaise, it being thought that she might be a case of pulmonary tuberculosis without physical signs. She developed multiple infarction of the spleen, and blood cultures were positive. Eventually she died of cerebral embolism. *Post mortem* there was found a small area of fungating auricular mural endocarditis, situated well above the mitral orifice, the cusps of which were natural. The importance of knowing that such cases exist lies in the fact that the disease may be present in the absence of signs of valvular mischief. But, as already stated, such cases are rare.

PARASITOLOGY.

I pass now to a consideration of the parasitology of endocarditis. I need not dwell upon the infecting agent in the syphilitic cases, except to point out that all the evidence favours the view that the route of infection is by the vasa vasorum to the middle coat of the aorta, and that it is therefore probable that the aortic cusps are infected likewise from the depths rather than from the surface.

Nor must I dwell long upon the old controversy anent *the causative agent in acute rheumatism*. Of late years there has been a growing tendency to consider the streptococcal origin of acute rheumatism as proved. But clearly this is not so, and it seems to me that we do but obstruct further research by so premature a conclusion. With due deference to Poynton and Paine, whose thorough and masterly work all must admire, it is to be doubted if the real picture of acute rheumatism has yet been experimentally produced in animals by the use of the *Diplococcus rheumaticus*. Nor is there so far anything like unanimity amongst the many observers who have given pains to the question of blood cultures in rheumatic fever and to the bacteriological investigation of fatal cases of the disease. Unfortunately the opportunities for this particular research become less and less with the decrease in incidence of severe rheumatic fever, but when the disease was rife, and even now, when it occurs, the number of negative results in the hands of skilled bacteriologists were, and are, strikingly large; and this, too, when the most approved culture methods are adopted. Such strains of cocci as are occasionally found in these cases seem to possess no special features, and considerable weight must be attached to the fact that the blood in cases of acute rheumatism has failed to yield any specific serological affinity, even for those homologous streptococci that have been isolated from the circulation of rheumatic patients. Such is the experience of Swift and Kinsella, who record the following striking case. A streptococcus was isolated from the blood of a patient in a first attack of rheumatic fever. A relapse occurred after a year of good health, and a second streptococcus was this time isolated. The two streptococci differed culturally and serologically. No complement-fixing antibodies against the first streptococcus could be demonstrated in the blood at the time of the second infection. Clawson and Bell have quite recently claimed to obtain a streptococcus by blood culture in 50 per cent. of cases of rheumatic fever. Yet they, again, failed to find antibodies in the blood at a serum dilution higher than 1 in 50. On the other hand, Clawson considers that he has produced lesions in rabbits' hearts which were morphologically identical with the Aschoff nodule, by the use of rheumatic strains of streptococci. He therefore concludes that streptococci, generally of the *viridans* type, are responsible for rheumatic heart lesions in man. This vexed question must still be considered as undecided.

In *acute cases of septic endocarditis* the nature of the infection calls for no special comment. Positive blood cultures are forthcoming in nearly all cases, and, as already

remarked, the micro-organisms are of a highly virulent type. Until the role of the streptococcus in acute rheumatism is more clearly defined—whether, for example, it is the primary cause or only present in the disease as a secondary infection—we cannot profitably discuss the question if some of the cases of *chronic septic endocarditis* may not be justly regarded as cases of "malignant rheumatism." Such a conception is only rendered probable by assuming, with Poynton, that the rheumococcus remains latent in the endocardium for, it may be, many years. This seems less probable than that the disease is the result of a new infection grafted upon the old damaged valve, and this view is the one most generally accepted at present.

Positive blood cultures in the chronic cases are, as already mentioned, by no means invariable. In my early series of mixed acute and chronic cases I found micro-organisms in the blood in nearly 90 per cent. of cases at some stage of the disease. Libman gives the same figure for his cases. But in a second recent series of 162 cases at St. Bartholomew's Hospital the number of positive blood cultures was only 47 per cent. This was largely due to the inclusion in the series of a much larger proportion of chronic cases, and especially of twenty ex-service cases; in these twenty cases the number of positive blood cultures was only 30 per cent. This paucity of positive cultures in the ex-service class corresponds with the experience of other observers. The micro-organisms found in these cultures are almost entirely streptococci; the exception is the strange one of Pfeiffer's bacillus, which crops up with extraordinary constancy in the series of all observers, provided the number of cases in any series be not too small.

There seems little reason to doubt that the cocci recovered from the circulation during life, and also those isolated from the diseased endocardium after death, by various observers, have been of the same type, though called by different names. The difference in names has depended upon the different principles adopted in the segregation of the streptococcus and pneumococcus groups. My original description of these cocci was based upon Gordon's well known work, in which the morphological and cultural characters of these micro-organisms were supplemented by biochemical reactions in various sugars. Working in conjunction with Andrewes we were able to trace very close affinities between the streptococci associated with chronic septic endocarditis and the salivary and faecal types as differentiated by Gordon. Schottmüller's nomenclature was based largely upon the fact that these streptococci reacted in a special manner on blood-agar plates; hence his term "*Streptococcus viridans*." Rosenow, on grounds which need not be entered upon here, claimed to have obtained evidence that these comparatively non-virulent cocci are modified pneumococci, and that by frequent passage through animals, and by special anaerobic cultural methods, they could be converted into micro-organisms indistinguishable from pneumococci and possessed of considerable pathogenicity. I am unaware that this work of Rosenow has been confirmed. Libman is content to term the coccus most commonly found in chronic septic endocarditis, "*Streptococcus endocarditidis*." But when we consider questions of pathogenesis it is obvious that the nature and origin of these streptococci become matters of great importance. Too much attention cannot, therefore, be paid by bacteriologists to the life-history of these cocci and to their probable source.

THE BACTERIA-FREE STAGE.

This is perhaps a convenient place in which to refer to Libman's views upon what he terms the "bacteria-free stage" of chronic septic endocarditis. I have already confessed to my inability to accept Libman's concept of the disease we are now considering as being a "subacute" rather than a "chronic" process. I gather that others have the same difficulty. I find that the last edition of Osler and McCrae's textbook of medicine includes two separate paragraphs; one is headed "Subacute bacterial endocarditis," and the other, immediately following it, is headed "Chronic infective endocarditis." But Libman makes it clear that by introducing the term "subacute bacterial endocarditis" he intends it to supersede the older name of "chronic

infective endocarditis," and to include the cases formerly put into this category. I must now confess to another inability to follow Libman when he uses the term "bacteria-free stage" of the disease as being synonymous with "healed stage." This writer speaks frequently of "healed and healing cases" in one and the same term. Now I can understand a "healed" case; there seems no doubt, largely as the result of Libman's own observations, that cases of septic endocarditis do occasionally undergo spontaneous cure, and that the residues of the old infection are found *post mortem*. I can also understand a "healing" case; in many chronic infections we get evidence, both during life and after death, that the lesions show constructive as well as destructive changes—to mention only pulmonary tuberculosis as one example. But to group "healed and healing cases" together under this single term seems to suggest some new type of case the criteria of which have been made by no means clear.

Libman admits that in the so-called "bacteria-free stage" of the disease some degree of pyrexia is often present, that anaemia is marked, that embolism goes on, that Osler's nodes and petechiae appear, that the patients get progressively more and more toxic and eventually die. But is not this passage from a more active stage of the disease to a more passive stage exactly what we see in some, indeed in a good many, other chronic infections?—in chronic pulmonary tuberculosis, again; in lymphadenoma; in chronic *Staphylococcus aureus* pyaemia; in syphilis; in malaria. In chronic septic endocarditis, as in these other diseases, patients not infrequently reach a cachectic stage in which the infection peters out, as it were, at the same time as the patient. The fight has been to a finish and neither party has won. Actually, the micro-organism has won, but only just. It can generally be demonstrated, though perhaps with difficulty, dug in and out of sight; and Libman admits this fact. I instance *S. aureus* infections of a chronic kind in particular as giving us a picture somewhat similar to that which is sometimes seen in chronic septic endocarditis. After a long and tedious illness the patient—cachectic, wasted, anaemic, enfeebled by his prolonged toxæmia—dies exhausted. Blood cultures have been sterile for weeks, even months, and the temperature has been at a much lower level than formerly. At first we were jubilant when these things happened. But they availed nothing, and we became aware that, though the fire of the interaction burned much lower, the disease was still progressing. We make a *post-mortem* examination perhaps; there is no obvious lesion; then, tucked away in some remote corner, we find a collection of inspissated pus—in the sheath of the psoas muscle it may be, or in the centrum ovale of the brain. From these old but still smouldering foci *S. aureus* is recovered in scanty numbers.

We must, of course, distinguish these so-called "bacteria-free" cases from the periods occurring earlier in the disease during which blood cultures are oftentimes negative, yet the patient is obviously in an active stage of his infection. There are possible reasons for these times of relative, or perhaps absolute, abacteraemia. (1) They may be due to the covering over of the colonized bacteria in the valve cusps by a layer of fibrinous material, which for the time being prevents the paying out of cocci into the blood stream. (2) Or they may be the result of a rise in the bactericidal or other immunizing antibodies in the blood, so that the circulation is rendered sterile within the limits of the amount of blood taken for purposes of the culture. Doubtless there are other causes which are as yet hidden from us. Mervyn Gordon has raised the question whether there may not be some filtering mechanism at work; he also reminds us of the great tendency of bacteria to yield to gravity. I should like to add the suggestion that in these cases something akin to the process of centrifugalization may go on, by which the bacteria, which are thrown into the circulation, are sedimented in various peripheral organs, leaving the blood stream relatively free. A close study of the cases makes it more and more apparent how innumerable are the embolic events that take place, and therefore how consonant with actual facts such an hypothesis may be.

DIAGNOSIS.

As the result of my earlier experience I was led to the view that to establish a diagnosis four cardinal points were necessary: multiple embolism, the signs of endocarditis, the isolation of a micro-organism from the blood, and pyrexia. Now that we are more familiar with the clinical picture, and have added certain other well recognized signs, the diagnosis becomes highly probable, though perhaps never quite certain, without the third, and certainly without the fourth, of these features. Thus, signs of multiple embolism, with endocarditis, in a patient having clubbed fingers and an otherwise unexplained anaemia, constitute a syndrome which scarcely admits of any other conclusion. In arriving at a decision, however, it is well to remember what a very grave prognosis a positive diagnosis carries with it in the present state of our ignorance of effective treatment. No doubt we shall be able, in years to come, to detect the disease at an earlier stage of its course, in which case we must be satisfied with less severe criteria. It may even be desirable to treat many patients as suspects, and remain uncertain, in the event of a satisfactory issue, if they were, or were not, larval instances of the disease.

In other words, we must strive to anticipate, rather than merely to recognize when present, the fully developed picture. There are other very suspicious combinations of signs and symptoms than that just given, but, granted that neither pyrexia nor a positive blood culture is essential to the diagnosis, it is impossible at present to construct a syndrome that does not include the feature of multiple embolism; and it is questionable if, once this process is in operation, we are not already too late in our efforts to arrest the disease.

We do not know, unfortunately, if there is an early apyrexial stage in the disease. We certainly do know that, though every case is probably at some time in its course pyrexial, apyrexial periods of one, two, or even three weeks are by no means uncommon during the later stages. Starling tells of an extraordinary instance of prolonged apyrexia lasting seventeen weeks. It is clear, therefore, that the absence of pyrexia at any particular time of observation by no means excludes the diagnosis.

Be the significance of negative blood cultures what it may, it is agreed that the diagnosis can frequently be made without evidence of bacteraemia at the time of examination, and, indeed, even though one or more subsequent efforts are also negative.

Libman has described localized tenderness over the lower end of the sternum with light pressure as a common symptom. I have found this present in several cases, but since I have also found it to be not uncommon in cases of severe anaemia, without evidence of endocarditis, I conclude that its importance in diagnosis depends upon the absence of this latter condition. Such tenderness is sometimes very marked, and very localized, in Addisonian anaemia.

MILD AND RECURRING CASES.

We are beginning to see light on the clinical side, and also on the side of gross morbid anatomy, in relation to the earlier stages of the disease, and this light may soon help in the histological and bacteriological sides by suggesting new lines of research. Several authors have described cases of mild bacteraemia, the cocci being of the same type as those associated with chronic septic endocarditis, and in which the clinical analogies with this latter disease are such as to suggest that they may have been abortive cases of it. Some of the cases have been followed for a period sufficiently long to make sure that they have recovered. It is tempting to consider them instances in which, as it were, the disease, as we usually know it, has missed fire.

Cases of recurrence, too, are being brought to light. I have seen two such cases. In one of these I was very doubtful, when the patient first came under observation, if I was not dealing with a case of septic endocarditis. There were signs of aortic regurgitation, and the patient was admitted to hospital on account of mild pyrexia, purpura, and arthritis. The spleen was palpable. Blood cultures were negative. The man was an ex-soldier with no history of any cause for his valvular disease. After two months' observation he was discharged, being given the benefit of

the doubt. He worked continuously as a postman for twelve months, feeling quite well. He was then admitted again to hospital, pyrexia and joint pains of an erratic kind having returned. The diagnosis of chronic septic endocarditis did not now admit of any doubt. In the other case there was again a clear interval of twelve months of good health between an attack of right hemiparesis associated with mitral regurgitation, slight pyrexia, clubbed fingers, and anaemia, and a second admission on account of a left hemiplegia, which was followed a month later by cerebral haemorrhage. It is possible, of course, that in neither of these cases was the interval between the two periods of observation sufficiently long to exclude the question of very protracted infection with unusually long remissions. But Libman and others have reported cases in which the interval between the attacks has been much longer. So that, unless we again take the view that the coccus can lie dormant in the endocardium over a period of years, we must consider the cases as true reinfections.

THE MECHANISM OF INFECTION.

When we turn to questions of *pathogenesis* we are faced with a whole series of unknown factors. We seem to know a good deal about the mechanism of the disease once the endocardial infection is established, and even our knowledge of the associated bacteria is by no means small, but the initial phases in the process of endocardial colonization are still hidden. We assume, perhaps rather too readily, that the source of the invading and infecting bacteria is one or other of the areas which for convenience we term areas of "focal sepsis." Such areas are conceived of as portals of entry of bacteria into the circulation. These areas have been recorded in many cases of the disease as though the relation between them and the heart infection is actually proved. Blumer has collected these records. It does not surprise us to read that the teeth and the tonsils head the list, that the female generative organs come next, and that the bronchial tract follows. But between the very common finding of salivary streptococci in apical tooth abscesses and the relatively uncommon finding of salivary streptococci in the endocardium there is a wide gulf to bridge. With the whole alimentary tract teeming with streptococci of this and of allied types it is quite a question if the area of focal sepsis is more than an epiphenomenon in the process of deep-seated infection.

If we now consider the mechanism of invasion of the infected valve we are equally in the dark. Does the coccus invade the valve from the coronary route or from the general blood stream bathing the outside of the valve? The argument for and against both routes, though old, is still open. Carey Coombs has quite recently convinced himself that, whereas the rheumatic virus reaches the cusps, and produces a valvulitis from within these structures, the bacteria in septic endocarditis attack them from the blood circulating around the cusps. The author's important work in connexion with the endocarditis of swine erysipelas is adduced in support of his views. But we still lack adequate demonstration of this difference of the modes of invasion in the two diseases. Whereas some authors adduce the fact of extra vascularization resulting from old inflammation as evidence that the coronary route is the likely one in septic endocarditis, others consider the scarring of the tissues resulting from the same process as liable to favour invasion from the surface. Certainly if analogy elsewhere goes for anything, it seems more likely that scarred tissues in this situation would be invaded from the surface rather than from the depths. But this latter hypothesis presupposes an initial septicaemia, or at any rate a bacteraemia, and probably of a massive kind. Of this there does not seem to be any clinical evidence; the disease is very insidious in its onset in nearly every case. Moreover, we are now faced with a difficulty with which the war cases have for the first time familiarized us—namely, that in many of these cases there appears to have been no old valve injury, or none the existence of which was apparent. Yet when we recollect that it is in the hearts which possess minor valve injuries, and not in those in which the valves are seriously damaged, that by preference the disease develops, we must

pause before we conclude that the aortic cusps in these ex-soldiers were above suspicion. In this connexion are to be considered the remarks already made concerning congenital defects, such as fusion of cusps, and the effects of strain upon such mechanically handicapped structures. It is rather a terrible thought, and yet it may well be true, that starting life with two aortic cusps instead of three determines a man's ultimate downfall by means of slow but inevitable sepsis, be the conditions of his life what they may. There are many persons in the possession of relatively good health who have minor degrees of valvular disease with good myocardial tone. Is there any way of ascertaining which of these are to be regarded as candidates for endocardial infection? At present the answer is that there is no such way. It is a point worthy of consideration, for if some observations arose by which such predisposition might be recognized, this would be a matter of great importance.

But if we are still much in the dark concerning the mechanism of the valve invasion and colonization, we are still more in the dark as to why it is that such feebly virulent bacteria gain so firm a foothold and pursue such relentless warfare. Is it mainly the general resistance that is at fault, or is it mainly the local tissue resistance? Does the coccus succeed in immunizing itself against the natural protecting substances of the blood and tissues? These are some of the questions that still await our answers. To which may be added the fact that the process of chronic ulceration in general in the body still holds some mysteries we have never yet explained.

RHEUMATIC AND SEPTIC ENDOCARDITIS COMPARED.

I have spoken of one great contrast between rheumatic endocarditis and septic endocarditis—namely, the great tendency to early and considerable involvement of the heart in the former, and the great freedom from intrinsic disease of the heart in the latter condition. I now turn to another great difference between these two diseases. In rheumatic heart disease we feel convinced that we are dealing with the work of a specific agent, and this conviction is not shaken by some doubt as to the causative nature of the infecting agent in certain cases of mitral stenosis. In septic endocarditis, on the other hand, we appear not to be dealing with a specific disease at all—that is, if we are right in our conclusions that the micro-organisms found to be associated with the disease during life and in the *post-mortem* room represent the only infecting agents present. I say this because, although I do not know that anyone has advanced evidence for such a view, it is just possible that all the bacteria associated with the pyaemic state in which the endocardium and various peripheral organs are concerned are of the nature of secondary infections, the primary infection being as yet unknown, and hardly suspected. But if we assume that the micro-organisms that we deal with every day in the disease are the sole causes of the infection, then we are faced with this striking fact—that the same disease picture may be produced by a variety of different micro-organisms. Even if it be argued that Rosenow's conclusions relative to the association of pneumococci with the disease are not yet accepted, and that the gonococcus cases are not really chronic (though two patients in Thayer's series lived over six months), there still remain, in addition to the streptococcal cases which bulk so largely in the whole number, the cases due to Pfeiffer's bacillus. Between these last-named cases and those due to streptococci there cannot, so far as I know, be distinguished any difference either clinically or by naked-eye morbid anatomy. And yet we know of no affinities whatever between the streptococcal group of micro-organisms and the group of which Pfeiffer's bacillus is a prominent member. But the lack of specificity in the disease would appear to go further than this. Individual cases within the streptococcal group show a strange lack of uniformity when investigated serologically. Kenneth Stone, working in Gordon's laboratory upon complement fixation in streptococcal infections, found that the serum from cases of chronic septic endocarditis gave positive reactions with the homologous cocci obtained by blood culture, with a titre even as high as 1 in 4,800; but that this same serum gave very little cross-fixation

with heterologous cocci (that is, with cocci obtained from other cases), and frequently no cross-fixation occurred at all. It would almost appear, therefore, as though the cases, far from being specific as a group, are specific only as individuals. The bearing of all this upon the difficulties of immunotherapy is obvious.

There is, it seems to me, still another striking fact in connexion with the bacteriology of the disease, and that is the absence of any evidence that more than one strain of streptococcus is present in the same case. Nor has any case yet been described in which streptococci and Pfeiffer's bacillus have both been present. If the source of the endocardial infection is an area of focal sepsis, as is commonly supposed, it seems strange that there should not occur in the vegetations, and in the circulation, at least occasionally, more than one strain of these common invaders. That this is so strongly favours the view that the streptococci are performing the role not of secondary, but of primary, infections.

TREATMENT.

I shall not stay to deal with the treatment in cases of syphilitic disease. In rheumatic endocarditis the treatment is that of acute and recurring rheumatism. Into this again I shall not go, reserving my time rather for considerations that apply to septic cases.

When faced with a case of acute infective endocarditis the treatment is that of the septic focus, when this is present, and also of the pyaemia complicating it. Immunotherapy has perhaps a slightly better chance of rendering assistance here than it has in chronic cases; it should therefore be given a thorough trial. The vogue at present is the process known as immunotransfusion, and it is perhaps too early yet to say what the results of this method are. All cases should, whenever practicable, be treated in the open air.

I now turn to the treatment of the chronic type of septic endocarditis.

In one of his most recent communications Libman is good enough to credit me with being the first to emphasize the importance of *prophylactic measures* in the treatment of this disease. Although there is no doubt he is correct in this, he is kind enough not to point out the paucity of the constructive suggestions which I made under this heading in 1909. I dealt almost entirely with the importance of treating the various forms of oral sepsis, and with considering certain methods by which the streptococci of the intestinal tract might be kept from transgressing the barriers which usually suffice to keep them outside the blood stream. That these measures of preventive treatment are of more importance in patients who have residual endocardial lesions, of whatever origin, than in other persons, will scarcely be questioned. Yet it is by no means an uncommon experience to find devitalized teeth with demonstrable apical sepsis in these patients. The well established sequence of a septic endocarditis arising as a direct consequence of the extraction of such teeth under local anaesthesia, together with the isolation of a salivary type of streptococcus from the blood in such cases, should surely lead to a rule of treatment by the observance of which no dead teeth and no obvious pyorrhoea are permitted to be present in such patients. It is unfortunate that a recent obsession in regard to sacrificing all teeth that are in the least degree suspicious in every patient has militated in the public mind against such a preventive measure being followed in selected cases. The question of septic tonsils is much less simple, because the criteria by which we judge these organs are notoriously vague, whether we consider the matter from the point of view of the general physician, the throat specialist, or the bacteriologist. Tonsils are sometimes condemned because cultures taken from them grow streptococci of the haemolytic, long-chained, or *pyogenes* type, on the ground that this is a more highly pathogenic type than others. But it is obvious, from what has been said, that in the present connexion such a finding should not condemn the tonsils any more than if the cultures yielded the *viridans*, short-chained, or salivary type; if, indeed, the condemnation should be as strong. The present state of our knowledge of

the streptococcus group makes the statement so often occurring in bacteriological reports, that "cultures from the tonsils give no pathogenic strains of streptococci" of no service when we are considering the prophylactic treatment of endocarditis. Until we have more definite guidance along these lines we shall probably act most wisely by deciding the question of the enucleation of tonsils on their general merits rather than upon their bacteriological content.

In the direction of "intestinal disinfection," so called, prophylaxis gropes in even greater darkness. There are problems here which we have scarcely begun to probe, but to think that security from subinfection lies in merely avoiding constipation, good though such advice may be, is to invite a rude awakening. We do not even know for certain that subinfection from the bowel bears any definite relation to the quantitative content of streptococci in this situation, or to the relative proportions of streptococci to coliform bacilli, though both of these things are generally taken for granted. Is it not a fact that we not infrequently make use of these and analogous findings to support a scheme of therapeutics, when the premises upon which such a scheme is based are quite lacking in proof? The suggestion of Besredka and others, that it might be well to employ antigens by the intestinal route in cases in which it is presumed that the initial interaction resulting from infection takes place in this situation, has scarcely received so thorough a trial as it deserves. We may get some help from such a trial. We may also get some help from well controlled observations relative to the effect of different diets upon the intestinal flora. Up till now very little work has been done on this point.

The injunction against undue strain, both physical and emotional, in persons having evidence of slight valvular defects, though theoretically indicated, is not likely to carry much weight. Yet it becomes our duty to give such advice in view of all the facts.

Curative measures now call for consideration.

Chemotherapy, despite the enormous number of drugs that have been tried at one time or another, and which I will not stay to catalogue, has so far been of little real help; and this is true by whatever route the drugs have been used. Yet it must not be concluded that we shall not ultimately find some remedy of a chemical nature which shall assist the tissues in their interaction with the infecting agent; for the crude notion that a chemical remedy can only help in microbial infections by a direct bactericidal action is, of course, no longer tenable. Of late years new claims have been made on behalf of arsenic, and especially when given intravenously. Needless to say, when the arsenobenzol series of drugs arrived they were given full trial in septic endocarditis, but, so far as I can find, without any permanently good results. Of immediately serious results by way of cerebral embolus I saw not a few, and I gather this is the experience of others. I have given Capps's sodium cacodylate treatment a very thorough trial, but have so far seen nothing to lead me to the conclusion that the patient has benefited more than is usual with so good a haematinic remedy as this proves to be in many infections. Capps gives daily injections of the drug intravenously, beginning with 1 grain and increasing gradually up to 5 grains. In all I have treated twelve cases, and I have in half of these given larger doses than Capps has recommended. I have also, following Capps's suggestion, followed up the treatment for many weeks. There is certainly this to be said for the drug, that it is singularly free from ill effects.

I think it is clear, from all we know of the disease, that recovery, whether by the aid of remedies used or occurring spontaneously, must of necessity be very slow if it is to be safe. When we remember the characters of the vegetations, and the ease with which they separate off as emboli, it is obvious that any remedy which acted as quickly as, for example, a *grand lavage* of the blood stream by some reputed blood antiseptic, would endanger death from cerebral embolism. And when we recollect the deep colonization of the infecting micro-organisms in the valves, it is equally obvious that no such lavage is likely to dislodge or kill these, seeing that they are to a large extent outside the direct blood stream.

As little credit can be given so far to measures of *immunotherapy* as to those of chemotherapy. And this applies to all the permutations and combinations of antigen and immune serum that the mind of the immunologist—not a mind lacking in fertility and inventiveness—has so far devised. The latest of these is immunotransfusion, which, though it is claimed that this method raises the bactericidal power of the blood, has not so far been more successful than other methods. A method of treatment which raises the bactericidal power of the blood as tested outside the body gives us no guarantee that it will do this inside the body; or, if it does, that the rise in bactericidal power will be sufficient, within the limits of the method, to turn the scale against the infecting agent and in favour of the patient. These things would be very puzzling did we not know of stranger facts—the fact, for example, that, apart from any immunotherapy whatever, the blood in many cases of chronic septic endocarditis is extremely rich in certain antibodies specific to the micro-organism isolated from the patient's circulation. And yet such patients may, all the time, be losing ground slowly but surely.

In opening a discussion upon chronic septic endocarditis at Cambridge in 1920, when speaking of curative treatment, I raised the point as to whether we ought not to deal with these patients on much the same lines as we follow in cases of chronic tuberculosis, bearing in mind, of course, the difference in the organs affected. I have of late years concentrated more and more upon non-specific measures, as for a disease of "low resistance." I treat as many cases as possible in the open air, with sunlight, natural and artificial. I supplement this by a long series of intravenous and intramuscular injections of sodium cacodylate. Sometimes I have found, as others have, that simple transfusions of blood are of considerable help. These are the only measures I yet know of that seem to give the patients the best chance of overcoming their usually intractable infection.

It remains for me to thank you, Sir, and the Fellows, for your patience in giving me your attention during the delivery of these lectures.

CHRONIC PYLORIC OR DUODENAL ULCER: POSTERIOR GASTRO-JEJUNOSTOMY WITH JEJUNO- JEJUNOSTOMY.

BY

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THE operation of a no-loop posterior gastro-jejunostomy has had a long trial, and, although the ulcer heals, the after-history of these patients, as regards well-being and comfort, is in a very large number of cases unsatisfactory.

A-C' = 3½ in.; A-A = 3 in.;
B-B = 2½ in.; C-C' = 1½ in.;
P-V = 3½ in.

The new pylorus is at A,A, and the dotted line along the duodenum from Vater's ampulla (V) to the jejunal opening at C,C' shows the course of the secretions from liver and pancreas to join the food stream issuing from the stomach at A,A. The two tubes of jejunum, marked by

THE MAKING OF A NEW PYLORUS.

A modification of this operation¹ is jejun-jejunostomy, done at the same time as the posterior gastro-jejunostomy so as to ensure the making of a new pylorus, by which the *status quo ante* as regards the physiology of the parts concerned is brought about.

The illustration represents a horizontal section of stomach and bowel after the operation is completed; for clearness' sake the gastro-colic oval omental attachment is not indicated.

arrows, function at the first part of the duodenum. C' is at a point 3½ in. below the new pylorus (A,A), which is the precise distance that the normal Vater's opening (V) is situated from the normal pylorus (P). A 10-inch loop of proximal jejunum, brought to the surface, gives enough bowel to work with, and no kinking ensues. The extra time required for the second anastomosis is only some fifteen minutes.

In effect, the whole physiological plan of the pylorus and the duodenal exit of the digestive fluids is simply removed some inches to the left. The gastric anastomosis is 3 inches and the jejuno-jejunal 1½ inches long. The patients enjoy very good health afterwards, with no unpleasant after-effects.

I have just learnt that one of the surgeons of the Mayo Clinic has begun to do this operation and intends to report his results.

REFERENCE.

¹ *Lancet*, January 31st, 1920; *Practitioner*, June, 1920; *Epitome*, *New York Medical Journal*, 1920.

GANGRENE IN AN INFANT SEVEN DAYS OLD: RECOVERY.*

BY

W. R. GROVE, M.D.CANTAB.

A PRIMIPARA, aged 33, who had had no miscarriages and been married two years, was, on January 30th, 1925, confined naturally, after an easy labour of six hours, of a female child. On the morning of February 5th the child's right leg was found blue from the knee downwards. The cord had separated the day before, and the umbilicus was a perfectly clean scar without redness; there was no rise of temperature, and the heart appeared normal. There seemed little pain, only a slight whimpering when the limb was handled. The leg was kept warm in cotton-wool, and the blueness gradually decreased downwards, until in about ten days there was a line of demarcation straight across the dorsum of the foot at the base of the toes, but on the sole of the foot it extended in a triangle nearly to the point of the heel. This gangrenous area was dry. It was decided to leave events to Nature, but, with the experience of gangrene in the old, the parents were told to expect a weary waiting of months for the separation of the slough. The mother was unable to nurse the child, but on undiluted milk it thrived apace, so that in each week from the beginning there was a gain in weight. On March 18th I was amazed to hear that the toes had separated, the factor of the child's growth away from the dead part never having entered my head. Within three weeks afterwards, very little more than two months from the onset, the foot was completely healed, the triangle on the sole of the foot having been only skin.

An attempt to get a photograph in the gangrenous stage failed from movement, an indoors time exposure being necessary. But the accompanying illustration in the healed state, when the child was 7 months old, shows the want of toes and the ridge on the sole of the foot. The separated toes have been placed in the Pathological Museum, Cambridge.

It is almost certain that the gangrene was due to an embolus caught at the bifurcation of the anterior and posterior tibial arteries, and that the circulation was re-established except in the toes and sole of the foot.

As to the origin of this embolus there must be some doubt; it is possible that it came from the umbilical veins, by way of the ductus venosus, inferior vena cava, and the right auricle, thence either through a patent foramen ovale, or into the pulmonary artery and by the ductus arteriosus

* A paper read before the Cambridge Medical Society, October, 1925.