A research upon combined mitral and aortic disease of rheumatic origin : a contribution to the study of rheumatic malignant endocarditis / by F.J. Poynton and Alexander Paine.

Reprinted from

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The Quarterly Journal of Medicine

July 1912 (*Vol. 5 No. 20*)

A RESEARCH UPON COMBINED MITRAL AND AORTIC DISEASE OF RHEUMATIC ORIGIN. A CONTRIBUTION TO THE STUDY OF RHEUMATIC MALIGNANT ENDOCARDITIS

By F. J. POYNTON and ALEXANDER PAINE

With Plates 27–29

Section I.

(*a*) *Object of the communication.* We return in this investigation to the consideration of the second statement that we made in our paper upon the causation of acute rheumatism published in the *Lancet* in September, 1900. This statement was to the effect that *acute rheumatism produces a malignant as well as a simple endocarditis.*

At the outset we would insist upon the exact wording of this assertion in order to avoid the mistake being made that we are thought to maintain that rheumatism is the only cause of this condition.

It has been repeatedly proved that there are many causes of malignant endocarditis, and we would venture to make the generalization that any infection which attacks the valves of the heart may produce this lesion, and to express our belief that when an infection which only produces endocarditis exceptionally does happen to attack the valves then the malignant form of endocarditis is prone to result.

On many previous occasions we have commented upon the peculiar attitude that has been adopted to rheumatism, in that it has been almost universally taught that it is a cause of simple or healing endocarditis, but needs the assistance of a secondary infection to produce the malignant form. Surely this is a curious example of seeking a difficult path, when the plain and easy one lies before us.

In this paper we are approaching our subject from a somewhat different point of view to that from which we dealt with it in a former paper ('A contribution to the study of malignant endocarditis,' *Medico-Chirurgical Transactions*, Vol. 85, 1903), for we are here studying a form of heart disease which we believe every one must allow may be the result of the rheumatic infection itself and not of any added infection.

In the course of this communication we shall quote from our former paper which established certain facts that may be lawfully utilized to illustrate our present contention, which is to this effect: *That from a study of severe heart*

disease of rheumatic origin involving lesions to two important valves, we find all gradations between simple and malignant endocarditis, and additional and striking proof of the existence of a malignant rheumatic endocarditis.

We would also add, in opposition to a statement by Horder[1] to the effect that the original distinction between non-infective and infective as applied to endocarditis may be allowed to remain, that such a division is in our opinion a survival of an obsolete pathology only supported by imperfect investigations and conceptions, and as such is a hindrance to advance in the study of heart disease.

(*b*) *Acute rheumatism a specific disease.* We are desirous at this point of dealing with a criticism of our investigations which has been frequently repeated, and has been recently made again at a meeting of the Pathological Section of the Royal Society of Medicine in March, 1912. It is one to this effect, that *we assume the fact that there is a specific disease, acute rheumatism.* It is impossible for any but skilful speakers to answer such a criticism as this in a short debate, but we are prepared to put in writing the reasons for our contentions, to which we firmly adhere and by the truth or falsity of which we are prepared to stand or fall.

The question is one the answer to which necessarily brings us in contact with fundamental conceptions of human disease, and we would urge at once that diseases such as acute rheumatism are not and never will be conditions that can be pigeon-holed into compartments with rigid walls. The farthest one can see clearly concerning such a problem is this: That certain pathological processes may produce results in the human body, which, when they prove fatal, can be studied sufficiently thoroughly, sufficiently accurately, and sufficiently frequently to permit the statement that they clinically and pathologically present a process of disease unlike any other. Such a disease we hold must be built up upon the study of fatal cases, although it may be frequently delimited at the bed-side when not fatal.

It is not in our opinion any scientific objection to the view that we put forward for a critic to quote a case which has been thought by many doctors to be acute rheumatism and yet has proved to be of a different nature because, for example, a staphylococcus has been isolated and the patient cured by a vaccine! What scientific weight can such a statement as that possibly have? We should be the first to allow that we have made and shall make errors in the clinical diagnosis of acute rheumatism, and that other diseases may resemble it very closely. We do not suppose acute rheumatism is the only cause of a transient polyarthritis in man; or that it is the only disease that produces heart affections, or even arthritis and heart disease combined. Twelve years ago we were conversant with these cardinal difficulties in the study of acute rheumatism which from time to time are presented to us by critics as though they were new suggestions. We have, indeed, ourselves pointed out that some cases of infection that result from middle ear disease are almost impossible to distinguish from

[1] *Quarterly Journal of Medicine*, ii. 290.

acute rheumatism. Yet no one would attempt to study any disease by the uncertain light of exceptional cases, for such a procedure would be foredoomed to failure, and it is essential, we think, in studying acute rheumatism to investigate the classical examples of which in our Hospital note-books there are ample records.

The first step that we have believed essential for establishing the specific nature of this disease has been to study side by side post-mortem records and clinical histories of acute rheumatism. In this way we have obtained not only the results of our own experience, but the independent observations of many different skilled physicians and pathologists. The remarkable records at the Hospital for Sick Children, Great Ormond Street, alone contain upwards of 200 fatal cases, and in addition to this we have many examples in older subjects recorded in recent years at St. Mary's Hospital and University College Hospital. Further, we have investigated microscopically on many occasions the important cardinal lesions and the exudations of the disease. Lastly, we have investigated the bacteriology in nearly 100 cases, and studied the experimental lesions.

The outcome of these investigations has been that we hold that there is decisive evidence from clinical and pathological observations of fatal cases that acute rheumatism is one of the most special of diseases in this country—a view we believe to be supported by nearly every physician of eminence who has studied in a Children's Hospital. Evidence such as this is not to be lightly set aside by the relation of unusual cases, or of cases unsupported by accurate clinical and post-mortem investigations.

It is as the infective agent of this specific disease that we claim the diplococcus, and would add that the statement made by critics that various bacteria have been isolated from cases of rheumatism should carry now no real weight. The only evidence we hold that can be now admitted as worthy of consideration is that which brings with it the proof that these various bacteria have not only been isolated, but have reproduced the lesions of the disease, as has the diplococcus. Those who maintain that the cause of the disease is still unknown should in all fairness now, after a period of at least ten years has elapsed, during which positive results have been obtained by others, justify their cause by some slight positive contribution of their own to our knowledge.

In a recent and admirable review of the study of rheumatism during the last decade by Sanderson,[2] our position and that of others who support our views has been described as becoming more isolated. Even if we admit this—which we do not—we would venture to ask of the impartial looker-on, whether scientific inquiry is to be measured by the number of investigators or by the character of the results? As far as acute rheumatism is concerned, with the increasingly isolated group of investigators remain such results as the demonstration of experimental arthritis both acute and chronic, endocarditis simple and malignant, pericarditis, myocarditis, pleurisy, peritonitis, pneumonia, nodule

[2] *Guy's Hospital Reports*, 1911, p. 193.

formations, appendicitis, choreiform movements, large white kidney, and infarctions—all obtained by a micrococcus isolated from the cardinal lesions of acute rheumatism, and most of them previously quite unknown in the experience of pathologists in this country.

Various Types of Rheumatic Infection.

If acute rheumatism is a specific disease, the result of infection with a diplococcus of the streptococcal group, what clinical types of the disease may be reasonably expected to be met with? The answer to this question has important bearing upon our investigation of 100 cases of mitral and aortic disease of rheumatic origin, for we wish to show that this infection is not extraordinary in its behaviour but quite in accord with what may be reasonably expected of such a condition.

Firstly, it may produce a more or less general infection and damage many organs. Sometimes it does this very acutely, but more frequently with a moderate degree of severity. In this group will be found, as is the case with other infections, many examples in childhood. In such, mitral and aortic disease is only one incident, and there are in our list classical examples of such cases which have proved fatal.

Secondly, the severity of the infection may fall on certain organs, notably the heart, or even upon certain parts of the heart, for example the valves.

These lesions may heal and leave scars which in the case of valvular lesions may introduce a new train of symptoms the results of mechanical heart disease. In our list there are convincing examples of this occurrence.

Again, the lesions may heal, or rather let us add appear to heal, almost entirely and yet exacerbate, or arise anew as a result of fresh activity, with the result that we find after death evidences of scarring and activity combined. Thus, thirdly, the active lesions in the valves in such cases may be only incidents in a but renewed general infection, or, fourthly, they may, as we shall hope to show, be the cause of death by a virulence and activity which are recognized under the name of malignant endocarditis.

Fifthly, from the first the endocardial lesions may show this malignancy and be the cause of death.

Such various results of infection as these are in no way remarkable; indeed, as we have previously stated, it would be much more remarkable if they did not occur.

Sixthly, it is only to be expected that in a long series of cases of mitral and aortic disease examples will occur which are exceedingly difficult to group. The result is we arrive at the conclusion that as a consequence of the rheumatic infection we may find every grade, from a primary malignant endocarditis to long healed lesions, which have caused death, not from any active process but entirely from a mechanical disability of the circulatory apparatus, the result of the scarred and deformed valves.

Necessity for considering Mitral and Aortic Disease in Rheumatism as an Event in the History of an Infective Process.

There are few physicians who have not been struck with the paralysing effect of nomenclature in the study of disease. We have here, we think, a very good example of such an occurrence. In looking through records it is brought home to us that a condition such as combined mitral and aortic disease of rheumatic origin is repeatedly looked upon as an example of 'heart disease'. We must emphasize that for our purpose such a conception is practically useless, and moreover it is frequently not correct. The condition is undoubtedly in a sense one of heart disease, and when these lesions represent the scars of some long dead infection such a description is correct, but when, as reference to our list of cases will at once make clear, there are not only valvular lesions but active valvular disease, the condition is not one of heart disease but of active heart disease; that is, it is a phase in the life-history of a prolonged infective process. Our paper rests in great part on this study of these valvular lesions as active events in acute rheumatism, and we shall endeavour to place them in the picture of a rheumatic infection, and not to isolate them under the benumbing title of heart disease.

The combined lesion can be produced experimentally both as the result of a single and of a repeated infection, and in some instances the involvement of the two valves has appeared to be the result of a direct spread of the infection from one valve to the other, the segments being in very close proximity. The usual sequence on account of the greater frequency of mitral disease is for the aortic valve to be affected the later of the two, but we would not deny the possibility of the reverse occurrence, although up to the present we have had no experimental proof in its support.

At the bed-side also we find the two lesions appearing in various ways. Sometimes the aortic disease follows rapidly upon the mitral during a prolonged attack of endocarditis. Sometimes after a pause in the activity of the infection, but before the patient is well enough to leave bed, there is a definite recrudescence with the appearance of an aortic lesion. Again, aortic disease may arise in a subsequent attack, and then it is very difficult to decide whether it is an independent infection of the valve by rheumatism or whether it is that this lesion is recognized by the appearance of new clinical signs, but its origin in reality is a spread from the older mitral endocarditis which has simultaneously reawakened to activity. Lastly, the aortic lesion may be the first event, although this is a less frequent occurrence.

The combination of valvular disease is of interest because it shows that in the young mitral regurgitation due to relative incompetence of an undamaged valve is decidedly rare as a result of aortic regurgitation, for in such case there is almost invariably active disease of the mitral valve also. It is, however, of far greater interest because it suggests *the dawning of a malignant tendency in the endocarditis.* We believe also that in man, as in animals, there may be

a direct spread of infection from one valve to the other, and that when this is the case we have one of the great features of the malignant type. In the post-mortem records of malignant endocarditis emphasis is invariably laid upon the spread of vegetations to the heart wall, to the chordae tendineae, to the musculi papillares, or the wall of the aorta. A direct spread from one valve to another in immediate proximity in no way differs from these occurrences.

The clinical study of rheumatic mitral and aortic disease illustrates well that behaviour of the rheumatic infection in the tissues which we have already foreshadowed.

Thus, first, the valvular lesions may be but one incident in a fatal general infection, as for example in the case of a boy aged 4½ years, who died in a first attack of acute rheumatism after twelve weeks' illness. During life there were polyarthritis, nodules, and aortic and mitral disease with pericarditis. After death, subacute pericarditis was demonstrated with acute mitral and aortic endocarditis. In such cases we are dealing with acute rheumatism invading many tissues.

In the second place, the endocardial lesions may completely heal and the patient die of cardiac disabilities (asystole), aortic or mitral in type, in accord with the predominance of the particular lesion.

Thus, for example, a man aged 42, who had suffered repeatedly from acute rheumatism, came under observation for mitral and aortic disease with dyspnoea and repeated attacks of angina pectoris. There was no fever and death was sudden. The necropsy showed thickened aortic and mitral valves with atheroma of the aorta. There was no active disease, and the course of the case was aortic in character.

Again, a man aged 50, who had suffered from acute rheumatism at 8, 25, 36, and 49 years, had been failing for many weeks with progressive dyspnoea, dropsy, and the other signs of mitral asystole. There was aortic and mitral disease and death ensued. The necropsy showed mitral stenosis with shortening of the chordae tendineae, and calcification of both mitral and aortic valves, proof of a dead infection. The last illness had been afebrile.

Thirdly, death may occur in a recurrent attack of a more or less general rheumatic infection in which once more the valvular lesions are but an incident, but in which after death both recent and old injuries are demonstrable.

Thus, for example, a boy aged 10 years, who had suffered from acute rheumatism at 6, had been ill for twelve weeks before death. During this last illness there had been pericarditis, arthritis, and nodules, and there was also aortic and mitral disease. The necropsy showed recent pericarditis and thickened aortic and mitral valves with, in addition, recent vegetations.

Fourthly, the disease of the valves may in a subsequent attack become the salient feature of the illness and show that persistence and virulence which is described as malignant. Thus, a boy aged 13 years, who had acute rheumatism with severe carditis at 10, was under observation for twenty-four weeks with pericarditis which subsided, and aortic and mitral disease which steadily progressed,

accompanied by high fever and embolisms. The necropsy showed a recently adherent pericardium and malignant endocarditis of both aortic and mitral valves.

Fifthly, from the first the valvular disease may be malignant in type, as in the case of a boy aged 7 years whose sister and mother were the subjects of acute rheumatism, and who himself in an illness of four weeks developed first a polyarthritis, then a rheumatic erythema, and then pericarditis. The necropsy showed recent pericarditis, malignant mitral and simple aortic endocarditis.

Sixthly and lastly, every sort of transitional case may occur, of which we will give three examples:—

(i) A boy aged 16 years, who had suffered from attacks of acute rheumatism at 6, 8, 10, and 12 years, was under observation in his final illness of eight weeks. During this period he developed a polyarthritis which subsided, and the combined valvular lesion with which he was already crippled steadily progressed with high fever and embolisms. During life, and after death, the case was described as a malignant endocarditis, but the vegetations upon the aortic and mitral valves were pointed out as small and resembling those of rheumatic endocarditis.

(ii) A man aged 19 years had suffered from acute rheumatism at 11, 14, 17, and 18. Since the last attack his health had been failing for months, and a sore throat had preceded his final breakdown. Under observation his temperature never rose above 99·5° F., and when sudden death occurred the natural diagnosis was 'heart disease'. The post-mortem examinations showed a calcified mass on the aortic valve with malignant vegetations around it, and malignant endocarditis of the mitral valve.

(iii) The third case is a clinical example only. A male aged 38, who had previously suffered from three attacks of acute rheumatism, was under observation with the combined valvular lesion and cerebral embolism. For six weeks there was persistent fever with gradual asystole, but eventually there followed a slow and partial recovery, the temperature quieting down and the signs of hemiplegia improving. Such a case would be difficult to place with any confidence either as a simple or a malignant type of endocarditis.

This brief outline of salient examples brings us to the end of the introductory division of this paper, for we know that there will be no dispute as to the nature of the first three types we have exemplified, but that over the last three classes, namely the malignant cases supervening on old rheumatic endocarditis, the primarily malignant ones, and the transitional cases, there will be dissension of opinion, and it is these cases that bring to a focus the main issue of this contribution.

In the next section we shall frequently use the term malignant rheumatic endocarditis, but we do not use it, as Horder asserts ought to be done, as connoting rheumatism complicated by streptococcal or other infections of the endocardium. According to this writer, the name is only 'permissible' in that sense; we would, however, modify this statement of his, and we would state that the name malignant rheumatic endocarditis is only permissible when it is used to express the fact that the diplococcal rheumatic infection may produce a malignant endocarditis.

Section II.

I. *The Establishment of a Working Basis for the Thesis.*

It appears to us that the most simple and direct method of presenting our facts is to give first of all examples of rheumatism with mitral and aortic disease which we hold to establish the following claims: 1. That acute rheumatism may cause aortic and mitral endocarditis. 2. That this endocarditis may eventually prove malignant, although coincident with the appearance of this malignancy other non-malignant or simple manifestations of acute rheumatism may appear and quiet down. 3. That the endocarditis in these malignant cases is caused by a strepto-diplococcus indistinguishable from that obtained from simple rheumatic endocarditis. 4. That this strepto-diplococcus will produce in animals on intravenous injection both simple carditis and malignant endocarditis.

Case I. A boy, aged 10 years, was admitted suffering from active heart disease. Twelve months before he had had a severe attack of acute rheumatism, during which both the mitral and aortic valves were damaged. His final illness had commenced six weeks before, with breathlessness, anaemia, and wasting, and shortly after admission pericarditis developed. Two weeks later arthritis of the ankles and knees appeared. There seemed very good reason to look upon this condition as the result of another attack of severe rheumatism, a view favoured by the disappearance of the pericarditis and arthritis. In spite, however, of these signs of improvement the temperature remained high and the child lost ground. The explanation that now seemed feasible was that there was an unusually intractable simple endocarditis in progress, but during the next two months infarctions, sweating, anaemia, and fever pointed to the condition as malignant. Death occurred from sudden heart failure.

The necropsy demonstrated a generally adherent pericardium of recent date, the subsidence of all arthritis, extensive malignant endocarditis of the aortic and mitral valves, and renal and splenic infarctions.

A pure growth of strepto-diplococci was obtained from the valves, indistinguishable from that we have isolated from simple rheumatism. The first rabbit intravenously injected developed polyarthritis and malignant endocarditis of the *aortic and mitral valves*. The diplococcus was recovered in pure culture. The second developed malignant aortic endocarditis; the third, polyarthritis and simple cardiac dilatation; the fourth, malignant mitral endocarditis; the fifth, general pericarditis and polyarthritis; the sixth, polyarthritis only.

It appears to us that this case illustrates the four points we have put forward as rigid tests of our contention. We have the rheumatic origin of the lesion, the non-malignant evidences of active rheumatism during the final illness, and the complete experimental chain of evidence.

The next case (Case II) is not quite so complete because of the absence of a multiple arthritis during the final illness.

Case II. A boy, aged 13 years, had suffered from severe rheumatic fever at the age of 10, leaving him with mitral and aortic disease. For two months previous to his coming under observation he had been ill with precordial pain, dyspnoea, anaemia, and wasting. He was evidently suffering from active carditis, and succumbed after an illness of four months. Throughout the whole of this time there was irregular fever, and there was considerable enlargement of the spleen with other signs of a progressive endocarditis.

The necropsy showed general and recent pericardial adhesions, malignant aortic and mitral endocarditis, and a large spleen with infarctions.

A pure growth of strepto-diplococci was obtained. The first rabbit injected developed a mitral murmur for a while and eventually died many weeks afterwards—when no lesion was forthcoming. No. 2 died of malignant mitral endocarditis with infarctions. No. 3 died with simple mitral endocarditis and dilatation. No. 4 died of fibrinoplastic pericarditis. No. 5 died with general recent adhesion of the pericardium.

II. *Histological Support.*

For many years emphasis has been laid upon the frequency of a history of a previous attack of rheumatic fever in cases of malignant endocarditis, and it is this that has led to the suggestion that antecedent damage to the valves favours the development of the malignant endocarditis.

With this view we are in agreement, but our explanation differs very distinctly from that usually accepted. First of all, however, we would point out that those who have opposed our views upon acute rheumatism have strangely neglected to publish and show any microscopical studies of the valvular lesions of rheumatism and malignant endocarditis in their various phases in man and animals. Yet this omission is, we think, a serious defect in their case, for in experimental endocarditis it is possible to trace every step from the earliest invasion of the valvular tissues to the exuberant malignant vegetation, and in human endocarditis to study nearly every phase of simple and malignant endocarditis and the methods of their healing.

If rheumatic endocarditis is not infective in origin it is remarkable that its lesions are indistinguishable from those of an infective process. If, on the other hand, it is the result of some unknown infection it is interesting to find that microscopy is unable to distinguish between the nature of the results produced by this infection and the malignant endocarditis that may occur in the rheumatic.

It is also interesting to find that in the malignant form numerous streptodiplococci can be demonstrated in the vegetations and are generally admitted to be the cause of the lesion, but that in simple endocarditis, in which the streptodiplococci can also be demonstrated—though in scanty numbers, for simple endocarditis does not kill—the causal nature of these bacteria is brushed aside. This is the more remarkable when it is pointed out that the experimental lesions of simple and malignant endocarditis, when obviously caused in both instances by the diplococcus isolated from the human lesions, show the same variation in the number of diplococci in accord with their nature, a point we demonstrated to the Pathological Society of London in 1900.

Although there may be difficulty in isolating the diplococcus from rheumatic lesions, a fact which has been forced upon us, we may add rather to our surprise, through the reports of other pathologists, we can hardly think that there can be any justification for a failure to demonstrate diplococci in acute simple rheumatic endocardial lesions. This is but a matter of accurate technique and sufficient

diligence, and that this may not seem a boast, we will support it by a quotation from a recent paper in *Heart* by H. G. Butterfield, Graham Research Scholar in University College Hospital Medical School. This writer, undertaking an entirely independent research upon acute carditis and heart-block, of which we were quite unaware, reports thus on the mitral valve of a case of classical rheumatic carditis:

'Bacteriological examination showed the presence of numerous Gram-positive diplococci with a tendency to short chain formation and in some cases to only partial retention of the methyl violet stain used. Some of these organisms were very small, and in general they were smaller than the ordinary streptococcus pyogenes.' In our first paper we pointed out the minute size of the streptococcus and its only relative Gram-staining properties in tissues.

We may add that since seeing his sections we asked him to be good enough to undertake the examination of another classical case in which Graham Forbes had isolated the micrococcus from the pericardial exudation. In this he demonstrated the diplococci in the lesions of acute rheumatic pericarditis.

Why deny the causal agency of these micrococci in the simple lesions and accept it in the malignant, in the face of the positive experimental results that have been published and specimens of which may be seen by any interested person in the Hunterian Museum?

There is, however, another point that is established by microscopy, which is that in the partially healed lesion of rheumatic endocarditis foci of necrotic tissue are found shut off by fibrous tissue or by proliferating tissue cells.

These foci we look upon as areas of danger in which the micrococci may long exist in a latent state. Further, it is, we believe, certain both from pathological study and clinical investigation that the vegetations often described in rheumatism as recent may have been of long standing. Even in a case of fatal carditis where there was much thickening and fibrous change in the mitral valve, we found on section that within the fibrous tissue there were still areas of necrotic tissue present. In such an occurrence there is nothing remarkable when it is remembered that sometimes rheumatic nodules may remain for many months, and that a section through the centre of one of these will show necrotic tissue; and also that in chronic pericarditis the same phenomena can be demonstrated.

The examination of malignant vegetations throws very interesting light on the sequence of events. We need not delay by dwelling upon the well-known fact that in the most active part of the vegetations thousands of diplococci will be found. The point of importance is that in many of the slow cases there are well-marked attempts at cure in the vegetation, and if this process is studied we find that the necrotic areas become less filled with clearly staining micrococci and numerous refringent granules become visible. These are soon extremely difficult to differentiate from the groundwork in which they lie, and at last an area is reached where it is difficult to decide whether the necrotic tissue does or does not contain micrococci. The alteration in the staining properties of these micrococci in rheumatic endocarditis is deserving of close attention, and

we are surprised that our opponents have never commented upon this point, which has such a close bearing upon the presence or absence of micrococci in this condition. Now if we turn for a moment to a study of some phenomena *in vitro* we find some suggestive points. The micrococcus of rheumatism does not thrive on agar-agar—a fact repeatedly ignored. If, however, we sow from this poor culture on to a mixture of bouillon, lactic acid, and milk, and the growth recovers sufficiently to clot the milk, we find that on examination of the amorphous clot numerous micrococci are beginning to appear. At first it is difficult to be sure whether one is looking at milk clot or micrococci, later the micrococci take the stain well, and later still they form obvious chains. This reverse process is very suggestive and leads us to believe that the necrotic tissue in damaged valves may contain micrococci much more frequently than is thought.

Our interpretation of the tendency for malignant endocarditis to occur in damaged valves is, then, that circumstances of increased virulence arise and latent micrococci *in* the valves produce this change in the lesion. This inception of a new virulence is not peculiar to the rheumatic infection.

Even these results of microscopy do not exhaust the valuable assistance that can be obtained from this branch of inquiry, and we must confess to a slight feeling of injustice when a distinguished pathologist at a public meeting criticized our investigations as largely dependent upon cultures from the throat, which, he maintained, were open to the most serious error.

Such cultures undoubtedly are, and our work in this direction was not attempted until we had isolated the micrococcus from all the important lesions and studied it by experiment in culture and in the human and animal tissues. The last points brought out by a study of the microscopy are these: that in some cases of very acute simple rheumatic endocarditis, such as occur, for example, in rare cases of fatal chorea, the vegetations, although minute, contain within them vast numbers of the micrococci. Such a section is indistinguishable from that through a malignant vegetation, and we have shown such examples on more than one occasion. Again, it is not rare to find in a fatal malignant endocarditis of the aortic and mitral valves simple vegetations upon one and malignant upon the other. On this account we have maintained that the essence of malignancy is not the size of the vegetations but the number and relative virulence of the micrococci, a statement borne out by the undoubted fact to be recognized in our series, that a case which has been diagnosed as malignant may at the necropsy only show minute vegetations.

III. *Support from Blood Cultures.*

We must now turn to the results of blood cultures which are taken during life in cases of acute rheumatism and malignant endocarditis. These have in our opinion been made responsible for statements which appear to us hardly justified by facts, for they require a very open-minded consideration of the pathological processes in acute rheumatism. To us the actual results that are obtained, far

from militating against the view we hold upon the causation, lend distinct support. If we interpret the reasoning of our opponents aright it is as follows: In many cases of malignant endocarditis a streptococcus is obtained by blood cultures, but in simple acute rheumatism the results are negative, therefore malignant endocarditis in the rheumatic is an epiphenomenon. We cannot accept these premisses or their interpretation. First let us ask the unbiased inquirer to picture the exact nature of the processes in acute rheumatism and we will postulate the original infection as tonsillar in origin. There is at once a gap in our knowledge which is not likely to be easily bridged over, and that is any idea of the number of micrococci which gain access to the blood stream. It is conceivable in the predisposed that a small infection only is requisite, and that this original supply multiplies in the local lesions. We do not yet know the number of micrococci that are sufficient in such people to produce a definite lesion; probably they are very few. This, however, is clear, that acute rheumatism consists of a number of *local foci* of infection in the tissues, and is not a general septicaemia. Further, there is great resistance to the disease, and the bacteria are rapidly destroyed in the blood and in these tissues. Now this being the case, it seems to us exceedingly unlikely that the withdrawal upon one or two occasions of some 5–10 c.c. of blood from the general circulation is going to yield a positive result. Why should it? If such an event were the rule we certainly should need to recast the pathology of this infection. Nevertheless in very severe and virulent cases with many grave lesions and evidences of systemic poisoning a positive result might be obtained. This is precisely our own experience, for all the cases of acute rheumatism in which we have succeeded have been of that type. Thus, for example, a girl aged 17, the victim of chorea at 12, and rheumatic fever at 15 years of age, was seized with acute illness commencing with sore throat, multiple arthritis, and purpura. She was admitted under Dr. D. B. Lees for fever, multiple arthritis, severe purpura, and general carditis, pericardial friction appearing eight days after admission. Venesection was ordered on two occasions, and on both a pure culture of strepto-diplococci was obtained. Three months later the patient had so far improved as to be allowed on a couch, but asystole gradually developed and death ensued.

The post-mortem examination showed recent pericardial adhesions; the mitral aortic and tricuspid valves were all thickened, but there were no recent vegetations, still less evidences of malignant endocarditis, recent or old. The cause of death was myocardial disease from the severe carditis.

Here is proof that during the acute course of a severe rheumatic fever strepto-diplococci can be isolated from the circulation, and incidentally conclusive evidence that such a result was not due to agonal infection. This result is one of very real importance, for it disproves the loose statement that is sometimes heard, that the isolation of bacteria from the blood in active heart disease is proof of malignant endocarditis.

We must add, though it is perhaps obvious, that to look upon a positive

culture of streptococci from the blood in a case of malignant endocarditis as evidence that the infection is not rheumatic is, in our opinion, quite unjustifiable.

The rheumatic diplococcus in fluid media tends to become streptococcal in character, and believing, as we do, in a rheumatic malignant endocarditis we should expect a streptococcus might be obtained in such cases. We would venture to add that the great majority of investigations in this country upon malignant endocarditis stop short of throwing any real light upon the essential point in dispute, for they almost always end either with the statement that a streptococcus was isolated, or with some primitive remarks upon the morphology, which we look upon as valueless, as we note also does Beattie, or with an attempt at classification by some laboratory tests *in vitro* which we and others cannot accept. What more, it may be fairly asked, would we demand? Our answer is, a careful series of experimental and histological investigations. If as a result of these both malignant endocarditis and simple rheumatism result, the answer can be given as nearly as is possible in the present stage of our knowledge. Experimental proofs far outweigh in our opinion tests *in vitro*.

We have had other cases of acute rheumatism which have recovered and from which we have isolated the diplococcus from the blood stream, but this one, from the fact that there was a necropsy, stands out as a clear proof of the nature of illness.

When we have a malignant endocarditis in rheumatism we have an unusual situation to deal with, in that there is then a focus teeming with micrococci actually impinging on the general circulation. Under such circumstances it is only to be expected that blood culture will prove to be positive in a far greater proportion of attempts, and if such were not the case we should have also to recast our views upon the pathology of this affection. Yet even in these circumstances, if the disease is of low virulence and the blood examination be made early, repeated negative results may be obtained by skilled bacteriologists—an event which is again only to be expected, but does not justify the assertion that the case is not malignant.

It is clear that we differ in one important respect from our opponents upon this question of blood culture, for we dispute the statement that results in *acute* rheumatism are *always* negative.

IV. *Additional Evidence from a Study of the Series of* 100 *Cases.*

We believe now that we have reasonably established a claim to adopt this attitude toward cases of malignant endocarditis which are associated with previous acute rheumatism or which commence as attacks of rheumatism, viz. that the onus of proof that such are not rheumatic rests with those who deny that such a condition exists.

It must not be expected that in this series of 100 examples of mitral and aortic cases from various sources complete chains of evidence are to be forth-

coming, seeing that few physicians look upon the malignant types from our point of view, and that no bacteriologist, unless devoting himself to such a special study, will be likely to have made more than the routine investigation of the blood or vegetations. Then again, in the non-malignant cases the lesions have often been considered as examples of heart disease and no particular stress laid upon them as phases in a prolonged rheumatic infection. Our evidence must then be of necessity fragmentary, but it is lawful for us, we think, to build up our thesis upon the carefully prepared basis of our complete investigations—that is, upon the four claims set out at the beginning of this section, strengthening the position by the aid of numerous other important fragments of evidence. It remains for any opponent to demolish the structure by bringing forward equally clear evidence that cases of this type are due to some other cause which is clearly of a different nature to the one we claim.

In order to avoid any suspicion that we are now trying to evade a plain issue, we will illustrate the character of our evidence by concrete examples of malignant endocarditis. The first case we quote is for the purpose of showing that we have weighed our evidence in every incomplete case.

A child, aged 4 years, had been ill ten days with arthritis of the shoulder, hips, and wrist joints; high fever and mitral disease. Pneumonic signs developed and death occurred.

In our opinion, if we published such a case as this as an example of a virulent first attack of rheumatism we should deserve the most drastic criticism.

The necropsy showed periostitis of the right femur, multiple suppurative arthritis, suppurative pericarditis, abscesses in the muscles, and early mitral disease. The *Staphylococcus pyogenes aureus* was isolated and was the cause of the illness.

On the other hand, a girl aged 11 had an attack of acute rheumatism at 9 and again at 10 years. Her final illness showed active carditis with persistent fever; no infarctions were observed. A strepto-diplococcus was isolated from the blood and at the necropsy malignant aortic disease was discovered with acute mitral of the simple type. Both valves showed former disease. The other viscera accorded with the diagnosis of a rheumatic infection. Such a case we claim to be rheumatic, until others can bring more convincing evidence to the contrary.

There is a very close clinical and pathological similarity in many of these cases of malignant endocarditis which becomes apparent from the short details of twenty-five examples that occurred in our series, and we feel justified in claiming some cases upon such clinical or clinical and pathological evidence, admitting at once that the proof is not complete, but believing the explanation as by far the most probable.

Case I. A man aged 27 years had chorea as a boy, and an attack of rheumatic fever at 26. He never laid up during the attack, but struggled on with his work, gradually losing ground. Compelled at last to give in, nine months after the neglected illness, he was found to have aortic and mitral

disease with fever and died in under a fortnight. The necropsy showed malignant aortic and mitral disease and evidences of previous cardiac rheumatism.

This case we would explain as a rheumatic malignant endocarditis, probably produced by neglect of the acute rheumatism, an explanation which would necessarily fail if opponents can produce a series of examples of such cases for which a better solution can be given. We think that in this case also the endocarditis had probably been active the entire nine months and was only under observation in the terminal phase.

Case II. The next case, which is of interest as an aortic and mitral one that cannot be included in our series, illustrates the difficulties that have to be encountered in any attempt at the study of disease in man, and to which we are fully alive.

A woman, aged 28, had suffered from rheumatic carditis after scarlet fever as a child and had never been well since her confinement thirteen months before. At the time of her confinement there was fever. After ten weeks of acute illness with purpura, paroxysmal fever, multiple embolisms, and progressive weakness she succumbed. No organism was isolated. The necropsy showed large vegetations, some with calcareous deposits in them, on the aortic valve and the anterior flap of the mitral. There were no abscesses, but white infarcts. Those who claim that this was a secondary infection of septic nature dating from the confinement have as strong evidence in their favour as those who would suggest that there was a lurking rheumatic endocarditis, which, in the puerperal state, awoke to virulence. The data are therefore insufficient and the case valueless on this account.

There is another difficulty to be faced over the determination of the nature of a carditis which is from the first malignant and is apparently the solitary lesion, or almost so. No one disputes the occurrence of a primary simple rheumatic endocarditis, that is, a pure cardiac rheumatism—and we naturally go a step further and ask, if this is admitted, why deny the possibility of the same, but in a malignant form, occurring in a first attack of rheumatism? Experiment proves that the rheumatic organism can produce malignant endocarditis in a previously healthy valve.

Example I. Thus, for example, a child of fourteen years who gave no history of previous illness was seized with a sudden hemiplegia. There were irregular fever and wasting for seven weeks, and evidence of mitral disease. Blood culture was negative. Malignant mitral endocarditis and old mitral disease were present with infarctions.

This was not a mitral and aortic case, but even if it had been we should not have included it in our series for lack of data. Nevertheless, it is most probable that this was an example of malignant rheumatic endocarditis.

Example II. The ground is far safer in the following example, already quoted in the first section, of a boy aged 7 years, whose mother and sister were the subjects of acute rheumatism, and who himself in an illness of four weeks developed polyarthritis, a rheumatic erythema, and then fatal pancarditis. Simple aortic and malignant mitral disease were found with pericarditis and the strepto-diplococcus isolated. In this case we have other manifestations of acute rheumatism. Such a case we look upon as undoubtedly rheumatic and as a link with that group which for the present purpose we may call transitional, in that they are clinically on the border line between simple and obviously malignant rheumatic endocarditis.

Example III. Again, a girl of nine years had been ill four months with moderate and persistent fever. Polyarthritis had developed early in the illness and passed off; then severe mitral and aortic disease developed, with an enlarged spleen and multiple embolisms. After death, malignant aortic and mitral endocarditis was present.

We are quite aware, as one of the cases we have chosen has illustrated, that a polyarthritis in a child need not be rheumatic. A transient affection of the joints such as occurred in the above case is, however, much more suggestive of acute rheumatism than any other disease. When a series of cases of this kind is studied and all the evidence we have put forward deliberately weighed, we believe that we are justified in asking that those who dispute the nature of such an arthritis and endocarditis should produce definite facts in support of their contention, and not generalize from the well-known fact that there are many causes of arthritis.

We repeat that the preceding cases have been quoted in order to show that now that we are dealing with examples of malignant endocarditis which have not been completely investigated we have not assumed that they are necessarily rheumatic, but have balanced the evidence both for and against this view. The appended list from our series given in brief will enable the reader to form his own opinion upon the value of our evidence. We may add that nine examples of malignant endocarditis have been excluded because they were obviously the result of other infections, and fifteen were of uncertain nature and open to grave criticism.

It is very interesting to find in the list below all grades of virulence in the rheumatic process, and there are some cases which lead us to the next group. This is, we admit, quite an artificial one and called by us transitional because it bridges over the gap between the certainly malignant and the third group, which contains examples of acute rheumatism showing damage to the mitral and aortic valves of the simple type. As we pass to the transitional group the conclusive evidence becomes more and more difficult to obtain, because recovery is more likely to occur, and among these examples it may well have been that some were in reality of the malignant type and others of the simple. It is, if our view is correct, much more scientific to abandon these two terms simple and malignant and to substitute for them active rheumatic endocarditis. Such a term is much more satisfactory from every point of view, for it is less alarming to the patient; it represents more accurately the true pathology and in no way blinds our eyes to the meaning of this activity when it reaches the degree in which the embolic phenomena and consequent systemic poisoning show that life is clearly threatened. Possibly the objection may be raised that such a condition of malignancy is utterly unlike any other manifestation in rheumatism, but we would point out that no other severe lesion in this disease could run a parallel course, however malignant it might be, for no other rheumatic lesion stands in the same relation to the general blood stream.

There is a statement that has been made about the relation of an attack of malignant endocarditis to previous rheumatic heart disease which we would

traverse as a very misleading one. It is to the effect that the two conditions, though associated, are as a rule quite independent of one another. Our series shows that there may be every variety of relation from immediate to remote, and we would add that because the relation is a remote one it is no proof at all that the malignant process is non-rheumatic. If any statement can be made about such cases it would be that the final condition, other things being equal, is more likely to be rheumatic than the result of any other infection.

Analysis of 100 *Cases of Rheumatic Aortic and Mitral Disease.*

At this point, before we give the first table of cases illustrating rheumatic mitral and aortic lesions, it will be convenient to give a brief analysis of the complete series of 100.

1. *Sex.* 51 were females and 49 males.

2. The age incidence was as follows :

1–10 years . . .	15 per cent.
11–20 „ . . .	32 „ „
21–30 „ . . .	23 „ „
31–40 „ . . .	15 „ „
41–50 „ . . .	10 „ „
51–60 „ . . .	3 „ „
61–70 „ . . .	1 „ „
71–80 „ . . .	1 „ „

3. *Clinical groups.*

I. Cases developing from the first or in subsequent attacks malignant endocarditis, 25.

II. Cases on the border line between malignant and simple endocarditis, at least 13.

III. Cases illustrating acute rheumatic simple endocarditis, either as an incident in a widespread infection or as the predominant lesion, 33.

IV. Cases illustrating mechanical disabilities from the results of scarred valves :

A. Symptoms chiefly aortic : 7 cases.

B. Symptoms chiefly mitral : 22 cases.

4. *Fatal cases.*

44 cases were fatal—and some of the others who left the hospitals were taken away on account of their hopeless condition.

23 of the 25 examples of malignant endocarditis in Group I succumbed, and the remaining 2 only returned home in a dying condition.

4 of the 13 cases in Group II were fatal, but this group is an artificial one, made for the purpose of exposition, and is not to be looked upon as an entity.

11 of the 33 in Group III were fatal.

6 (2 in Group A and 4 in Group B) were fatal of the 29 cases in Group IV.

5. Bacteriological evidence is necessarily incomplete, for in the majority of cases none was made. 12 positive results were obtained in the 25 malignant cases and 6 were reported negative. The comparative success in this group is entirely in accord with the view of the pathology we have put forward.

Negative results in the simple rheumatic cases (Group III) are the rule, but there are exceptions. We would repeat that a single or even two such examinations of the blood are but little evidence of the presence or absence of an infective process when the result is negative, and that in our opinion far too much weight has been laid upon the occurrence of these negative results when the morbid processes in acute rheumatism are thoroughly realized.

6. The relation of the final illness, when fatal, to the last attack of rheumatism can be readily studied from our lists. The facts thus obtained are only relative, for, when a patient has been the victim of repeated attacks of acute rheumatism, the more closely the history is investigated the more frequently will be found evidence of some activity of the rheumatic processes between the definite attacks: these minor attacks are frequently not recorded and not mentioned by the patients.

7. All the observations upon the duration of the illness are also only approximate, but they serve to illustrate how prolonged the illness may be and how difficult it is to ascertain the commencement or the end of the active processes.

8. We would lay special stress upon the following histories from the groups of the malignant cases. First, three in which the malignant process dated from the first illness; two in which it followed upon an attack of rheumatism six months before, from which illnesses the patients had never really recovered; one in which there was a continuous history of failing health for twelve months after the fourth attack of acute rheumatism; one in which the patient neglected a previous attack of rheumatism which had occurred less than a year before and after which he had been ill fed and had kept at work; one in which there had been failing health following a rheumatic polyarthritis five months previously.

These 8 cases out of a series of 25 show the close relationship of the rheumatic process to malignant endocarditis. 9 more illustrate the malignant endocarditis emerging from other and transitory symptoms of acute rheumatism. Thus 17 of these 25 cases show a close relationship to the occurrence of acute rheumatism.

Group No. I.

Mitral and Aortic Cases Malignant in Type.

No. 1. Male, aged 10. **History of acute rheumatism** at 9 years. **Main symptoms of final illness**: Admitted with mitral and aortic disease—developed transient polyarthritis and pericarditis. Later infarctions, persistent fever, &c. **Approximate duration**: 18 weeks. **Bacteriology**: Strepto-diplococcus isolated from valves. **Result**: *Death*. Malignant mitral and aortic, recent pericardial adhesion, white infarctions in spleen and kidneys.

No. 2. Male, aged 13. **History of acute rheumatism** at 10 years. **Main symptoms of final illness**: Mitral and aortic disease, transient pericarditis. Infarctions and persistent

high fever. **Approximate duration**: 24 weeks. **Bacteriology**: Strepto-diplococcus isolated from valves. **Result**: *Death*. Malignant mitral and aortic, recent and old pericarditis, infarctions.

No. 3. Male, aged 16. **History of acute rheumatism** at 6, 8, 10, and 12 years. **Main symptoms of final illness**: Mitral and aortic disease, transient polyarthritis, fever, infarctions. **Approximate duration**: 8 weeks. **Bacteriology**: Strepto-diplococcus isolated. **Result**: *Death*. Malignant in the clinical course and in the post-mortem evidence of infarctions, but the vegetations on the two valves resembled those of *severe simple endocarditis*.

No. 4. Female, aged 37. **History of acute rheumatism** at 23 years. **Main symptoms of final illness**: Polyarthritis (subsiding), aortic and mitral disease, enlarged spleen, high fever, progressive course. **Approximate duration**: 18 weeks. **Bacteriology**: Strepto-diplococcus isolated from blood stream. **Result**: *Death*. Simple aortic endocarditis. Malignant mitral. Infarctions in the spleen.

No. 5. Male, aged 7. **History of acute rheumatism**: First attack. **Main symptoms of final illness**: Polyarthritis, pericarditis, erythema multiforme, acute aortic and mitral disease, high fever. **Approximate duration**: 4 weeks. **Bacteriology**: Strepto-diplococcus from pericardial fluid. **Result**: *Death*. Sero-fibrinous pericarditis, acute simple aortic malignant mitral endocarditis.

No. 6. Female, aged 14. **History of acute rheumatism** at 12 and 13 years. **Main symptoms of final illness**: Transient polyarthritis, mitral and aortic disease with continuous fever, evidences of infarction and nephritis. **Approximate duration**: 6 weeks. **Bacteriology**: Negative. **Result**: *Death*. The endocarditis was in character of the simple type; the lesions *qua* infarctions and nephritis, and the clinical course, were of the malignant type.

No. 7. Female, aged 21. **History of chorea** at 7 years; **acute rheumatism** at 20 years. **Main symptoms of final illness**: Mitral and aortic disease with irregular fever, infarctions, and nephritis. **Approximate duration**: 16 weeks. **Bacteriology**: No report. **Result**: *Death*. Malignant type of vegetations on the mitral valve. On the aortic and tricuspid valves small vegetations.

No. 8. Female, aged 37. **History of acute rheumatism** as a child and 6 months before final illness. **Main symptoms of final illness**: This illness imperceptibly followed upon an attack of rheumatic arthritis 6 months before. There were aortic and mitral disease. Moderate intermittent fever and infarction. **Approximate duration**: Gradual; probably 6 months. **Bacteriology**: Negative. **Result**: *Death*. Malignant endocarditis of the mitral and aortic valves with infarctions in spleen.

No. 9. Male, aged 19. **History of acute rheumatism** at 11, 14, 17, and 18 years. **Main symptoms of final illness**: This patient had never recovered from his last attack of acute rheumatism, but his symptoms increased after a sore throat, being those of mitral and aortic disease with slight fever never above 99·5° F. Sudden death occurred and the case was not suspected to be malignant. **Approximate duration**: Gradual over 12 months. **Bacteriology**: None made. **Result**: *Death*. Malignant mitral endocarditis recent and some vegetations on the aortic segments which were thickened and calcified.

No. 10. Male, aged 50. **History of acute rheumatism** at 42 years. **Main symptoms of final illness**: An illness of some months' duration with transient polyarthritis in the articulations of the fingers. Aortic and mitral disease, later infarctions and purpura. The pyrexia persistent but at first mild, gradually increased in severity. **Approximate duration**: Some months. **Bacteriology**: Strepto-diplococcus from the circulation. **Result**: *Death*. Malignant endocarditis of the mitral, aortic, and tricuspid valves.

No. 11. Female, aged 16. **History of acute rheumatism** at 12 years. **Main symptoms of final illness**: A long illness with polyarthritis, persistent fever, aortic and mitral disease, and infarctions. **Approximate duration**: 14 weeks. **Bacteriology**: Strepto-diplococcus from the circulation. **Result**: *Death*. No necropsy, but a case of the malignant type.

No. 12. Female, aged 11. **History of acute rheumatism** at 9 and 10 years. **Main symptoms of final illness**: A comparatively rapid case in which there was high fever and severe aortic and mitral disease. **Approximate duration**: 7 weeks. **Bacteriology**: Strepto-

diplococcus isolated from circulation. **Result**: *Death*. Small vegetations on the mitral, malignant on the aortic valve. No infarctions.

No. 13. Male, aged 27. **History of chorea** as a boy; **acute rheumatism** at 26 years. **Main symptoms of final illness**: During the attack of acute rheumatism at 26 the patient would not rest but persisted with his work—steadily losing ground with cardiac symptoms until within 10 days of his death. During this time there was fever with severe mitral and aortic disease. **Approximate duration**: About 9 months; 10 days' acute illness. **Bacteriology**: None made. **Result**: *Death*. Malignant aortic and mitral endocarditis.

No. 14. Female, aged 16. **History of acute rheumatism** at 12 years. **Main symptoms of final illness**: Admitted with multiple arthritis, which subsided, and also mitral and aortic disease. For some 3 months there was high fever. The spleen enlarged and was tender. **Approximate duration**: About 12 weeks. **Bacteriology**: None made. **Result**: *Death*. No post-mortem.

No. 15. Male, aged 11. **History of acute rheumatism** at $7\frac{1}{2}$ years. **Main symptoms of final illness**: A case of progressive mitral and aortic disease—pericarditis with transient polyarthritis, infarctions, enlarged spleen, and irregular fever. **Approximate duration**: 11 weeks. **Bacteriology**: Strepto-diplococcus from blood stream. **Result**: *Death*. Recent pericarditis. Malignant mitral and small aortic vegetations.

No. 16. Male, aged 13. **History of acute rheumatism** at 7 years. **Main symptoms of final illness**: A case of progressive mitral and aortic disease with irregular fever and infarctions. **Approximate duration**: 17 weeks. **Bacteriology**: Negative. **Result**: *Death*. Aortic malignant vegetations, mitral small vegetations.

No. 17. Female, aged 9. **History of acute rheumatism**: First attack. **Main symptoms of final illness**: Admitted with multiple arthritis and mitral and aortic disease; there was moderate irregular fever throughout. The spleen enlarged, and emboli occurred, finally cerebral haemorrhage. **Approximate duration**: 16 weeks. **Bacteriology**: None made. **Result**: *Death*. Malignant aortic and mitral endocarditis.

No. 18. Female, aged 8. **History of acute rheumatism**: First attack. **Main symptoms of final illness**: Ill for 3 weeks with acute heart disease. **Approximate duration**: 3 weeks. **Bacteriology**: Strepto-diplococcus from aortic valve. **Result**: *Death*. Recent small vegetations on mitral and tricuspid, larger on aortic.

No. 19. Female, aged 17. **History of chorea** and **morbus cordis** at 12 years; **acute rheumatism** at 15 years. **Main symptoms of final illness**: An acute illness with typhoidal character of fever, commencing with a stiff neck. Delirium, purpura, and infarctions followed mitral and aortic disease. **Approximate duration**: 4 weeks. **Bacteriology**: Strepto-diplococci from blood stream. **Result**: *Death*. Extensive mitral malignant endocarditis spreading on the anterior flap of mitral and the neighbouring aortic cusp. Infarctions in spleen and kidneys.

No. 20. Female, aged 24. **History of chorea** at 8, 13, and 15 years. **Main symptoms of final illness**: Six months previously acute rheumatic arthritis, since then never well, severe aortic and mitral disease—persistent irregular fever, infarctions in spleen and kidneys. **Approximate duration**: 8 weeks. **Bacteriology**: Strepto-diplococcus from blood. **Result**: *Death*. No post-mortem.

No. 21. Female, aged 48. **History of acute rheumatism** at 38 years. **Main symptoms of final illness**: Failing health for 12 months—signs of cardiac asystole with irregular fever and aortic and mitral disease. **Approximate duration**: Gradual. **Bacteriology**: None. **Result**: *Death*. Malignant endocarditis, aortic and mitral.

No. 22. Male, aged 28. **History of acute rheumatism** at 18 years and minor attacks since. **Main symptoms of final illness**: Acute illness—typhoidal in character, high fever, aortic and mitral disease with multiple embolism. **Approximate duration**: 6 days' acute illness. **Bacteriology**: None. **Result**: *Death*. Malignant aortic and mitral disease.

No. 23. Female, aged 27. **History of acute rheumatism** at 13 and 17 years. **Main symptoms of final illness**: Failing health for 8 months with moderate irregular fever. Aortic and mitral disease and renal and splenic infarctions. **Approximate duration**: 5 weeks' acute illness. **Bacteriology**: Negative. **Result**: *Death*. No post-mortem.

No. 24. Female, aged 12. **History of acute rheumatism** at 7 years. **Main symptoms**

of final illness: Mitral disease, later developed aortic regurgitation with high irregular fever and haematuria. **Approximate duration**: 10 weeks. **Bacteriology**: Negative. **Result**: Left with the diagnosis of malignant endocarditis.

No. 25. Female, aged 32. **History of acute rheumatism** and **chorea** as a child. **Main symptoms of final illness**: 5 months' history of pains in the joints and limbs, 6 months under observation with irregular fever, aortic and mitral disease, pallor and emaciation. **Approximate duration**: 11 months. **Bacteriology**: Negative. **Result**: Left with active fever thought to be malignant.

Group II.

Transitional Cases.

When experimental endocarditis is produced with the diplococcus, whether isolated from a simple or malignant rheumatic endocarditis, every grade of severity may result. Recovery may occur or speedy death, and vegetations of all sizes may develop. It is impossible when dealing with this experimental endocarditis to justify the use of the terms 'simple' and 'malignant', and it is evident enough that the particular result is a question of the virulence of the cardiac infection. If this is the case with a small animal such as a rabbit whose cardiac valves are so minute and whose resistance is so comparatively weak, it is much more evident in man, in whom the resistance to the rheumatic infection is so considerable and in whom the infection we can hardly believe occurs in such a gross fashion as by the method of intravenous inoculation. One link, however, in the chain is necessarily wanting in human pathology. We are not able, when we wish to observe the particular phase of an endocarditis, to look and see.

Transitional cases of rheumatic endocarditis, by which then we imply cases hovering on the border-line of the divisions, simple or non-infective, and malignant or infective endocarditis, are of frequent occurrence.

In records we repeatedly meet with cases which are thought to be malignant and have quieted down, or have been considered simple and proved to be malignant. From time to time a post-mortem examination shows us evidence of an old malignant process in a valve by the presence of a large calcified vegetation. There is, however, no necessity for this particular evidence, for the malignancy does not depend upon the size and shape of vegetations but rather upon the virulence and number of the infective agent.

As an example in illustration may be quoted the following case: A girl of twelve had suffered from an attack of acute rheumatism three months before she came under observation. From this attack she never thoroughly recovered and a relapse of polyarthritis occurred, with a slowly progressive endocarditis of the mitral and aortic valves. When death occurred five months later from cerebral embolism, a calcareous mass of vegetation was found upon the cusp of the aortic valve, and on the thickened mitral valve there were small recent vegetations.

This group of transitional cases is purely artificial and is not likely to content any one, for it is built up partly upon clinical, partly upon experimental,

and partly upon pathological evidence, and in some cases reliance has to be placed upon one source, in others upon another source of evidence.

We have, we repeat, only used the term here in order to show how advisable it is to abandon the terms 'simple' and 'malignant' as applied to rheumatic endocarditis, and by the formation of such a group to do what little we can to break down the barrier caused by the terms 'infective' and 'non-infective' endocarditis.

The examples that we give in this group can be supplemented by others in Group I and Group III.

Group No. II.

Transitional Cases. Linked to Group I by Cases 3, 6, 12, *and* 18 *in that Group.*

No. 1. Female, aged 10. **History of acute rheumatism**: First attack. **Main symptoms of final illness**: Admitted for multiple arthritis and heart disease. Ran a course with moderate irregular fever. The spleen enlarged and the mitral and aortic lesions proved fatal. **Approximate duration**: 11 weeks. **Bacteriology**: None made. **Result**: *Death.* The vegetations on the mitral and aortic valves were quite small, but the condition of the spleen and course of the case were in accordance with malignant endocarditis. There was no pericarditis.

No. 2. Female, aged 12. **History of acute rheumatism**: An attack 3 months before, never well since. **Main symptoms of final illness**: For many weeks slowly losing ground with multiple arthritis. Aortic and mitral disease. Fever for the last 3 weeks continuous, and finally cerebral embolism. **Approximate duration**: 20 weeks. **Bacteriology**: Negative. **Result**: *Death.* The mitral valve was thickened and there were some recent small vegetations. The aortic showed a calcareous mass on one of the segments—suggesting a healed malignant vegetation.

No. 3. Male, aged 46. **History of chorea** at 9 years. **Main symptoms of final illness**: A long illness commencing with polyarthritis. Mitral disease was followed by the appearance of aortic disease. There was continued fever, with enlargement and tenderness of the spleen and blood and albumin in the urine. **Approximate duration**: 16 weeks. **Bacteriology**: Negative. **Result**: There was *recovery* from all the acute symptoms. It is difficult to explain the clinical course except as due to a transient malignancy.

No. 4. Female, aged 44. **History of rheumatic fever** at 25 and 34 years. **Main symptoms of final illness**: Admitted with aortic and mitral disease with continuous irregular fever; developed haemoptysis and sudden pain in the left side. **Approximate duration**: 9 weeks. **Bacteriology**: Negative. **Result**: There was a *slow recovery.* All the acute symptoms subsided.

No. 5. Male, aged 13. **History of acute rheumatism**: First attack. **Main symptoms of final illness**: Developed aortic and mitral disease with irregular fever. The clinical diagnosis was malignant endocarditis. **Approximate duration**: 10 weeks. **Bacteriology**: Negative. **Result**: *Relieved.* All acute symptoms disappeared.

No. 6. Male, aged 38. **History of acute rheumatism**: 3 attacks. **Main symptoms of final illness**: Aortic and mitral disease with persistent fever for 7 weeks and cerebral embolism. Later signs of asystole. **Approximate duration**: 12 weeks. **Bacteriology**: Negative. **Result**: *Relieved.* Eventually all acute symptoms subsided and the patient made a partial recovery.

No. 7. Male, aged 28. **History of acute rheumatism** at 24 years. **Main symptoms of final illness**: Admitted for active mitral disease; developed aortic regurgitation with persistent fever for 12 weeks. No emboli noted. **Approximate duration**: 16 weeks.

Bacteriology: Negative. **Result**: *Relieved.* Thought to be malignant, but the acute symptoms quieted down.

No. 8. Male, aged 58. **History of acute rheumatism** at 30 and 42 years. **Main symptoms of final illness**: A case of aortic and mitral disease with irregular fever for 3 months and blood and albumin in the urine. **Approximate duration**: 12 weeks. **Bacteriology**: None made. **Result**: *Relieved.*

No. 9. Female, aged 22. **History of acute rheumatism** as a child; repeated attacks since. **Main symptoms of final illness**: Admitted with aortic and mitral disease, irregular fever, haematuria, and ophthalmoplegia. Recovered partially, but 5 months later readmitted with nephritis. **Approximate duration**: 4 weeks. **Bacteriology**: None made. **Result**: *Death.* The necropsy showed old pericarditis. Thickened mitral and aortic valves, a large spleen. Large white kidneys with scars of previous infarctions.

No. 10. Female, aged 25. **History of acute rheumatism** at 17 years. **Main symptoms of final illness**: Admitted with slight fever; ophthalmoplegia, renal infarctions. **Approximate duration**: 7 weeks. **Bacteriology**: Negative. **Result**: *Relieved.*

No. 11. Male, aged 15–17. **History of acute rheumatism** at 12 and 13 years. **Main symptoms of first illness** (at 15): Arthritis and mitral and aortic disease, fever. **Approximate duration**: 4 weeks. **Bacteriology**: None made. **Result**: Simple acute rheumatism. **Main symptoms of second illness** (at 16): Carditis and high irregular fever for 8 weeks. **Approximate duration**: 12 weeks. **Bacteriology**: None made. **Result**: Suspected to be malignant. **Main symptoms of third illness** (at 17): Carditis with 100 days' fever, pleurisy. **Approximate duration**: 17 weeks. **Bacteriology**: Negative. **Result**: Suspected to be malignant but *recovered.*

No. 12. Female, aged 14. **History of acute rheumatism** at 11 years. **Main symptoms of final illness**: Admitted with polyarthritis, aortic and mitral disease. There were no evidences of embolism, but persistent fever for 9 weeks. **Approximate duration**: 9 weeks. **Bacteriology**: None made. **Result**: *Relieved.*

No. 13. Female, aged 10. **History of chorea** and **rheumatism** at 8 and 9 years. **Main symptoms of final illness**: Admitted with polyarthritis, aortic and mitral disease, persistent fever for 9 weeks. **Approximate duration**: 9 weeks. **Bacteriology**: None made. **Result**: *Death.* Adherent pericardium. Aortic and mitral endocarditis of the acute rheumatic type, but the spleen enlarged.

Group III.

Acute Rheumatic Heart Disease (Simple Type).

This group needs no explanation. The classical examples are found in the young, and the fatal first attacks are valuable illustrations of the fact that death results from a pancarditis, and not from the simple endocarditis. Here we would again repeat that in most of the opportunities for examining the vegetations of simple rheumatic endocarditis the actual process in the valves is in a stage of retrogression; it is only in rare exceptions that a condition can be obtained comparable to an early experimental endocarditis in which an animal can be killed as soon as the signs develop.

In several instances the cases with recurrent attacks of rheumatism illustrate the increasing obstinacy of the cardiac infection, with its repetition, and also show that the relation of a recurrent attack to previous ones precisely resembles that which exists between the malignant cases and a previous attack of acute rheumatism, for the time interval may be short or long.

Group No. III.

Acute Rheumatic Endocarditis. Linked up to Group II by Cases 11, 12, *and* 13 *in that Group and* 3, 9, *and* 10 *in this.*

No. 1. Male, aged 4½. **History of acute rheumatism**: First attack. **Main symptoms of final illness**: Polyarthritis, subsiding. Aortic and mitral disease, pericarditis and nodules, persistent fever. **Approximate duration**: 12 weeks. **Bacteriology**: None made. **Result**: *Death.* Subacute pericarditis, acute simple aortic and mitral endocarditis.

No. 2. Male, aged 9. **History of acute rheumatism**: First attack. **Main symptoms of final illness**: 5 weeks' fever with arthritis, nodules, and aortic and mitral disease. **Approximate duration**: 5 weeks. **Bacteriology**: None made. **Result**: *Death.* Acute simple aortic and mitral endocarditis.

No. 3. Female, aged 9½. **History of acute rheumatism**: First attack. **Main symptoms of final illness**: Arthritis, carditis and chorea, persistent irregular fever. **Approximate duration**: 5 weeks. **Bacteriology**: Strepto-diplococcus isolated. **Result**: *Death.* Acute simple endocarditis, though aortic vegetations larger, resembling those of a malignant case. Recent pericarditis.

No. 4. Male, aged 9. **History of acute rheumatism** at 8 years (6 months ill). **Main symptoms of final illness**: Acute endocarditis and nodules; 9 weeks' fever. **Approximate duration**: 10 weeks. **Bacteriology**: None made. **Result**: *Death.* Adherent pericardium. Mitral and aortic endocarditis, recent vegetations, thickened valves.

No. 5. Male, aged 10–11½. **History of acute rheumatism**: First attack at 10 years; second attack at 11½ years. **Main symptoms of first illness**: Arthritis, persistent fever for many weeks, of the typhoidal type; aortic and mitral disease. **Approximate duration**: 20 weeks. **Bacteriology**: None made. **Main symptoms of second illness**: Asystole. **Approximate duration**: 2 weeks. **Bacteriology**: None made. **Result**: *Death.* Thickened aortic valves, with minute vegetations, aortic atheroma.

No. 6. Female, aged 7. **History of acute rheumatism** at 6 years. **Main symptoms of final illness**: Arthritis. Continuous irregular fever, aortic and mitral disease. **Approximate duration**: 12 weeks. **Bacteriology**: None made. **Result**: *Death.* Slight recent aortic endocarditis. Old and recent mitral.

No. 7. Female, aged 6½. **History of acute rheumatism** at 4 and 5 years with pericarditis. **Main symptoms of final illness**: Asystole, with slight fever. **Approximate duration**: 5 weeks. **Bacteriology**: None made. **Result**: *Death.* Mitral aortic and tricuspid endocarditis of the acute rheumatic type. No evidence of pericarditis.

No. 8. Female, aged 16. **History of acute rheumatism**: First attack. **Main symptoms of final illness**: Commenced with polyarthritis, 10 weeks' fever, gradually subsiding. Aortic and mitral disease. **Approximate duration**: 13 weeks. **Bacteriology**: None made. **Result**: *Relieved.*

No. 9. Female, aged 6–8. **History of acute rheumatism**: First attack at 6 years; second attack at 7 years; third attack at 8 years. **Main symptoms of first illness**: Arthritis, chorea, nodules, persistent carditis, aortic and mitral disease, waves of fever extending over many weeks. **Approximate duration**: At least 18 weeks. **Bacteriology**: None made. **Result**: *Relieved.* **Main symptoms of second illness**: Carditis, persistent fever. **Approximate duration**: 12 weeks. **Bacteriology**: None made. **Result**: *Relieved.* **Main symptoms of third illness**: 10 days' fever, asystole. **Approximate duration**: 10 days. **Bacteriology**: Strepto-diplococcus isolated from mitral valve. **Result**: *Death.* Recent and old pericarditis, aortic valves inflamed from base to margin.

No. 10. Male, aged 11–16½. **History of chorea** at 3 years; **acute rheumatism** at 11, 12, 14, 16, and 16½ years. **Main symptoms of first illness**: Aortic and mitral disease, nodules, persistent fever. **Approximate duration**: 20 weeks. **Bacteriology**: None made. **Result**: Simple mitral endocarditis. **Main symptoms of second illness**: Sent in for 'a rest', persistent fever and tachycardia for 3 weeks. **Approximate duration**: 3 weeks. **Bacteriology**: None made. **Result**: *Relieved.* **Main symptoms of third illness**: Three weeks' palpitation and fever. **Approximate duration**: 5 weeks. **Bacteriology**: None made.

Result: *Relieved.* **Main symptoms of fourth illness**: 10 weeks' pericarditis and carditis. **Approximate duration**: 12 weeks. **Bacteriology**: Blood culture negative. **Result**: *Relieved.* **Fifth illness—Result**: *Sudden death.* No post-mortem; probably the simple type. Note persistent carditis with fever.

No. 11. Female, aged 17. **History of acute rheumatism** at 10 years and 2 attacks since. **Main symptoms of final illness**: Admitted with mitral regurgitations and slight fever; developed aortic regurgitations and died suddenly. **Approximate duration**: 3 weeks. **Bacteriology**: None made. **Result**: *Death.* No post-mortem.

No. 12. Male, aged 22. **History of acute rheumatism** at 11 and 17 years. **Main symptoms of final illness**: Multiple arthritis. Aortic and mitral disease with irregular outbursts of fever, synchronous with which there was precordial pain. **Approximate duration**: 8 weeks. **Bacteriology**: None made. **Result**: *Relieved.*

No. 13. Male, aged 22. **History of acute rheumatism** at 18 and 20 years. **Main symptoms of final illness**: 5 months' history of recurrent anginal attacks, also multiple arthritis, aortic and mitral disease and recurrent attacks of fever. **Approximate duration**: 8 weeks. **Bacteriology**: None made. **Result**: *Relieved.*

No. 14. Male, aged 50. **History of acute rheumatism** in childhood and at 25 years. **Main symptoms of final illness**: Aortic and mitral disease, with irregular fever for 7 days. **Approximate duration**: 6 weeks. **Bacteriology**: None made. **Result**: *Relieved.*

No. 15. Female, aged 10. **History of acute rheumatism** at 7 and 8 years. **Main symptoms of final illness**: Polyarthritis, aortic and mitral, tachycardia, high irregular fever followed by a normal temperature and relapse. **Approximate duration**: 5 weeks. **Bacteriology**: None made. **Result**: *Relieved.* Severe type of simple carditis.

No. 16. Male, aged 38. **History of acute rheumatism** at 6, 12, and 21 years. **Main symptoms of final illness**: Mitral and aortic disease with 3 attacks of fever, in one of which an attack of pericarditis. **Approximate duration**: 10 weeks. **Bacteriology**: None made. **Result**: *Relieved.*

No. 17. Female, aged 20. **History of acute rheumatism** at 6 and 12 years; **chorea** at 15 years. **Main symptoms of final illness**: Double mitral and aortic regurgitation with slight transient fever. **Approximate duration**: 4 weeks. **Bacteriology**: None made. **Result**: *Relieved.*

No. 18. Male, aged 25. **History of acute rheumatism**: Several mild attacks. **Main symptoms of final illness**: Polyarthritis, transient fever, mitral and aortic disease. **Approximate duration**: 7 weeks. **Bacteriology**: None made. **Result**: *Relieved.*

No. 19. Male, aged 32. **History of acute rheumatism** at 11, 16, and 26 years. **Main symptoms of final illness**: Mitral and aortic disease, left with a rising temperature. **Approximate duration**: 13 weeks. **Bacteriology**: None made. **Result**: Left at own request, nature of endocarditis doubtful.

No. 20. Female, aged 18. **History of acute rheumatism**: 6 attacks. **Main symptoms of final illness**: Mitral and aortic disease, 3 weeks' irregular fever, pericarditis, several relapses of fever. **Approximate duration**: 13 weeks. **Bacteriology**: None made. **Result**: *Relieved.* Severe type.

No. 21. Female, aged 24. **History of chorea** at 9 years; **acute rheumatism** at 16 years. **Main symptoms of final illness**: Mitral and aortic disease with slight fever. **Approximate duration**: 5 weeks. **Bacteriology**: None made. **Result**: *Relieved.*

No. 22. Female, aged 20. **History of acute rheumatism**: First attack. **Main symptoms of final illness**: Multiple arthritis, aortic and mitral regurgitations, always a slightly swinging temperature. **Approximate duration**: 11 weeks. **Bacteriology**: Blood culture negative. **Result**: *Relieved.* Note persistent slight fever.

No. 23. Male, aged 13. **History of acute rheumatism** at 11½ years. **Main symptoms of final illness**: Aortic and mitral disease, arthritis, nodules, slight fever. **Approximate duration**: 7 weeks. **Bacteriology**: None made. **Result**: *Relieved.*

No. 24. Male, aged 27. **History of acute rheumatism** at 21 years. **Main symptoms of final illness**: Dyspnoea, mitral and aortic disease, slight irregular fever. **Approximate duration**: 5 weeks. **Bacteriology**: None made. **Result**: *Relieved.*

No. 25. Male, aged 21. **History of acute rheumatism** at 10 and 11 years. **Main**

symptoms of final illness: Subacute arthritis, mitral and aortic disease, slight fever. **Approximate duration**: 3 weeks. **Bacteriology**: None made. **Result**: *Relieved.*

No. 26. Male, aged 24. **History of acute rheumatism** at 11 years. **Main symptoms of final illness**: Arthritis, mitral and aortic disease, and irregular fever. **Approximate duration**: 7 weeks. **Bacteriology**: None made. **Result**: *Relieved.*

No. 27. Male, aged 22. **History of acute rheumatism**: First attack. **Main symptoms of final illness**: Arthritis followed by mitral and then aortic regurgitations, always a slight fever, never rising above 100° F. **Approximate duration**: 17 weeks. **Bacteriology**: None made. **Result**: *Relieved.* Note the mild but progressive course.

No. 28. Female, aged 35. **History of acute rheumatism** at 14 years. **Main symptoms of final illness**: Arthritis, mitral and aortic disease and slight fever. **Approximate duration**: 5 weeks. **Bacteriology**: None made. **Result**: *Relieved.*

No. 29. Female, aged 11. **History of acute rheumatism** at 8 and 9 years. **Main symptoms of final illness**: Mitral and aortic disease; only in hospital 10 days. **Approximate duration**: 10 days. **Bacteriology**: None made. **Result**: *Relieved.*

No. 30. Female, aged 34. **History of acute rheumatism**: 6 attacks. **Main symptoms of final illness**: Mitral and aortic disease. **Approximate duration**: 5 weeks. **Bacteriology**: None made. **Result**: *Relieved.*

No. 31. Male, aged 10. **History of acute rheumatism** at 6 years. **Main symptoms of final illness**: Pericarditis, aortic and mitral disease, nodules and arthritis, fever for 14 days ill 12 weeks. **Approximate duration**: 12 weeks. **Bacteriology**: None made. **Result**: *Death.* Thickened aortic and mitral with recent vegetations (small). Recent pericarditis.

No. 32. Female, aged 19. **History of rheumatism and chorea** at 13 years. **Main symptoms of final illness**: Severe aortic and mitral disease with continuous fever for 5 weeks; anginal attacks. **Approximate duration**: 5 weeks. **Bacteriology**: None made. **Result**: *Relieved.* Note prolonged fever, carditis, and angina.

No. 33. Female, aged 38. **History of acute rheumatism** at 14 years. **Main symptoms of final illness**: Mitral and aortic disease, admitted with transient polyarthritis and fever. **Approximate duration**: 5 weeks. **Bacteriology**: None made. **Result**: *Relieved.*

Cases in Group IV.

The last group of cases will not need any prolonged explanation, for they are examples of heart scars with consequent mechanical disabilities. There is a sufficient number of fatal cases among them in which a necropsy has proved the reality of such an interpretation, and their chief importance is to emphasize the power that the human frame possesses to resist the rheumatic infection. This very fact bringing it strictly into line with other great infections only serves to throw into relief the overwhelming probability that these healing processes may also fail, as they do undoubtedly succeed, in such a struggle. What an assumption it must be to assert that such an infection as the rheumatic could always be overcome in the cardiac valves! Even if we were deprived of all the clinical, pathological, and experimental evidence we now possess such an assumption would be open to the gravest questioning, but with such evidence at hand it must surely be abandoned as a survival of an older pathology which existed when acute rheumatism was looked upon as of nervous or lactic acid origin. Old beliefs die very hard, and oftentimes in medical literature may be seen the strange results of attempting to graft upon an old stem the new shoots of another plant of knowledge. The relationship of rheumatism to malignant endocarditis is a beautiful example of such an attempt. Every sort of ingenious device has been invented to graft the old stem with the new shoots, but they have all failed.

Among the most remarkable must be placed that one which suggests that rheumatism is a mysterious and unknown disease akin to simple scarlet fever, upon which all the manifestations are to be grafted as secondary infections. When we can imagine on the one hand a scarlet fever which is not infectious and is without a rash save in exceptional cases, and on the other a rheumatism which is infectious and which possesses no manifestations except possibly a sore throat and an occasional rash, we may be able to appreciate the likeness between these two diseases. For us an infectious disease such as scarlet fever, whether complicated by secondary infections or not, possesses a peculiarity of its own, viz. its infectivity. Whereas acute rheumatism, deprived of its manifestations, is a disease still to be discovered, as also would be in our opinion a tuberculosis or pneumococcal infection without its manifestations.

Group No. IV.

Chronic Heart Disease due to previous Rheumatic Endocarditis.

A. Cases showing chiefly aortic symptoms.

No. 1. Male, aged 63. **History of acute rheumatism:** 3 attacks; **heart disease** at 13 years. **Main symptoms of final illness:** 2 days' illness. Sudden death, aortic type, mitral and aortic disease. **Approximate duration:** 2 days. **Result:** *Death.* Calcified valves.

No. 2. Male, aged 42. **History of much rheumatism. Main symptoms of final illness:** Angina pectoris—dyspnoea, aortic and mitral disease. **Approximate duration:** Many weeks. **Result:** *Death.* Thickened valves and aortic atheroma.

No. 3. Male, aged 40. **History of acute rheumatism** at 27. **Main symptoms of final illness:** Mitral and aortic disease, angina pectoris. **Approximate duration:** 4 weeks. **Result:** *Relieved.*

No. 4. Male, aged 40. **History of acute rheumatism:** Repeated attacks. **Main symptoms of final illness:** Mitral and aortic disease with angina. **Approximate duration:** 6 weeks. **Result:** *Relieved.*

No. 5. Female, aged 14. **History of acute rheumatism:** Slight. **Main symptoms of final illness:** Mitral and aortic disease, pallor, pain in chest. **Approximate duration:** 9 days. **Result:** *Relieved.*

No. 6. Male, aged 28. **History of acute rheumatism** at 18 years and since. **Main symptoms of final illness:** Mitral and aortic disease, dyspnoea. **Approximate duration:** 7 days. **Result:** Left at his own request.

No. 7. Male, aged 48. **History of acute rheumatism** at 35 and 39 years. **Main symptoms of final illness:** Mitral and aortic disease, angina. **Approximate duration:** 3 weeks. **Result:** *Relieved.*

B. Cases showing chiefly mitral symptoms.

No. 1. Male, aged 38. **History of acute rheumatism:** Several attacks. **Main symptoms of final illness:** Alcoholism. Mitral and aortic disease, jaundice, dropsy, dyspnoea. **Approximate duration:** 11 weeks. **Result:** *Death.* Sclerosis of aortic and mitral valves.

No. 2. Male, aged 50. **History of acute rheumatism** at 8, 25, 36, and 49 years. **Main symptoms of final illness:** Mitral and aortic. Oedema, dyspnoea, &c.; asystole. **Approximate duration:** Many weeks. **Result:** *Death.* Calcified aortic and mitral valves; shortening of chordae tendineae.

No. 3. Male, aged 72. **History of acute rheumatism** at 17 years. **Main symptoms of**

final illness : Mitral and aortic. Myocardial weakness. Asystole. **Approximate duration :** 4 weeks. **Result :** *Death.* Thickened mitral and aortic valves. Atheroma.

No. 4. Female, aged 52. **History of acute rheumatism** at 40 years. **Main symptoms of final illness :** Mitral and aortic. Asystole, with oedema, &c. **Approximate duration :** 4 weeks. **Result :** *Relieved.*

No. 5. Female, aged 60. **History of acute rheumatism :** Slight attacks. **Main symptoms of final illness :** Mitral and aortic. Asystole, with cyanosis and dropsy. **Approximate duration :** 5 weeks. **Result :** *Relieved.*

No. 6. Female, aged 79. **History of acute rheumatism :** 6 attacks. **Main symptoms of final illness :** Mitral and aortic. Asystole—mitral type. **Approximate duration :** 5 weeks. **Result :** *Relieved.*

No. 7. Male, aged 35. **History of acute rheumatism** at 20 years. **Main symptoms of final illness :** Mitral and aortic. Alcoholism, asystole. **Approximate duration :** 5 weeks. **Result :** *Relieved.*

No. 8. Male, aged 20. **History of acute rheumatism** at 11 years. **Main symptoms of final illness :** Mitral and aortic. Asystole—mitral type. **Approximate duration :** 3 weeks. **Result :** *Relieved.*

No. 9. Female, aged 18. **History of acute rheumatism** at 13, 14 and 15 years. **Main symptoms of final illness :** Mitral and aortic. Murmurs. **Approximate duration :** 2 weeks. **Result :** *Relieved.*

No. 10. Female, aged 26. **History of acute rheumatism :** Repeated attacks. **Main symptoms of final illness :** Mitral and aortic. Severe asystole, mitral type. **Approximate duration :** 24 weeks. **Result :** *Relieved.*

No. 11. Female, aged 20. **History of acute rheumatism :** 6 attacks. **Main symptoms of final illness :** Mitral and aortic disease. Signs of mitral asystole. **Approximate duration :** 4 weeks. **Result :** *Relieved.*

No. 12. Male, aged 40. **History of acute rheumatism** at 19 years. **Main symptoms of final illness :** Mitral and aortic disease. Signs of mitral asystole. **Approximate duration :** 10 weeks. **Result :** *Relieved.*

No. 13. Male, aged 48. **History of acute rheumatism** at 12 and 38 years. **Main symptoms of final illness :** Mitral and aortic disease. Signs of asystole. **Approximate duration :** Some weeks. **Result :** *Relieved.*

No. 14. Male, aged 22. **History of acute rheumatism** at 19 years. **Main symptoms of final illness :** Mitral and aortic disease. Signs of asystole, mitral. **Approximate duration :** 3 weeks. **Result :** *Relieved.*

No. 15. Male, aged 22. **History of acute rheumatism** at 16 years. **Main symptoms of final illness :** Mitral and aortic disease, prolonged asystole. **Approximate duration :** 18 months. **Result :** *Relieved.*

No. 16. Female, aged 32. **History of acute rheumatism** at 14, 19, 21, 23, and 25 years. **Main symptoms of final illness :** Mitral and aortic disease, with palpitation. **Approximate duration :** 7 days. **Result :** *Relieved.*

No. 17. Female, aged 32. **History of acute rheumatism** at 17 and 31 years. **Main symptoms of final illness :** Mitral and aortic disease, with signs of mitral asystole. **Approximate duration :** 4 weeks. **Result :** *Relieved.*

No. 18. Female, aged 33. **History of acute rheumatism** as a child. **Main symptoms of final illness :** Mitral and aortic disease. Palpitation, &c. **Approximate duration :** 10 days. **Result :** *Relieved.*

No. 19. Female, aged 21. **History of acute rheumatism** at 11 and 12 years. **Main symptoms of final illness :** Mitral and aortic disease. Anaemia, palpitation, &c. **Approximate duration :** Many months. **Result :** *Relieved.*

No. 20. Female, aged 28. **History of acute rheumatism** as a child and at 18 years. **Main symptoms of final illness :** Mitral and aortic disease. Asystole. **Approximate duration :** Many weeks. **Result :** *Relieved.*

No. 21. Male, aged 14. **History of acute rheumatism** at 12 years. **Main symptoms of final illness :** Mitral and aortic disease. Severe asystole. **Approximate duration :** 4 weeks. **Result :** *Death.* Aortic and mitral valves thickened, adherent pericardium.

No. 22. Male, aged 30. **History of acute rheumatism** at 16 years. **Main symptoms of final illness:** Mitral and aortic disease. Signs of asystole. **Approximate duration:** 3 weeks. **Result:** *Relieved.*

We wish now to put very briefly our conception of acute rheumatism—or, as we would prefer to call it, rheumatism—side by side with the pictures of other similar infections.

1. First of all comes the gonorrhoeal infection.

From a local focus in the urethra there may follow a systemic invasion, producing multiple arthritis and other lesions, including a carditis. The arthritis may be transient, but often is exceedingly stubborn and drifts into a condition of rheumatoid arthritis. The heart affection may be a pancarditis, or a transient endocarditis, or a malignant endocarditis.

2. The rheumatic infection from such a focus as the tonsil may produce an arthritis and other lesions, including a carditis. Two features are well recognized. One is that the arthritis is usually transient, although we maintain that a rheumatoid arthritis may result from this infection. The other is the great prominence of cardiac lesions. Carditis is very frequent, and both simple and malignant endocarditis may result.

3. With the pneumococcal infection the lungs and pleurae take the position that the heart occupies in rheumatism, but arthritis of all grades of severity may result, and also a carditis, in which suppurative pericarditis and malignant endocarditis are liable to develop.

4. In staphylococcal infections, from a local infection such as an acute osteomyelitis, there may follow multiple arthritis and carditis. The processes here are essentially suppurative, and multiple nodular subcutaneous abscesses, myocardial abscesses, and acute malignant endocarditis may all result.

5. Virulent streptococcal infections of the type caused by the *Streptococcus pyogenes* show a similar picture. The arthritis, if not exceedingly acute, is suppurative; profound myocardial poisoning is much more frequent than endocarditis, and this, when it occurs, is usually malignant in type. A general septicaemia is frequent, and in classical cases the entire process differs widely from that of acute rheumatism. It is a difference in the type and not in the degree of virulence.

We believe that this conception of acute rheumatism as a peculiar streptococcal infection fills a gap in our knowledge of this important disease, in a way that is unequalled, not only for its simplicity, but for the completeness of the explanation which it affords of the symptoms and course of the affection.

The strong hereditary element in the disease supports the view that the exciting cause possesses some peculiarity by which in these particular tissues it can form the special poisons that make it so definite an affection.

Concluding Remarks.

We believe that the view we support in this research is not one of academic interest or a mere battle of words. It will be a distinct gain if we succeed in overthrowing the remarkable view that the nature of rheumatic endocarditis—whatever the infection may be—is always benign and requires an added infection to produce a progressive lesion. The survival of such a view implies such a subversion of the natural principles of the infective processes as to unsteady one's whole outlook upon these diseases. The disappearance of such a mystery, on the other hand, must be a clear gain to connected thought upon all rheumatic processes and a forward step in cardiac pathology.

Far more important is its bearing upon the clinical side of malignant endocarditis. The rheumatic form is no exception to the rule that it is a disease which is almost invariably fatal when the signs are well established. Theoretical considerations lead to the belief that occasional recoveries may occur, and there is good clinical evidence in support; but these exceptions are rare, and our series alone shows the great fatality.

We are doubtful of the efficacy of serum or vaccine at present in use, though we would neither dispute the records of such recoveries while such treatment was being employed, nor the advisability of trying any method that holds out the least prospect of success.

It is the prophylaxis that is encouraged by our investigations. There must clearly be some peculiar factors at work to produce the progressive endocarditis, and we sometimes find suggestive evidence in support of this. The cardiac rheumatism may have been neglected, the patient ill-fed, the surroundings unhealthy. Anaemia—a prominent feature of some rheumatic attacks—may have persisted, and this in our opinion favours the malignant process. The danger of large unhealthy tonsils in the rheumatic is well established, and this danger can be cautiously dealt with. Above all, we believe that more clinical study is necessary of the course and history of acute rheumatic endocarditis. We believe that a smouldering activity of the rheumatic process is more common than is suspected, and very possibly we may not yet possess the necessary clinical accuracy for ascertaining the limits of this activity. This seems the more likely when we bear in mind that even a gross and progressive lesion may elude our observation until the end is close at hand.

There is more hope that we may protect a patient against the development of a known danger than against a mysterious secondary infection which prefers scarred valve tissues and which appears usually without any particular cause or reason.

The disappearance of the terms 'malignant', 'infective', or 'pernicious' as applied to endocarditis will be a great advantage, and the substitution of the term 'active' will answer every purpose, for the physician can judge of the degree

of this activity by the well-known signs that may arise. 'Active tuberculosis' expresses sufficiently a progressive pulmonary lesion, and we need no term 'malignant tuberculosis' to bring home to us the fact that the activity is getting beyond all control. Why then use such a term as 'malignant endocarditis', or perpetuate such an unproven conception as a non-infective endocarditis, by the use of the adjective 'infective'?

DESCRIPTION OF FIGURES.

PLATE 27. To illustrate the view that direct spread of infection may occur from one valve to another.

FIG. 1. The heart of a rabbit showing endocarditis of the mitral and aortic valves. The heart has been greatly enlarged for the more convenient comparison with the human heart. The vegetations on the mitral valve are very extensive and are in continuity with equally extensive ones upon the aortic cusps.

FIG. 1 *a*. A human heart showing aortic and mitral endocarditis. The vegetations on the aortic flap of the mitral are in continuity with extensive vegetations on the contingent aortic cusp. The other cusps are affected in lesser degree. The mitral valve is not opened.

PLATE 28, FIG. 2. The heart of a rabbit showing mitral endocarditis of the malignant type, the result of infection with the *Diplococcus rheumaticus*.

FIG. 3. The heart of a rabbit showing fibrino-plastic pericarditis, the result of infection with the *Diplococcus rheumaticus*.

FIG. 4. The heart of a rabbit showing aortic endocarditis of the same causation.

FIG. 5. Rheumatic endocarditis, human (simple type), showing the presence of the diplococci.

FIG. 6. Rheumatic endocarditis, experimental (simple type), showing the presence of the diplococci.

FIG. 7. Rheumatic endocarditis, human (simple type), showing the necrotic tissue in a vegetation.

PLATE 29, FIG. 8. Rheumatic endocarditis, experimental (simple type), showing the necrotic tissue in a vegetation.

FIG. 9. Rheumatic endocarditis, human (malignant type), showing numerous diplococci in necrotic tissue.

FIG. 10. The same experimentally produced in a rabbit.

FIG. 11. Early rheumatic endocarditis (human) showing numerous diplococci.

FIG. 12. Transitional type of endocarditis in a rabbit.

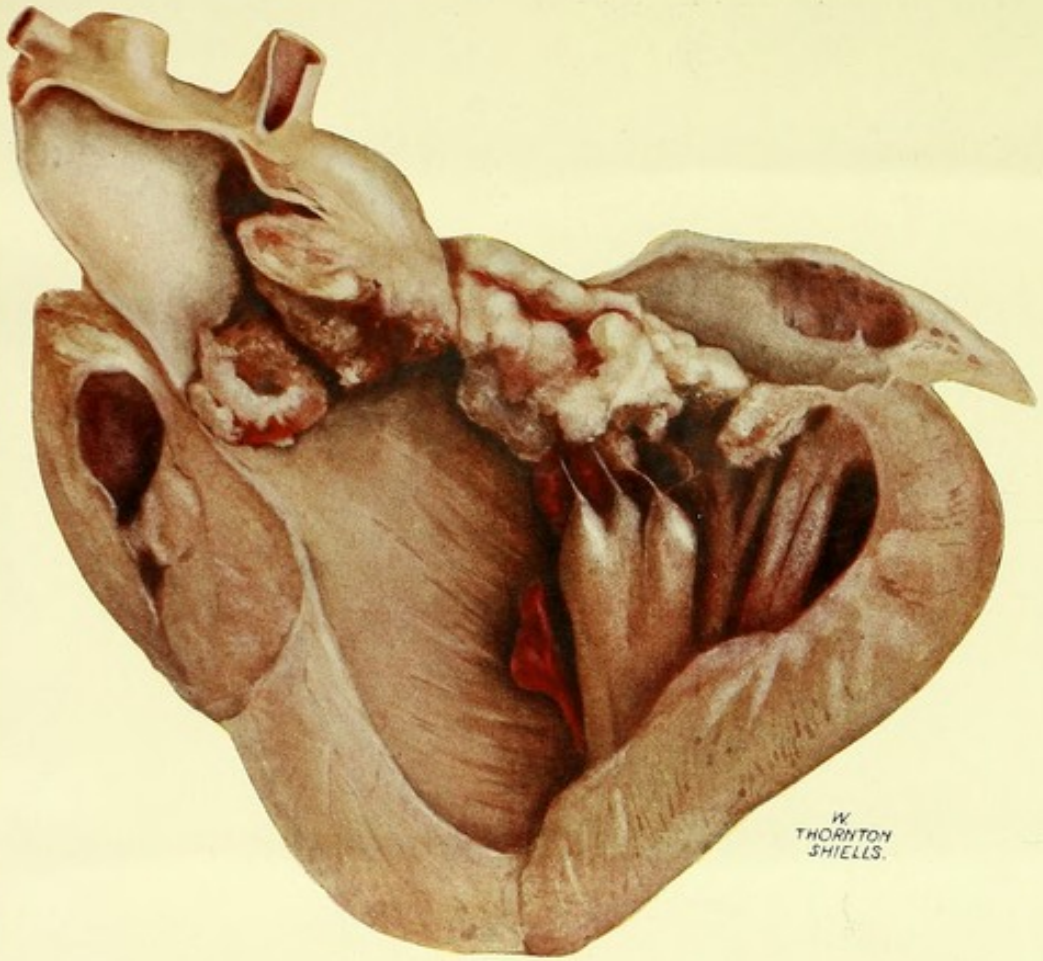

FIG. 1

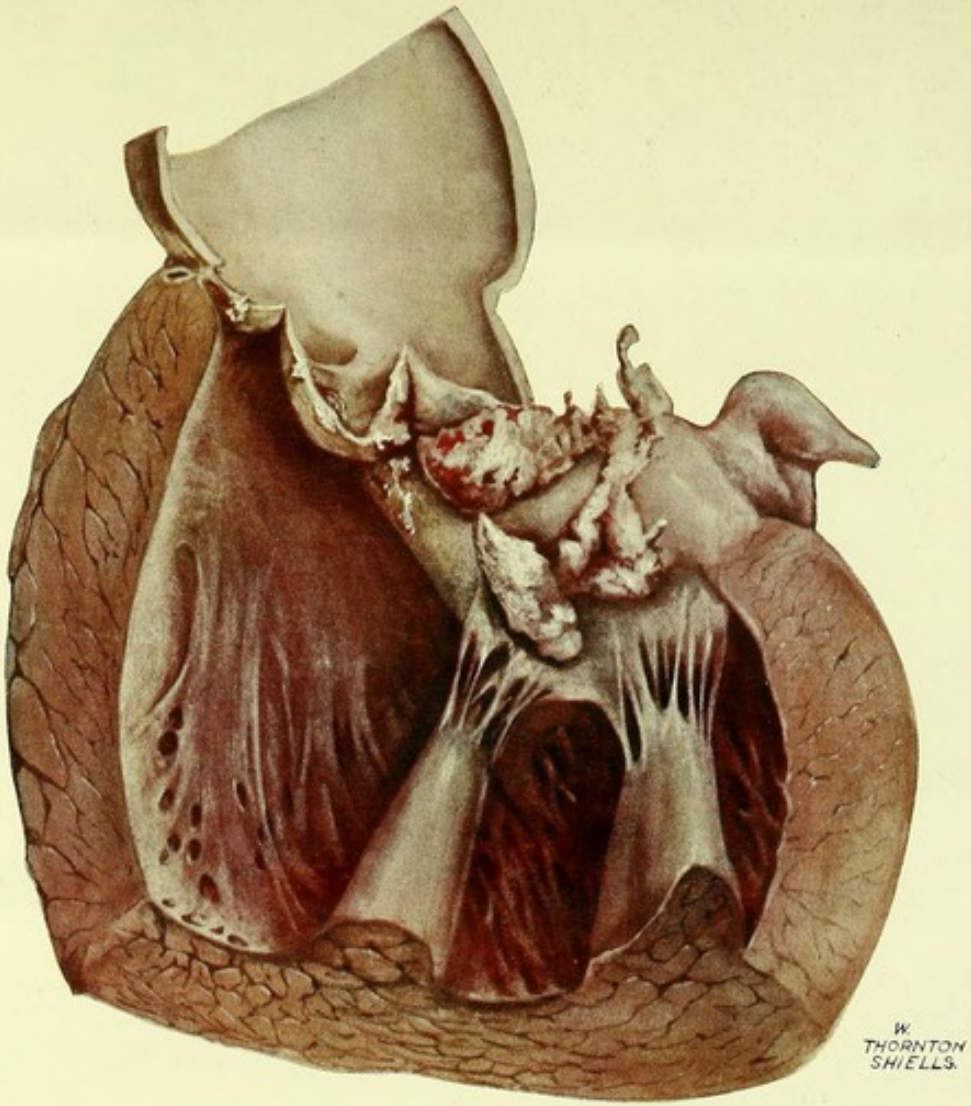

FIG. 1a

Fig. 2

Fig. 4

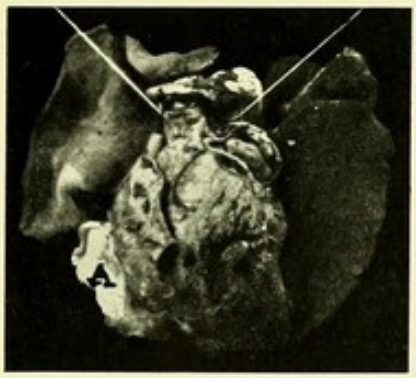

Fig. 3

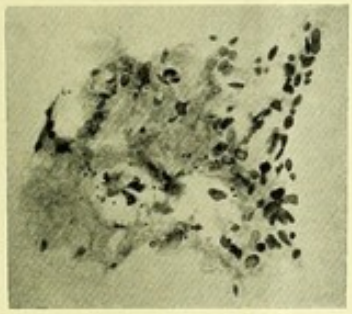

Fig. 5

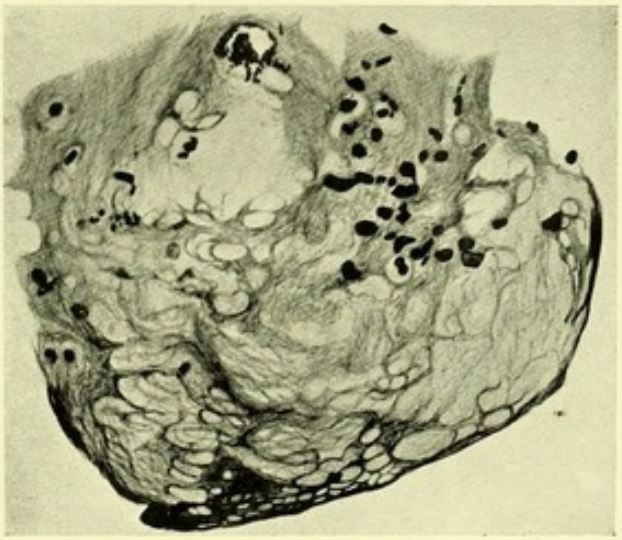

Fig. 6

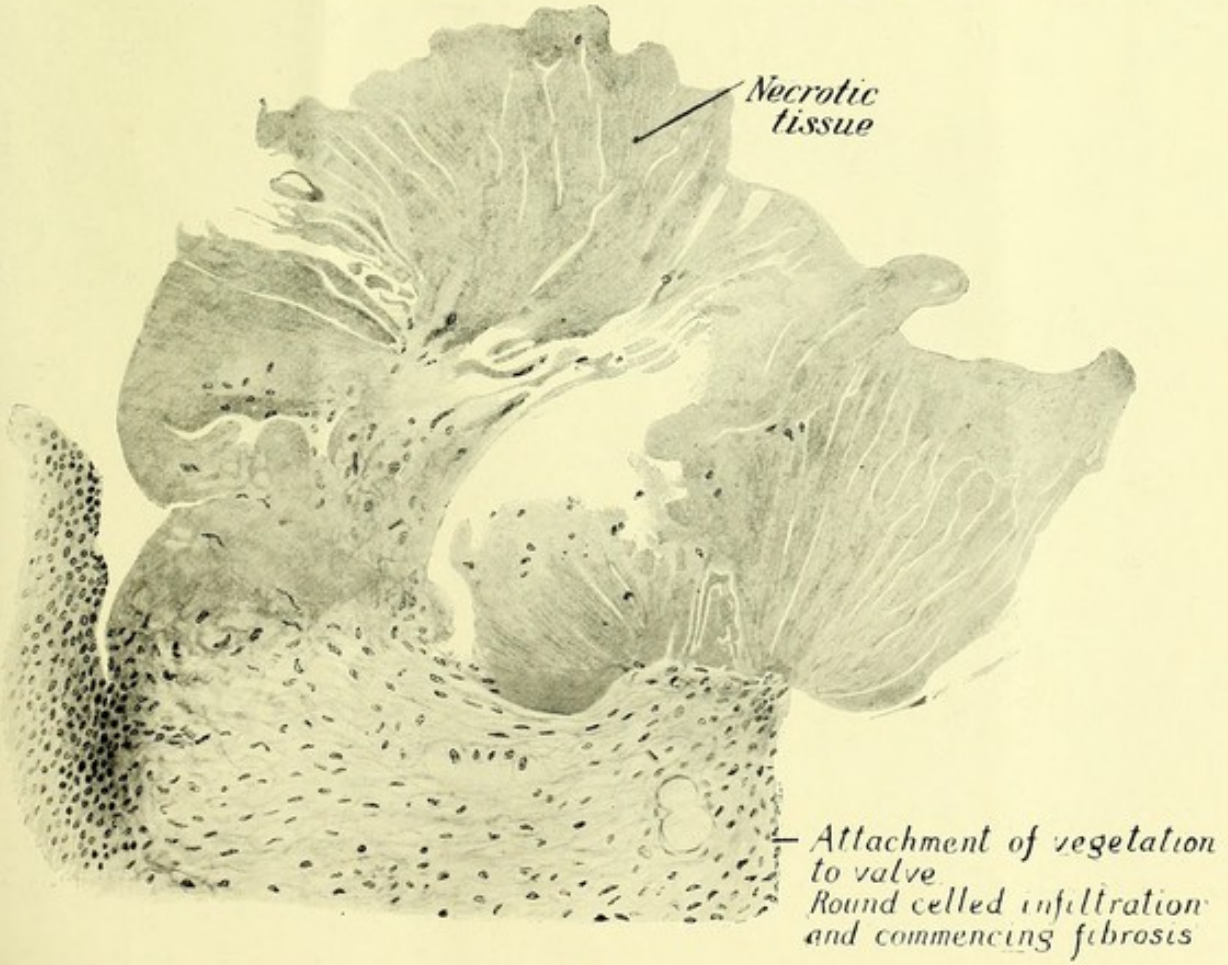

Fig. 7

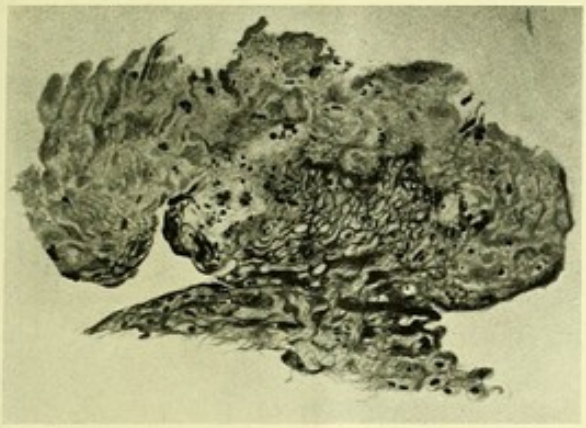

FIG. 8

FIG. 9

FIG. 10

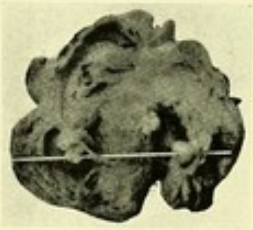

FIG. 12

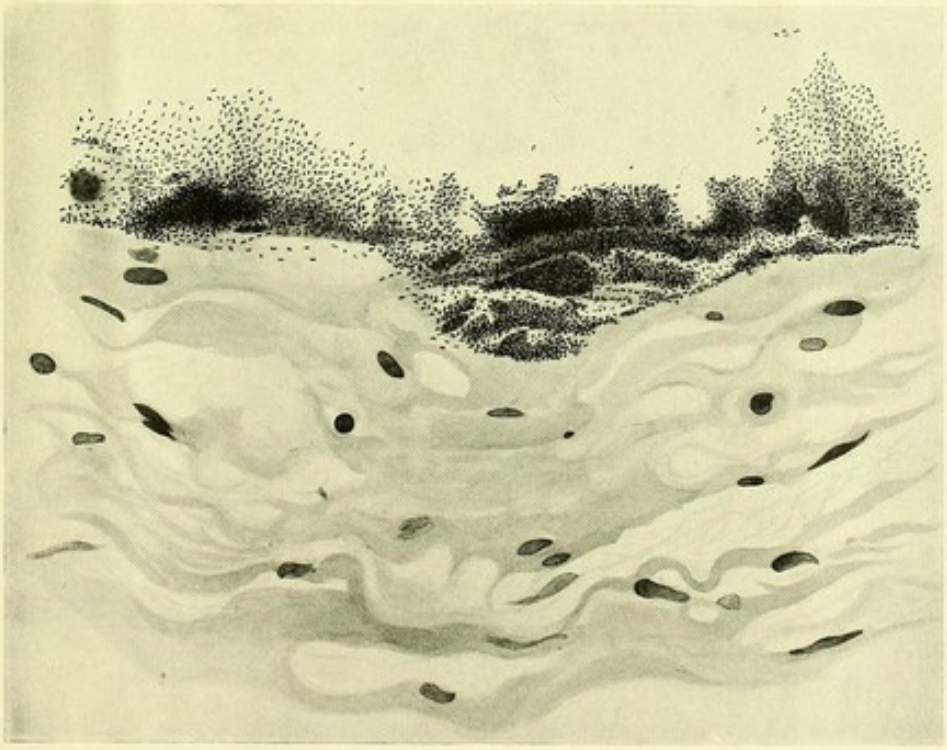

FIG. 11