STUDIES ON THE MYOCARDIAL ASCHOFF BODY *

II. LIFE CYCLE, SITES OF PREDILECTION AND RELATION TO CLINICAL COURSE OF RHEUMATIC FEVER

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This report represents an attempt to throw further light on the nature of the myocardial Aschoff body, its life cycle, sites of predilection, frequency of occurrence, and its possible relation to the clinical course of rheumatic fever. In a previous publication [1] we have shown that the Aschoff body occurring in the heart should be considered apart from the corresponding rheumatic lesions found in other tissues, such as skin, diaphragm, tendinous insertions, and so on, inasmuch as the myocardial lesions present specific characteristics that are either lacking in the other sites or have been insufficiently studied as yet. Furthermore, within the heart proper the Aschoff bodies appear to present characteristics that are definitely influenced by their site. Thus, the subendocardial, left auricular endocardial and perivascular lesions occur in a compressed form which modifies markedly the topography of the evolutionary stages. Within the looser milieu of the interstitial connective tissue between the myocardial bundles the Aschoff body passes through the various stages of its life cycle relatively unhampered by dense fibro-elastic tissue and, accordingly, presents its more characteristic and fully developed metamorphoses. For these reasons the studies presented here will concern the Aschoff bodies situated between the myocardial bundles — lesions that we have referred to as myocardial Aschoff bodies.

Despite reports, particularly in recent years, in which some doubt is expressed concerning the specificity of this lesion in its relation to rheumatic fever, a review of the literature dealing with the development of our knowledge concerning the Aschoff body reveals sufficient evidence to warrant the definite assumption that this lesion does not occur in the myocardium if rheumatic fever, past or present, can

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safely be ruled out of consideration. We shall assume, therefore, for purposes of this study, that it is absolutely specific of this disease.

It is pertinent to this report to mention that one of the reasons for doubting the specificity of this lesion has been the fact that the Aschoff body assumes allegedly protean forms and that one cannot, therefore, speak of a "typical Aschoff body." In a paper presented before the American Association of Bacteriologists and Pathologists [2] we have shown that the supposed protean appearance of the Aschoff body is due to the fact that the published descriptions have not infrequently referred to different stages in the life cycle of the lesion and that, on the contrary, there is a remarkable constancy in the appearance that these inflammatory nodules assume. We have been able to show [1] that each stage in the development of the lesions apparently presents such a uniformity in characteristics that the Aschoff bodies in their specific forms (the earliest stages — collagen swelling and mesenchymal cell proliferation — cannot be considered a specific picture) may be classified into seven relatively clear-cut and easily recognizable types. Occasionally hybrid forms may be encountered, which undoubtedly represent transitions from one type to another. In order that the argument throughout this report may be followed more easily we shall first present a short description of the seven types of Aschoff bodies found in the myocardium. A discussion on the classification of these lesions, together with a fuller demonstration of their histological characteristics, will be found elsewhere.[1]

Abstract of Classification of Aschoff Bodies

1. *Small Cell Coronal Type:* This consists of a central swollen mass of eosinophilic collagen surrounded by round or oval cells somewhat larger than lymphocytes with a delicate mantle of basophilic cytoplasm which presents a sharply defined edge. The nuclei are of the three types that have been described by us as common to all types of Aschoff bodies in which, however, they occur in different proportions: (1) fibrocytoid, (2) owl-eyed, and (3) pyknotic. Giant cells are occasionally seen. This type of Aschoff body shows the beginnings of a network of argentophilic reticulum fibers.

2. *Large Cell Coronal Type:* This differs from the small cell type in the following respects: the cytoplasm is more abundant, the edges

may be diffuse and ragged, giant cells are seen somewhat more frequently and the network of argentophilic fibers is more prominent.

3. *Syncytial Coronal Type:* In this type the giant cells assume the form of large syncytial basophilic masses with ragged edges. These masses arrange themselves around generally small, centrally located fragments of swollen collagen. Owl-eyed nuclei are quite prominent and tend to assume a peripheral situation within the cytoplasmic masses.

4. *Reticular Type:* This consists of a feltwork of interlacing, swollen collagen fibers which frequently fuse at their points of intersection. Within the meshes of this network there are to be found small cells, round or ovoid, with scant basophilic cytoplasm. Occasionally larger cells with a scattering of owl-eyed, fibrocytoid and pyknotic nuclei may be found. Giant cells may be present. Variations occur in this type in which the collagenous meshwork may be extremely irregular, or where fusion may go on to the extent that larger collagenous masses are produced.

5. *Mosaic Type:* This type is characterized by a fairly regular intermingling of cells and collagen. The cells are abundantly cytoplasmic, deeply basophilic, somewhat fragmented and possess ragged edges. The collagen is swollen, eosinophilic and often fragmented. The cells may be squeezed between the crypts of the collagen masses and connected by delicate cytoplasmic streamers, or the mosaic may be of looser structure, in which case the cells tend to be extremely irregular in shape. The argentophilic fibers occur in the form of a net.

6. *Polarized Type:* In this type the cells begin to assume a spindle shape. They may still be somewhat irregular and elongated or they may present a somewhat smoother contour and still retain the basophilia of the cytoplasm. The entire collection of cells takes on a definite direction within the planes of the myocardial bundles. The argentophilic network is somewhat compressed.

7. *Fibrillar Type:* This is a stage that precedes complete metamorphosis of the cells into fibroblasts. As a consequence the cytoplasm is extremely scant, occurring at times as somewhat blunt basophilic knobs at either end of the much attenuated cell. The nuclei are largely fibrocytoid. Giant cells are infrequent. The collagen occurs predominantly in the fibrillar form. The argentophilic fibers are rapidly disappearing.

As to the origin of the cells, we have already stated that it is safest to assume that they arise from mesenchymal elements, understanding by this term an ultimate derivation from the mesenchyme which may or may not have passed through a differentiation into mature cell types such as lymphocytes, histiocytes or fibroblasts. It is also accepted by many observers that injury to the collagen framework of the heart plays the most conspicuous rôle in the determination of these lesions. As a consequence Aschoff bodies occur at those sites where the collagen is found in the greatest amount, *viz.*, in the planes between the myocardial bundles, in the fibro-elastic tissue around blood vessels and in the endocardium. It is the primary lesion to this collagen, with the subsequent development of cellular reaction of a specific type, that gives rise to the Aschoff body.

The first question with which we shall deal is whether a given heart presents a relatively uniform development of Aschoff bodies in respect to their type. Obviously, if this is not the case, any attempt to introduce a time component in the development of the life cycle of this lesion becomes fraught with such difficulty as to make it an apparently hopeless task. Furthermore, such a state of affairs would lend support to the argument that the Aschoff body may arise in a variety of forms. It may be said at once, therefore, that in an examination of 70 hearts possessing Aschoff bodies we have found that a given section usually presents one type of Aschoff body, occasionally two and rarely three. Furthermore, one frequently encounters in the heart a remarkable uniformity in Aschoff body types, particularly if the specimen is obtained from a patient dying in a first attack, or where the attack has taken place a long time (2 years or more) subsequent to a previous attack. This consistency in the structure and, therefore, in the age of the Aschoff body permits of the reasonable assumption that a given crop of lesions may be timed from the onset of a given attack; and since they reach the same evolutionary stages in development, as judged by their appearance at the time of death, it would seem that these lesions pass through an orderly and probably similar series of progressive changes.

Life Cycle of the Aschoff Body

Several of the published reports make mention of the ultimate fate of the cells concerned in the formation of the Aschoff body. Thus, Aschoff,[3] in 1904, believed that the cells eventually transform them-

selves into fibroblasts. Geipel [4] in 1905 observed the development of the lesion in the 5th to 6th week after the onset of the illness, the formation of giant cells and the swelling and later fibrillar change of the ground substance. Takayasu [5] in 1909 described what appears to have been a mosaic Aschoff body occurring 3 months after the onset of the illness. An excellent contribution along these lines was made by Talalajew [6] in 1929, who divided the evolution of the Aschoff body into three phases: (1) exudative, found at the end of the 2nd or during the 3rd week of the illness; (2) proliferative, occurring in the 2nd or during the 3rd month and lasting, at times, 6 months; and (3) sclerotic, appearing during the 2nd month and lasting, at times, 6 months. In 1930 we[2] presented evidence of many evolutionary phases in the development of the Aschoff body through coronal, mosaic, polarized and fibrillar stages. While a sequence of events was suggested, no intimation was made of the actual time component of each phase. Additional information concerning the time it takes to reach the several evolutionary stages of the Aschoff body was formulated by Klinge [7] and his associates in a series of papers (1929 to 1933). According to this work, at the end of the 2nd week of the illness this lesion is represented by swelling of the collagen fibers and increase of connective tissue and wandering cells, with the presence of occasional giant cells. After the 4th week many swollen and multinucleated cells are found arranged either in rosette form around swollen collagen or dispersed throughout it. From this period on involutionary changes take place through the disappearance of the giant cells and "fibrin" and the development of connective tissue cells.

Before proceeding with our own observations on the life cycle of the Aschoff body it may not be amiss to mention the criteria employed by us to determine the sequence of events and the time factors in the cycle. As mentioned before, 70 hearts, each presenting Aschoff bodies in the myocardium, were studied. These were described grossly, particular care being taken to note the extent of valvular damage. The specimens were generally fixed in formol-saline,* and blocks were cut and stained by a number of methods designed to demonstrate changes in the collagen, tinctorial properties of the cytoplasm, details in nuclear structure and presence of

* For a more detailed description of the methods employed see Gross and Ehrlich.[1]

bacteria, fibrin, argyrophilic reticulum and elastic tissue. The case records from all this material were studied in order to determine the clinical course and particularly to set the time of onset of the last attack.

Apart from the clinical records we attempted to fix the onset of the attack by the extent of the valvular damage, as determined by its macroscopic and microscopic appearance and by the histology of the left auricular lesion, when present. The most reliable guide, however, appeared to be the state of the collagen. In common with a number of observers we were impressed with the fact that the collagen was the first to show damage in the form of swelling and the assumption of eosinophilic properties. The earliest appearance of swelling was, therefore, taken as confirmatory evidence that we were dealing with the beginning of the cycle. In this stage (early phases) the reticular and small cell coronal Aschoff body type predominated. On the other hand, it seemed equally reasonable to assume that the late phases of the cycle were associated with the appearance of fibroblasts (metamorphosis of the Aschoff cells) and the transformation of the swollen collagen into the delicate fibrillar form. These stages were associated with the polarized and fibrillar forms of Aschoff bodies. Moreover, the clinical records confirmed the fact that these were late stages in the evolution of the attack. There remained, therefore, the large cell coronal, syncytial coronal and mosaic forms which, both by the nature of the collagen and on structural considerations, appeared to fall naturally in between these extremes in the age of their development (middle phases). At best, of course, these can be considered no more than an approximation to what actually happens in the human heart.

The material least subject to criticism on which it is permissible to attempt the reconstruction of the stages through which the Aschoff body passes is represented by cases where the individual died in his first attack, and where the time of onset of the disease is definitely known. For this purpose we had available 9 cases, all children who died from 2 to 13 weeks after the onset of the rheumatic fever symptoms, *e.g.*, joint pains and temperature. It is to be noted that in a discussion of the time component of these lesions we shall date their age from the onset of the rheumatic phenomena — disregarding what may be considered a prodromal period, namely, the possible preceding attack of sore throat, scarlet fever, and so on. It

is generally believed that this prodromal period may vary from several days to 4 to 5 weeks. A study of these "first attack" cases indicates that the earliest lesions are of the reticular type, and that fibrillar forms are not found by the end of the 13th week, at least in the limited number of cases available for study. On the other hand, a careful selection of material from cases where the individual suffered from more than one attack presents clear-cut evidence that in these clinical groups the initial lesions may be represented by reticular, as well as small cell coronal forms. Furthermore, an opportunity is thus made available to study the development and time factors of the fibrillar form.

As indicated in a previous publication, it seems fairly certain that the earliest stages consist of swelling, eosinophilic metamorphosis and a certain amount of fusion of the collagen fibers with, *pari passu*, proliferation of the mesenchymal elements. These non-specific early stages may occur in two forms which eventually develop into the coronal and reticular Aschoff body types.

Before entering into a description of the sequence of events that represent the life cycle of the Aschoff body it is of value to classify our material into four clinical groups representing the course taken by the rheumatic fever process in our 70 cases which came to autopsy and presented Aschoff bodies in the myocardium. This classification was undertaken because it appeared that the clinical course of the disease modifies to a certain extent the evolutionary process of the Aschoff body in a given case.

Clinical Classification of Rheumatic Fever Material

Group 1. Cases where the individual died in a first attack.

Group 2. Cases where one attack occurred prior to the final fatal recurrence.

Group 3. Repeated attacks with death during an acute recurrence.

Group 4. Cases where death was caused by decompensation without clinical evidence of a final recurrence. Some of these cases had no previous history of rheumatic fever.

Early Phases: In the "first attack" cases (Group 1), as well as in the other groups where the collagen in the interstices of the myo-

cardium exists in a somewhat loose fibrillar form, the reticular Aschoff body apparently represents the earliest specific lesion. In addition, however, in Groups 2, 3 and 4 the early lesion is also represented with about the same frequency by the small cell coronal Aschoff body type, both types existing side by side in the same blocks taken from the myocardium. The fact that the Group 1 cases show reticular forms exclusively (or, perhaps, predominantly) suggests that the form taken by the initial lesion is apparently influenced not only by the fact that the small cell coronal form begins around more compact collagen, but possibly also by the altered reactivity of the individual, due to the fact that he has already suffered an initial attack. These early stages (early phases) are found in from 2 to 4 weeks after the onset of the disease. Since we did not have any cases where the individual died sooner than 2 weeks after the onset of the disease we have been unable to determine precisely how soon the earliest specific lesion may be found before this time.

Middle Phases: Depending upon whether the earliest lesion is the reticular or small cell coronal Aschoff body type, the nodule may develop in one of two main directions during its middle phase. The reticular form rapidly shows increase in the size of the cells, during which time the collagen may either become more delicate, or fuse and undergo granular degeneration. If the collagen becomes relatively inconspicuous and delicate the cells elongate themselves and there develops the picture of the large irregular cell polarized type. If the collagen undergoes fusion and granular degeneration the resultant picture may be one indistinguishable from the mosaic type with necrotic collagen. This process apparently takes place between the 4th and 13th week after the onset of the illness.

The small cell coronal Aschoff body transforms itself into the large cell variety by swelling of the cell cytoplasm. These swollen cells soon appear to penetrate into the collagenous central mass and eventually permeate it in such a manner as to form the mosaic Aschoff body. If the intercellular collagen undergoes granular degeneration a picture is produced that simulates the corresponding form already described as derived from the reticular Aschoff body. The stage during which the cells begin to permeate the central collagenous mass can be referred to as the coronal mosaic Aschoff body. In some cases the cells of the large cell coronal Aschoff body undergo amitotic division, fusion and enormous enlargement, form-

ing huge syncytial masses which surround the relatively insignificant collagenous central portion (syncytial coronal Aschoff body). This lesion was found most frequently in the "first attack" group and generally appeared during the 9th week after the onset of the attack. Eventually, the syncytial masses disintegrate and produce a picture indistinguishable from the mosaic forms. As in the development that takes place from the reticular Aschoff body, these middle phases in the evolution from the small cell coronal lesion also occur between the 4th and 13th week after the onset of the disease.

Late Phases: The large irregular cell polarized Aschoff body, as well as the mosaic Aschoff body, whether derived from the reticular or small cell coronal lesion, now begins to show elongation of the cells to spindle forms. The cytoplasm still retains its basophilia but the outlines become sharp. The collagen becomes scanty and there is thus developed the polarized Aschoff body. Apparently, these lesions generally appear from the 9th to the 16th week after the onset of the disease. It is seen, therefore, that no matter which of the two initial lesions subsequently develops through the evolutionary stages of the Aschoff body, the lines of development apparently ultimately converge into the polarized forms.

From this point on, the spindle cells apparently transform themselves into fibroblasts. Delicate collagenous fibrils, which may ultimately fuse into dense collagenous bundles, appear between the cells. For some considerable time, however, the cells still retain rather blunt basophilic knobs of cytoplasm at either end of the elongated nucleus. Furthermore, whereas giant cells become extremely scarce and the nuclei become largely fibrocytoid, there are still to be seen a sufficient admixture of owl-eyed and pyknotic nuclei which, together with the peculiarity of the cells, distinguish this lesion as specific of rheumatic fever. We have designated these lesions as fibrillar Aschoff bodies. They apparently occur some time after the 13th week following the onset of the illness. The final stage in the evolution of this specific inflammatory lesion is the complete metamorphosis of the fibrillar Aschoff body into scar tissue which lies rather characteristically between the muscle bundles.

Figure 1 illustrates diagrammatically the lines of development of the Aschoff body, starting from the reticular and small cell coronal lesions and ending in the fibrillar type. An indication is given of the time component, although it must be realized that the attempt which

we have made at timing the development of these lesions represents an average arrived at from a study of relatively few specimens. There can be no doubt that considerable variations occur in the tempo, but this can be determined only from a much larger series of cases.

Relation of Aschoff Body Type to Clinical Course of Rheumatic Fever

In examining the types of Aschoff bodies found in the four clinical subdivisions of rheumatic fever outlined above several observations seemed to be worthy of note. Thus, the small cell coronal lesion was not found in the first group. This may have been due to the limited material available. On the other hand, as stated before, it may represent a difference in the reactivity of these "first attack" cases from the other clinical types. The large cell coronal, syncytial coronal and mosaic types were found more frequently in this group than in the other three. Fibrillar forms were not found. This may be due to the fact that death occurred within 13 weeks after the onset of the illness in the cases that comprised this group. In the second clinical group the incidence of small cell coronal and fibrillar types, as the initial lesions, was about equal. Mosaic forms occurred frequently, perhaps, however, slightly less often than in the first group. Fibrillar forms occurred with moderate frequency and large cell coronal types were relatively infrequent. The third group showed a further decrease in the incidence of mosaic forms, the lowest incidence of fibrillar forms found in any group with the exception of Group 1, and the highest incidence of polarized forms found in any group. Inasmuch as these two types of lesions are to a certain extent reciprocals of one another this observation does not indicate a fundamental difference in this group. No reticular forms were found in the fourth group, which otherwise showed approximately the same incidence of lesions as found in the second group. The conspicuous points in these observations appear to be the absence of small cell and fibrillar Aschoff bodies in Group 1, the high incidence of mosaic forms and the relatively high incidence of large cell coronal and syncytial coronal forms in this group, and the absence of reticular lesions in Group 4.

Incidence and Distribution of Aschoff Bodies in the Myocardium

The figures quoted in the earlier literature (see Clawson [10]) on the incidence of Aschoff bodies in the hearts of patients dying from rheumatic fever are considerably higher than those obtained by later investigators. The reason for this discrepancy undoubtedly lies in the fact that the earlier workers chose active cases on which to make their studies. On the other hand, the figures recently published have also been high, probably because of better recognition of these lesions and a more thorough search for them. In comparing the reported incidence it must be remembered that the type of material studied plays an important rôle. Unless the proportion of acute and chronic cases studied is indicated no true comparison can be made. Furthermore, as will be shown later, the number of blocks studied and, more particularly, the sites from which these blocks have been taken, will materially influence the results obtained. Of the more recently published figures it is of interest to note that Aschoff bodies were found in the myocardium in 18 of Libman's [8] 56 cases (32 per cent), 20 of Kugel and Epstein's [9] 24 cases (83 per cent), 31 of Clawson's [10] 50 cases (62 per cent), 24 of McClenahan and Paul's[11] 28 cases (85.7 per cent), 42 of Gross, Antopol and Sacks' [12] 79 acute and chronic cases (53 per cent), and in 60 of Thayer's [13] 64 cases (93.7 per cent).

In our present statistics, which are based on a study of the standardized blocks, Aschoff bodies were found in approximately 59 per cent of 161 hearts showing evidence of rheumatic infection, past or present, and in 90 per cent of hearts in cases that showed evidence of activity, clinically or pathologically. The clinical evidence of activity can be considered to consist of joint pains, choreic manifestations and fever. The anatomical evidences of activity consist of fresh verrucous lesions, fresh pericarditis and acute inflammatory phenomena in the myocardium, valve rings and valve leaflets. The question of the relation of activity to myocardial failure and the incidence of these phenomena during the first eight decades of life have been studied by Rothschild, Kugel and Gross,[14] who were able to show that during the first five decades of life myocardial failure is closely paralleled by activity in the myocardium.

Classifying our rheumatic material that presented Aschoff bodies in the myocardium into the four groups outlined above, we observed

that in the first group ("first attack" cases) myocardial Aschoff bodies are almost invariably found in the interventricular septum (T.V.*) and in the upper part of the posterior wall of the left ventricle (M.P.). The posterior wall (myocardium) of the left auricle (L.A.), left posterior papillary muscle (P.P.M.) and pulmonary conus (P.A.V.) show the presence of Aschoff bodies in about 60 per cent of the cases. The myocardial wedge between the aorta and left auricle (A.M.V.) shows Aschoff bodies in only a small percentage of the cases.

The Group 2 cases, *i. e.*, those where the individual suffered from one previous attack, show a decidedly lower incidence of auricular myocardial Aschoff bodies (approximately 20 per cent), but the same incidence of lesions in the upper part of the posterior wall of the left ventricle (M.P.). The distribution of Aschoff bodies in the other sections is similar to that in Group 1, but approximately 15 per cent lower in incidence. In Groups 3 and 4 myocardial Aschoff bodies were not found in the myocardial wedge between the aorta and left auricle (A.M.V.). They were rare in the posterior wall of the left auricle (L.A.). The distribution of Aschoff bodies in the left posterior papillary muscle (P.P.M.), the interventricular septum (T.V.) and pulmonary conus (P.A.V.) was in the same proportion as the corresponding sites in Group 1, but about 30 per cent lower in incidence. In Group 3 Aschoff bodies were found in the upper part of the posterior wall of the left ventricle (M.P.) in 90 per cent of the cases, in Group 4 in 64 per cent of the cases. Perivascular and subendocardial Aschoff bodies, on the other hand, in contrast to what we have termed "myocardial Aschoff bodies," seem to occur with greater frequency in Group 4 cases.

In summarizing our findings in these four groups it seems that when Aschoff bodies are found in all the standardized blocks the case almost invariably falls into the first group of our clinical classification. Furthermore, involvement of the myocardium of the posterior wall of the left auricle (L.A.) with Aschoff bodies occurs almost as frequently as it does in the posterior wall of the left ventricle (M.P.) and interventricular septum (T.V.). Conversely, the left auricular myocardium (L.A.) is seldom involved with Aschoff bodies in the remaining three groups. The incidence of Aschoff bodies in the up-

* These bracketed initials refer to the abbreviated terminology employed by Gross, Antopol and Sacks [12] to designate the standardized sections.

per part of the posterior wall of the left ventricle (M.P.) remains approximately the same (90 per cent) in the first three groups. It is somewhat lower in the fourth group. The incidence of Aschoff bodies in the interventricular septum (T.V.) is extremely high (almost 100 per cent) in the first group. It varies from 66 per cent to 88 per cent in this site in the remaining groups. This curious rearrangement in the incidence of Aschoff bodies in various parts of the heart, brought about by the clinical course of the disease, again suggests the possibility of some alteration in the reactivity of the tissues induced by the nature and frequency of previous attacks.

Quite apart from this clinical grouping of our material, it may be stated that when Aschoff bodies are present in the myocardium they will be found almost invariably either in the interventricular septum (T.V.) or posterior wall of the left ventricle (M.P.). The next most frequent sites in the order of frequency with which Aschoff bodies are found are the left posterior papillary muscle (P.P.M.), pulmonary conus (P.V.), posterior wall of the left auricle (L.A.) and myocardial wedge between the aorta and left auricle (A.M.V.).

Discussion and Summary

There has been presented in this report a study of the life cycle of the myocardial Aschoff body, based on an examination of the clinical records and autopsy material from 70 cases that presented Aschoff bodies in the myocardium. It appears that these specific lesions pass through three stages in development. The earliest phases, represented by small cell coronal and reticular Aschoff bodies, have been found to occur up to the 4th week after the onset of the illness. The middle phases, represented by large cell coronal, syncytial coronal, mosaic and large irregular cell polarized Aschoff bodies, have been found to occur between the 4th and 13th week after the onset of the illness. The late phases are represented by polarized Aschoff bodies which occur from the 9th to the 16th week after the onset of the illness, and subsequently by fibrillar Aschoff bodies which occur after the 13th week of the illness.

The earliest types of specific lesions are apparently influenced in their response by the reactivity of the tissue, depending on whether there has or has not been a previous attack of rheumatic fever, and also by the state of the collagen present in the interstices between the

myocardial bundles. As a consequence, the evolution of the lesion may follow one of two main courses, determined by the initial lesion. The latter may occur in the form of the reticular or the small cell coronal Aschoff body. The final phases of the life cycle of the Aschoff body are common to both main courses.

Dividing the material into four groups representing different clinical courses, there appears to be some change both in the incidence of the types of Aschoff bodies present in the myocardium and in their localization. The findings reported here, however, can by no means be considered as furnishing sufficient statistical evidence on which to base final conclusions on this point. That the tempo of the life cycle may be considerably faster or slower than what has been described in this report seems very probable. Some of the stages in the "model" of the life cycle presented by us may be absent in some cases, abbreviated in others, or indeed, appear in the reverse order from what we have suggested. These facts can be determined with greater accuracy only after examining a much more extensive series of cases and, in the last analysis, must await confirmation by the hitherto unsuccessful transmission of this disease to animals. It is hoped, however, that further studies will be made along these lines in order that some of these interesting relations may be placed on a firmer footing.

REFERENCES

1. Gross, L., and Ehrlich, J. C. Studies on the myocardial Aschoff body. I. Descriptive classification of lesions. *Am. J. Path.*, 1934, **10**, 467–487.
2. Gross, L., and Ehrlich, J. C. Histological studies on the Aschoff body. *Am. J. Path.*, 1930, **6**, 621.
3. Aschoff, L. Zur Myocarditisfrage. *Verhandl. d. deutsch. path. Gesellsch.*, 1904, **7** and **8**, 46–53.
4. Geipel, P. Untersuchungen über rheumatische Myokarditis. *Deutsches Arch. f. klin. Med.*, 1905-06, **85**, 75–88.
5. Takayasu, R. Zur Kenntnis der sogenannten Endarteriitis infectiosa und der Knötchenbildung bei rheumatischer maligner Endokarditis. *Deutsches Arch. f. klin. Med.*, 1908–9, **95**, 270–279.
6. Talalajew, W. T. Der akute Rheumatismus. *Klin. Wchnschr.*, 1929, **8**, 124–129.
7. Klinge, F. Der Rheumatismus. *Ergebn. d. allg. Pathol. u. path. Anat.*, 1933, **27**, 1–336.

8. Libman, E. Characterization of various forms of endocarditis. *J. A. M. A.*, 1923, **80**, 813–818.

9. Kugel, M. A., and Epstein, E. Z. Lesions in the pulmonary artery and valve associated with rheumatic cardiac disease. *Arch. Path.*, 1928, **6**, 247–262.

10. Clawson, B. J. The Aschoff nodule. *Arch. Path.*, 1929, **8**, 664–685.

11. McClenahan, W. U., and Paul, J. R. A review of the pleural and pulmonary lesions in twenty-eight fatal cases of active rheumatic fever. *Arch. Path.*, 1929, **8**, 595–610.

12. Gross, L., Antopol, W., and Sacks, B. A standardized procedure suggested for microscopic studies on the heart. *Arch. Path.*, 1930, **10**, 840–852.

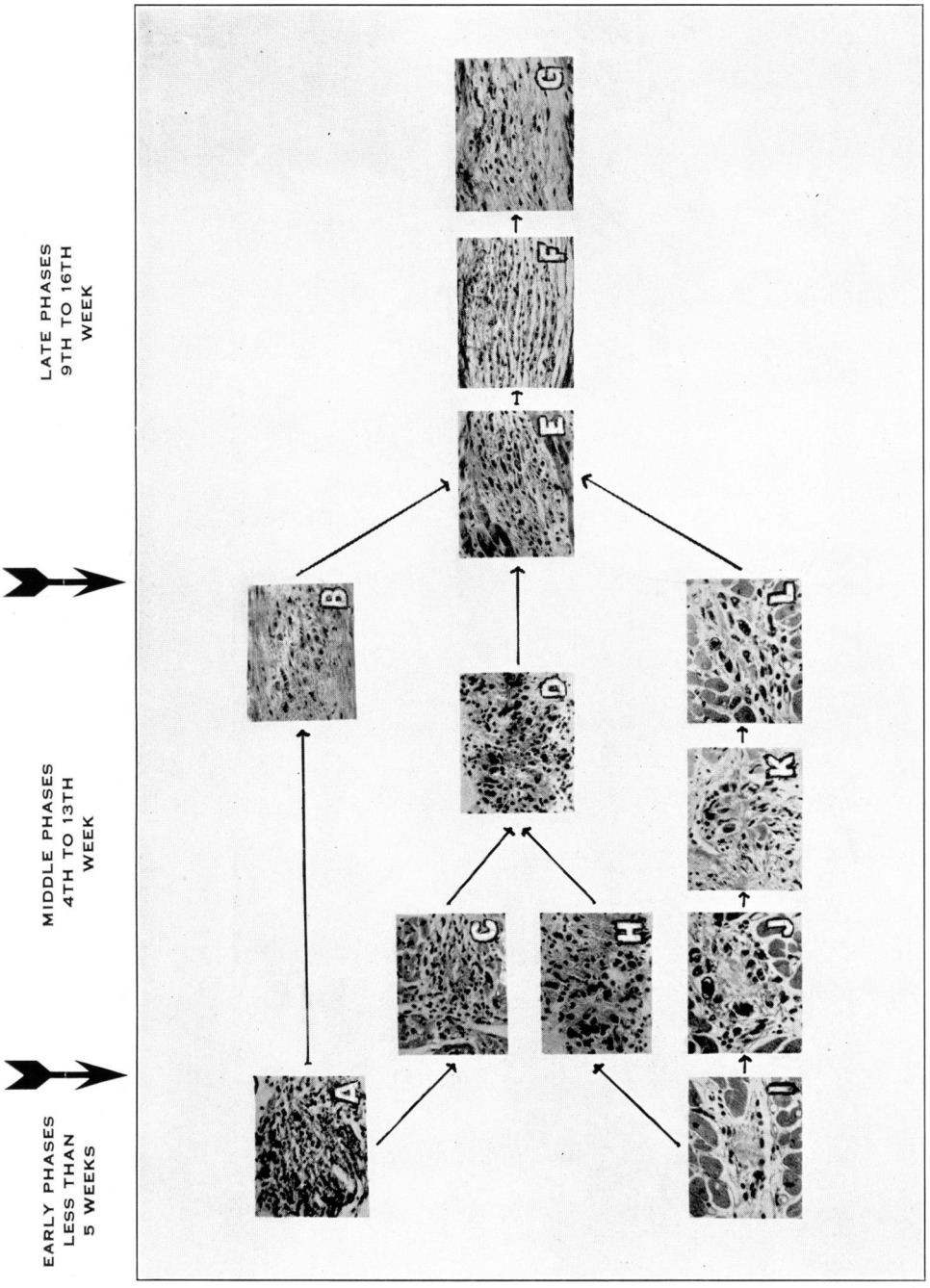
13. Thayer, W. S. Bacterial or infective endocarditis. *Edinburgh M. J.*, 1931, **38**, 237–265, 307–334.

14. Rothschild, M. A., Kugel, M. A., and Gross, L. Incidence and significance of active infection in rheumatic fever during the various age periods. *Am. Heart J.*, 1934, **9**, 586–595.

DESCRIPTION OF PLATE

PLATE 125

FIG. 1. Aschoff body types illustrating various stages in the life cycle of the lesion. A, reticular stage; B, large irregular cell polarized stage; C, reticular stage with fusion and granular degeneration of collagen fibers; D, mosaic stage with granular degeneration of collagen; E, polarized stage showing marked spindle cell formation; F, polarized fibrillar stage; G, fibrillar stage; H, large cell coronal stage with granular degeneration of collagen; I, small cell coronal stage; J, large cell coronal stage; K, coronal mosaic stage; L, mosaic stage, compact form with beginning polarization.


LATE PHASES
9TH TO 16TH
WEEK
MIDDLE PHASES
4TH TO 13TH
WEEK
EARLY PHASES
LESS THAN
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