CYTOLOGIC STUDIES ON RHEUMATIC FEVER

I. The Characteristic Cell of the Rheumatic Granuloma

By CURRIER McEWEN, M.D.

(From the Hospital of The Rockefeller Institute for Medical Research)

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Bang, in 1878 (1), described multinucleated giant cells in a rheumatic subcutaneous nodule, but it was not until Aschoff's (2) discovery of the myocardial submiliary node, in 1904, that attention was focused upon the characteristic microscopic appearance of the granulomata in rheumatic fever. Although a number of investigators (3–5) have questioned the specificity of the Aschoff body, and despite the fact that early and late stages of these lesions do not present all the features of the typical granulomata, it is generally conceded that few microscopic lesions are more characteristic of a given disease than are the fully developed Aschoff bodies. It is likewise quite generally accepted that the essential elements of the fully developed nodules are the large basophilic and often multinucleated cells found in them. Because of the uncertainty concerning the nature of these cells the present study was undertaken in an attempt to obtain additional information by examining the living cells supravitally stained. The terms "Aschoff body cell" and "cell of the rheumatic granuloma" employed in this paper, refer, of course, to the characteristic cells just mentioned, and not to the lymphocytes, plasma cells, and polymorphonuclear leucocytes which also may be present.

The myocardial submiliary nodules do not lend themselves to the supravital method of examination because of their microscopic size and the difficulty of obtaining them in the fresh state. Subcutaneous nodules, on the other hand, are macroscopic and can be easily excised; and, accordingly, they were selected as the material with which to work. It is obviously important for the purposes of this study, therefore, that the essential identity of these lesions and those in the

myocardium be recognized. Clinically, the relationship between the two has been thoroughly established. The modern appreciation of this fact is well illustrated by the statement of Coombs (6), who, in discussing the various rheumatic manifestations, described the subcutaneous nodules as "the most rheumatic of all." The pathologic evidence supporting this relationship is even more convincing, so that almost all pathologists who have studied the subcutaneous nodules have concluded that morphologically and genetically these lesions are essentially the same as those in the myocardium. Only two opinions to the contrary (7, 8) have been encountered in the literature (see Table I), and the convincing evidence in favor of the analogous nature of the granulomata occurring in different parts of the body in rheumatic fever makes logical the use of the subcutaneous nodules as an indirect means of studying the Aschoff body cells in the myocardium.

Table I summarizes the view of different authors concerning the nature or origin of the peculiar large cells which characterize these lesions. As indicated at the head of the table, the opinions recorded in the first column were derived from studies of subcutaneous nodules, while those in the second column were based upon investigations of the myocardial lesions. Only in those instances in which a different origin has been ascribed to the cells in the two lesions has the opinion of a single author been recorded in both columns. While this list makes no pretence at completeness, it does serve to show the lack of agreement among investigators who have expressed a definite opinion.

Grouping the data from the table in another way, one sees that the cell of the rheumatic granuloma has been thought to arise from different sources by various of these authors as follows: from muscle cells by 5, from endothelial cells by 5, from connective tissue cells by 21, and from wandering or fixed phagocytic cells by 19. This last class, referred to in this communication as clasmatocytes, probably includes all those cells listed in Table I under the names of adventitial cells, macrophages, mononuclear wandering cells, clasmatocytes, endothelioid cells, endothelial leucocytes, polyblasts, histiocytes, lymphocytoid elements, and epithelioid cells. By using supravital staining, Sabin and her coworkers (44) have shown the true epithelioid cells of the tubercle to differ from the clasmatocytes, but in the sense in which these terms were used by the authors in Table I, the names probably referred to cells of the same type.

TABLE I

Views of Different Investigators on the Nature of the Characteristic Cells of Subcutaneous Nodules and Myocardial Nodules

Date	Subcutaneous nodules	Date	Myocardial nodules
1878	Bang (1)—Connective tissue cells		
1883	Cavafy (9)—Lymphoid cells		
1883	Carvasy (10)—Young connective tissue cells		
1887	Gilly (11)—Embryonic connective tissue cells		
1889	Cheadle (12)—Connective tissue cells		
1895	Futcher (13)—Fibroblasts		
1904	Wick (14)—Epithelioid cells	1904	Aschoff (2)—Leucocytoid elements (adventitial cells)
		1905	Geipel (3)—Connective tissue cells
		1906	Aschoff and Tawara (15)—Lymphocytoid elements and connective tissue cells
		1907	Coombs (16)—Connective tissue cells
		1908	Saigo (17)—Epithelioid and muscle cells
		1909	Bracht and Wächter (18)—Connective tissue cells
		1910	Roy (19)—Connective tissue and mononuclear wandering cells
		1911	Coombs (20)—Either endothelial or connective tissue cells
		1911	Gallavardin (21)—Epithelioid cells
1912	Frank (22)—Connective tissue cells	1912	Fraenkel (23)—Adventitial connective tissue cells
1913	Voelcker (24)—Connective tissue cells	1913	Huzella (25)—Connective tissue cells
1914	Tilp (26)—Endothelial cells	1914	Huzella (27)—Muscle cells
1914	Patella (7)—Lymphatic endothelial cells	1914	Patella (7)—Connective tissue cells
		1917	Langmann (28)—Endothelial or mononuclear wandering cells
1918	Fahr (29)—Connective tissue cells		
1919	Jacki (30)—Polyblasts	1919	Aschoff (31)—Connective tissue cells
		1920	Mallory (32)—Endothelial leucocytes
		1920	Whitman and Eastlake (33)—Muscle cells

TABLE I—*Concluded*

Date	Subcutaneous nodules	Date	Myocardial nodules
1923	Perkins (34)—Endothelioid cells	1923	Kanatsoulis (35)—Epithelioid cells
1924	Swift (36)—Endothelial cells		
		1925	MacCallum (37)—Clasmatocytes
		1926	Letulle, Bezançon, and Weil (38)—Muscle and connective tissue cells
		1926	Sacks (39)—Histiocytes
1927	Gräff (40)—Adventitial and connective tissue cells		
1928	Symmers (8)—Connective tissue cells	1928	Symmers (8)—Muscle cells
		1929	Clawson (4)—Polyblasts
		1929	Gross, Loewe, and Eliasoph (41)—Histiocyte family
		1930	Klinge (42)—Mesenchymal cells
		1931	Donaldson (43)—Histiocytes

Material and Technique

It is especially important that the rheumatic nature of the nodules used in this study be firmly established because of the occurrence of somewhat similar lesions in other diseases. The so called juxta-articular nodules of syphilis, yaws, acrodermatitis chronica atrophicans, and scleroderma may be mentioned among these, although it is most improbable that they would be mistaken for rheumatic lesions. For accounts of them the reader is referred to the papers of the Harvard African Expedition (45), of Jessner (46), and of Hopkins (47). Subcutaneous nodules have likewise been reported in patients with infectious arthritis, by Hawthorne (48), Coates (49), Dawson and Boots (50), and others; as some of these authors have pointed out, however, this probably indicates merely the close connection between this disease and rheumatic fever. Finally, Coates and Coombs (51) have described similar lesions occurring in a patient with endocarditis lenta, although the nature of the disease apparently was not unquestionably established since there is no mention of a blood culture in the report and the patient, who had previously had rheumatic fever, recovered.

The present study is based upon an investigation of eleven subcutaneous nodules from ten patients with rheumatic fever, six of whom were from the Hospital of The Rockefeller Institute, while the remaining four were from the Children's Medical Service of Bellevue Hospital. From nine the material was obtained at biopsy, while from one it was obtained at autopsy within ½ hour of the patient's death. All the patients had typical rheumatic fever with carditis and polyarthritis in addition to the subcutaneous nodules, and all were between the ages of 5 and 22 years. The blood Wassermann reaction was negative in the six patients in

whom the test was performed, while in the other four, whose ages ranged from 5 to 12 years, there were no stigmata of congenital lues. In no case was there reason to suspect bacterial endocarditis and, in the one patient who died, autopsy revealed no evidence of that disease.

The control material comprised: skin and subcutaneous tissue from a patient with erythema nodosum and rheumatic heart disease, a piece of subcutaneous tissue and deep fascia from a boy with rheumatic subcutaneous nodules, an "ephemeral node" from a case of bacterial endocarditis, a bit of triceps tendon and deep fascia from the elbow of a nephritic patient, and numerous scrapings of the deep fascia, tendons, periosteum, and endothelial linings of blood vessels of rabbits and dogs.

Preliminary to excision in two of the cases, material was obtained by inserting a needle of wide caliber into the tumor mass and then withdrawing bits of tissue through it by means of a dental broach. This method, described by Forkner (52), is satisfactory for lymph nodes and other friable tumors, but was inadequate for obtaining a sufficient amount of material from subcutaneous rheumatic nodules. In both cases in which this method was employed, however, a few cells were obtained which could be identified from the previous experience with excised lesions.

Each of the excised nodules was cut in half and one piece was immediately placed in Zenker-acetic solution or in formol for the preparation of serial sections. The other half was freed from non-granulomatous material and was then scraped with a sharp scalpel. The small amount of material thus obtained was treated as follows:—

1. Films were made on clean glass slides by mixing the scrapings in a drop of physiologic saline, which was then allowed to dry. They were fixed in Zenker-acetic solution 15 minutes, washed in water for several hours, and finally stained in several ways, the most satisfactory of which was the malachite green-acridine red method of Hitchcock and Ehrich (53).

2. Supravitally stained preparations were made according to the technique described by Sabin (54). Dried films of neutral red and Janus green were prepared.[1] The scrapings from the nodules were mixed in a drop of physiologic salt solution upon cover-slips which were then inverted upon the prepared slides and

[1]The dyes used were those of the National Aniline and Chemical Company, New York. A stock solution of neutral red was made by dissolving 125 mg. of the powdered dye in 50 cc. of neutral absolute alcohol; and that of Janus green (diazine green) by dissolving 125 mg. in 62.5 cc. of absolute alcohol. From the stock neutral red a dilute solution was made by adding 50 drops to 10 cc. of absolute alcohol. All these solutions keep very well separately, but when neutral red and Janus green are mixed in solution they deteriorate rapidly; hence the combined stain for the preparation of the slides was made just before use. This was done by mixing thoroughly 2 drops of the Janus green solution in 3 cc. of the dilute neutral red. Carefully cleaned slides were then flooded with this mixture and were dried above a small flame so that the dyes remained as a thin, even film.

sealed with vaseline. In some instances the scrapings were mixed in a drop of dilute saline solution of neutral red or Janus green upon the prepared slides in order to increase the amount of available dye. These preparations were immediately examined under the oil immersion lens in a warm chamber at 37°C.

In one instance this procedure was altered to ascertain whether the intravital injection of particulate matter would lead to phagocytosis by the cells of the nodule. A sterile 50 per cent suspension of India ink in physiologic saline was injected into and around the nodule. Biopsy was performed 40 hours later and the excised material was subjected to the procedures already outlined.

RESULTS

All the supravitally stained preparations showed small masses of tissue composed of many cells lying in a fibrillar meshwork, and of wavy fibrils such as occur in similar preparations of tendons or deep fascia. Only at the margins of these masses, however, could the cells be clearly distinguished. Lying between the bits of tissue were large numbers of these same cells which, because of their isolated positions, could be more accurately studied. Of these, the great majority were of the type illustrated in Fig. 1 *A*, but all transitions were seen ranging from small cells about the size of intermediate lymphocytes to spindle-shaped cells and large, multinucleated giant forms. In addition, erythrocytes were always present, while in several preparations there were a few small lymphocytes, monocytes, and clasmatocytes. Occasional cells were encountered which had the appearance of plasma cells as described by Miller (55).

The predominating cell in supravitally stained preparations was from 15 to 20 microns wide by 20 to 30 microns long. The small cells, however, were sometimes only 8 x 15 microns in diameter, while the multinucleated cell in Fig. 3 measured 32 x 77 microns. The shape was usually oval, but many of the cells had pointed processes at one end which were often at a sharp angle to the rest of the cell, while the long, spindle-shaped elements shown in Fig. 1 *B*. were not uncommon.

The cell membrane in freshly studied preparations was very indistinct, but was more definite in those kept in the ice box for 48 hours. The cytoplasm had a coarse, ground glass appearance, and its pale yellowish gray color showed it to be slightly basophilic. The nucleus was oval and large, almost filling the small cells, but occupying relatively less of the larger ones. In sharp contrast to the vague cell

outline, the nuclear membrane was extremely distinct. The nuclear background had almost the same appearance as the cytoplasm, but the ground glass markings were coarser and the basophilia slightly greater. Indeed, the nucleus and cytoplasm were so similar that, if it had not been for the sharply outlined nuclear membrane, it would have been difficult to distinguish between them. One or two nucleoli were usually present.

Definite mitochondria were never seen, although in a few cells a faint suggestion of minute, pale blue dots was noted. A striking contrast to this was observed in the case of the lymphocytes present in small numbers in many of the preparations; in these cells the deep blue mitochondria were always easily seen, especially in scrapings stained with an additional drop of dilute saline solution of Janus green. The study of fixed material stained by Altmann's method (56) also failed to reveal mitochondria.

The failure of the cells to take up neutral red was their most striking characteristic. In a few cells two to four small, pale pink dots were seen which faded after about 30 minutes. The great majority, however, showed none of the dye at any stage of the examination, and there was a complete lack of phagocytosis even in preparations exposed to neutral red for 30 days at ice box temperature. A few small refractive bodies were seen in almost all the cells, but they seemed never to be stained by the dye.

Fig. 1 is a drawing of some of the cells from one nodule. At *E* can be seen the edge of one of the large masses of fibers and cells which were always present in the scrapings. At *A* is shown a cell of the type which comprised about 80 per cent of all those in the preparations. The coarsely granular character of the cytoplasm is better illustrated in Fig. 2, a microphotograph of a similar group of cells; but the drawing depicts very well the sharply outlined nuclear membrane, the refractive bodies in the cytoplasm, and the nucleoli. In Fig. 1 at *B*, *C*, and *D* are shown variations from this predominant type. Of these the small cell at *C* probably represents merely an earlier stage, while the others show definite alterations in form. The two cells labeled *B* show transition toward the long spindle-shaped elements which resemble fibrocytes, while that marked *D* is a giant cell with two nuclei. The best example of the latter type of cell, however, is seen in the microphotograph (Fig. 3), which likewise depicts very clearly the vague cell boundary and the very distinct nuclear membranes. The scrapings from this nodule contained a few clasmatocytes and two of these are shown for contrast (Fig. 1 *F*). In these clasmatocytes the definite cell boundary, the vague nuclear borders, and

especially the large number of neutral red-stained bodies serve to differentiate them very sharply from the characteristic cells of the rheumatic granuloma.

As has been mentioned, scrapings of all the nodules were fixed in Zenker-acetic solution and were stained by the malachite green-acridine red method. Such preparations showed cells having the same staining characteristics as those in the usual paraffin sections. The cytoplasm took the red dye with varying intensity, apparently depending upon the age, size, and state of preservation of the cell. The dark blue and sharply outlined nuclear membrane contrasted sharply with the pale blue of the nuclear background, and against this the deep red or blue nucleoli stood out plainly.

The study of supravitally stained scrapings from the nodule into which India ink had been injected was particularly interesting. Most of the cells were exactly like those described above, but a few contained particles of carbon as shown by a differential count of 200 cells, of which 95 per cent contained no India ink, 3 per cent contained 2 to 3 small particles, while in the remaining 2 per cent the carbon was present in fair amount. Even these phagocytic cells, however, failed to stain with the neutral red. Study of sections of this nodule bore out these results. A moderate amount of intercellular carbon was scattered diffusely through the nodule and surrounding tissue and there were many polymorphonuclear leucocytes, a large number of which contained ink granules. In the perinodular tissue were many typical clasmatocytes, completely filled with particles of carbon. In the characteristic nodule tissue, on the other hand, only a small percentage of the granuloma cells contained a few small particles, and typical clasmatocytes were entirely lacking in spite of the presence of much unphagocytosed carbon.

While all the rheumatic nodules consistently yielded large numbers of the characteristic cells illustrated in Figs. 1 and 2, nothing comparable was found in any of the control material. A few elongated cells occurred in scrapings of normal rabbit tendons or deep fascia and of similar tissue taken from patients who had died of other diseases. These were similar in many respects to cells of the type shown in Fig. 1 *B*, but were very infrequently encountered and the rounded forms and giant cells were never found. The piece of deep fascia from a

patient with rheumatic nodules which was mentioned among the control material, deserves further comment. This patient had definite nodules in areas not suitable for excision and in addition a very small one situated over the left patella. An attempt was made to excise the latter and the material obtained was immediately subjected to the procedures previously outlined but no cells of the rheumatic granuloma type were found in supravitally stained preparations. Subsequent examination of the paraffin sections of this material, however, revealed only normal connective tissue, and hence it was obvious that the nodule had been missed at the time of biopsy.

DISCUSSION

The success attained in identifying the cells in the lesions of tuberculosis and syphilis by means of the supravital staining method led to its employment in this study of the rheumatic granulomata. Sacks (39) had already suggested that the subcutaneous nodules would lend themselves to such an investigation; and Cecil (57) used vital staining to identify cells in the myocardial lesions of rabbits which had been injected intravenously with streptococci. He found these cells to be macrophages, but since he believed the experimentally produced lesions to differ from Aschoff bodies, the investigation did not cast much light on the nature of the cells in the latter.

As indicated in Table I, a number of possible origins have been suggested for the peculiar cells of rheumatic granulomata, and each of these will be considered.

First, it is fairly certain that fragments of cardiac muscle fibers lying in Aschoff bodies may sometimes have the appearance of multinucleated giant cells, especially when the fibers are regenerated and have been cut transversely. In all probability, however, this is not the source of the true Aschoff body cells; indeed, if one agrees with the generally accepted view that the granulomata in the cardiac valves and auricular endocardium are analogous to those in the myocardium (58), it is obvious that the characteristic cells of these lesions cannot be dependent upon muscle fibers for their origin.

The possibility that the cells of the rheumatic granuloma arise from endothelium is suggested by the great vascularity and extensive endothelial swelling and proliferation in histologic sections of many

subcutaneous nodules. On the other hand, such changes are not present in all nodules; and, conversely, similar endothelial swelling may occur in any area containing newly formed capillaries. Moreover, careful search of serial sections of myocardial Aschoff bodies sometimes fails to reveal the presence of any vessels in or near the lesions (59). Hence the close resemblance of the swollen endothelial cells to the typical Aschoff body cells, in ordinary histologic sections, is merely suggestive of a relationship between them. Unfortunately, the method employed in the present work has not given, as yet, a definite answer to the question thus raised. Endothelial cells obtained by scraping vessels differ greatly in appearance from the cells of the rheumatic granuloma, in that they are more spindle-shaped and lie in sheets; but those free elements in the circulating blood which Sabin and Doan (60) have called desquamated endothelial cells bear a close resemblance to cells of the type illustrated in Fig. 1 *B*.

The great majority of authors listed in Table I selected connective tissue cells or those of the clasmatocyte group as the source of the elements of the rheumatic granulomata. These two views can be conveniently discussed together, since the latter elements were probably included in the broad term "connective tissue cells" as it was employed by pathologists up to recent years. Indeed, opinions concerning the origin and nature of the Aschoff body cells hinge largely upon the nomenclature of the different elements of the normal and pathologic loose connective tissue. The omentum serves as an excellent example of such tissue, in which one can identify three chief cellular components: (*a*) the true adventitial cells of Marchand, which are actively phagocytic and belong to the group called clasmatocytes in this communication; (*b*) the fibrocytes; and (*c*) the primitive mesenchymal cells, which have a great capacity for further differentiation. The chief distinguishing feature of the first of these types, in supravitally stained preparations, is a marked ability to take up neutral red. The present investigation has shown that the typical cells of subcutaneous rheumatic nodules, on the contrary, are incapable of this; hence they cannot be clasmatocytes. This same characteristic tends to exclude the fibrocytes as the source of the cells in question, since Carrel and Ebeling (61) and others have shown that they, too, take up the dye in moderate amount, especially when actively dividing. In the scrap-

ings here examined there were some cells (Fig. 1 *B*) which in shape suggested fibrocytes. The characteristics of all the granuloma cells, however, including these spindle-shaped elements, were those of young connective tissue cells less differentiated than the fibrocytes. This study, therefore, points strongly to the primitive mesenchymal elements as the source of the cells under investigation.

In connection with the fact that both connective tissue and endothelium have been suggested as the source of the cells in rheumatic granulomata, the views of Klinge are of particular interest. This author (42) has interpreted rheumatic fever as a disease essentially of the mesenchyme. He believes that the characteristic cells arise chiefly from mesenchymal elements normally present in connective tissue, but, in addition (62), that perimysial cells and endothelial cells lining capillaries and lymph spaces may also take part, since they are of mesenchymal origin. Recently, Rinehart (63) has summarized the data favoring the view that capillaries and lymph vessels arise *in situ* from undifferentiated mesenchyme, and has presented additional evidence that the endothelial cells are only slightly differentiated from the primitive mesenchymal elements. These theories, although still debatable, offer a possible explanation of the apparent participation of both connective tissue and endothelial cells in the formation of some of the lesions; and it may be that, although the primitive mesenchymal cells respond most readily to the stimulus of rheumatic fever, other cells, not too highly differentiated, may also take part.

The microscopic lesions of tuberculosis, syphilis, and rheumatic fever are all composed of unit cells which bear a strong resemblance to one another in ordinary histologic sections and which probably all arise from the undifferentiated mesenchymal cells. It is of interest, therefore, to compare these unit cells in their reaction to the supravital dyes, and at the same time to note the different modes of development of the primitive mesenchymal elements in these three diseases. Sabin, Doan, and Forkner (64) have shown that in experimental tuberculosis there is, early, a great increase in the number of these undifferentiated cells, which rapidly evolve into monocytes and epithelioid cells (the latter term being restricted, here, to the typical elements of the tubercle characterized by the neutral red rosette which has been described by the same authors). By development in a different man-

ner under the influence of other stimuli it is probable that the same primitive elements become clasmatocytes (65), distinguished from the epithelioid cells by their more active phagocytosis and the different manner in which the engulfed dye is distributed through the cytoplasm. Following the work of Sabin and her coworkers, Morgan (66) showed the characteristic and predominating cell in experimental syphilis to be the clasmatocyte, although Pearce and Rosahn (67) found chiefly monocytes in the early lesions and clasmatocytes later. In the present study of rheumatic nodules, on the other hand, monocytes and clasmatocytes were only rarely encountered, and epithelioid cells, never. Through the kindness of Dr. Sabin, the author had the opportunity of studying material from guinea pigs injected with tuberculo-fatty acid; and, in very early lesions, many cells were found identical in every respect with the rheumatic granuloma cells of the type illustrated in Fig. 1 *A*. Even in these early lesions, however, the majority of cells had already begun to assume the staining characteristics expected in the cells of the tubercle. In rheumatic fever, as in tuberculosis, the number of primitive mesenchymal cells apparently increases markedly and they evolve into mono- and multinucleated forms. The cells of the rheumatic granuloma differ from those of the tubercle and the gumma, however, in their inability to stain supravitally with neutral red, and they continue to have the characteristics of undifferentiated, young, connective tissue cells at all stages of their development.

It has been recorded that some of the granuloma cells of the nodule into which India ink had been injected prior to biopsy contained particles of carbon. This probably indicates that they can acquire the function of phagocytosis when acted upon by proper stimuli. Such developmental potentialities would be entirely in keeping with the view that the cells are relatively undifferentiated functionally. Transition cells such as those illustrated in Fig. 1 *B* are, perhaps, further evidence that the elements of the rheumatic granuloma can change into other types, in this instance, into fibrocytes; and it is suggested that this latter transformation may explain the great tendency of these lesions to produce scar tissue.

SUMMARY AND CONCLUSIONS

Scrapings of subcutaneous nodules from ten patients with rheumatic fever were examined microscopically after being stained with supra-

vital dyes. From the uniform results obtained, the following conclusions have been drawn.

1. Supravital staining of cells from these lesions gives information unobtainable with ordinary histologic methods.

2. The scrapings show a great predominance of certain cells almost entirely devoid of phagocytic power and not characterized by the reactions with neutral red which distinguish monocytes, epithelioid cells, and clasmatocytes. Hence they differ from the essential cells of the lesions of tuberculosis and experimental syphilis. These differences are probably of a functional and developmental rather than of a genetic nature.

3. The cells probably arise from the undifferentiated mesenchymal elements of loose connective tissue, although it is possible that endothelial cells take part in their formation in some instances.

4. Since there is little doubt that the subcutaneous rheumatic nodules are pathologically identical with rheumatic granulomata elsewhere in the body, these conclusions are considered applicable also to the Aschoff body cells of the myocardial submiliary nodules.

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EXPLANATION OF PLATES

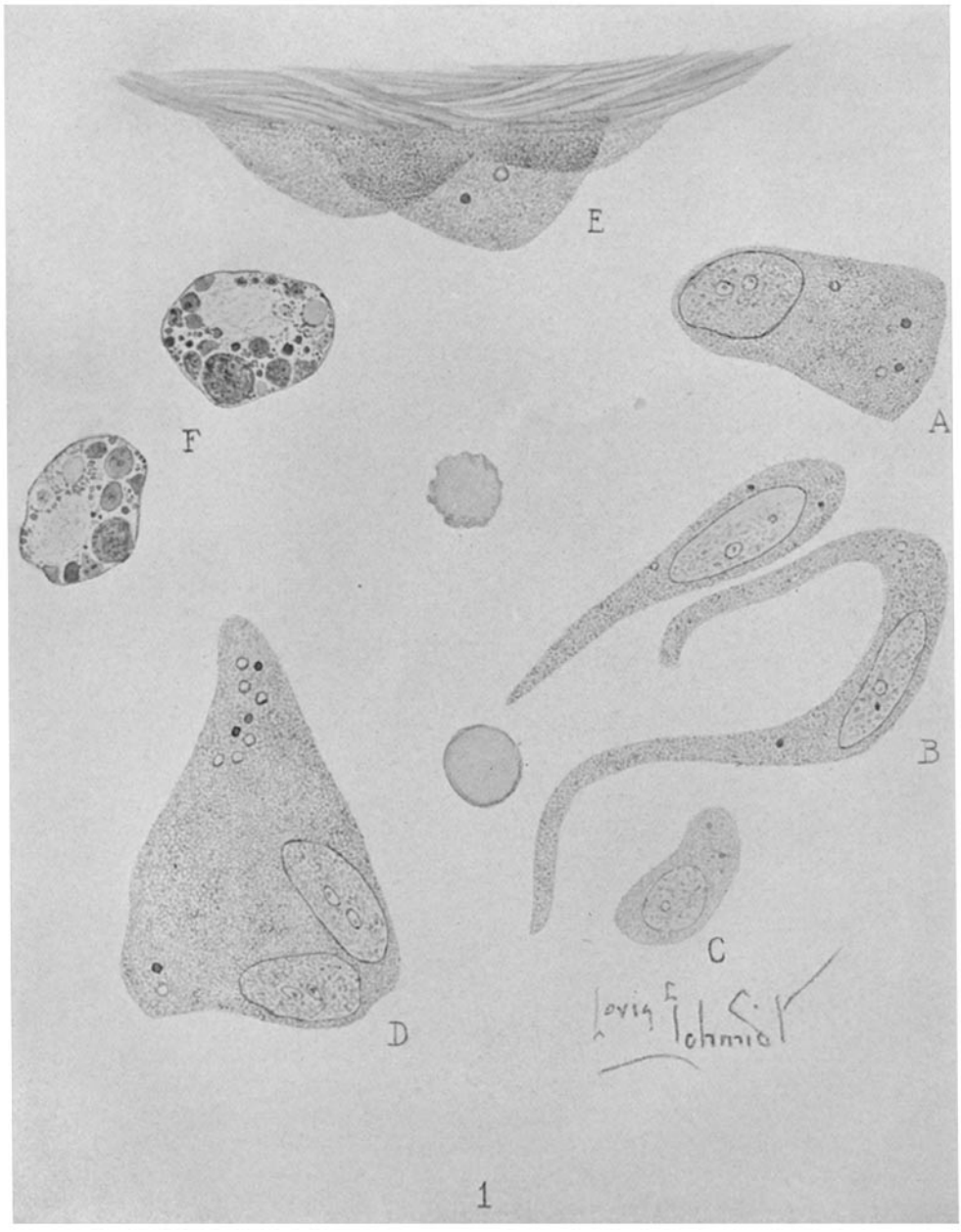
PLATE 29

FIG. 1. Drawing of cells from a subcutaneous rheumatic nodule. At *A*, *B*, *C*, and *D* are shown rheumatic granuloma cells, while at *E* is seen the edge of a small mass of tissue. *A* represents the predominant type of cell, *B* the long, spindle-shaped elements, *C* a small cell, and *D* a multinucleated form. The dark and light gray bodies in the two clasmatocytes (*F*) were actually dark and light shades varying from red to orange in the original. Two erythrocytes are included for comparison of size. Stained supravitally with neutral red and Janus green. × 1,700.

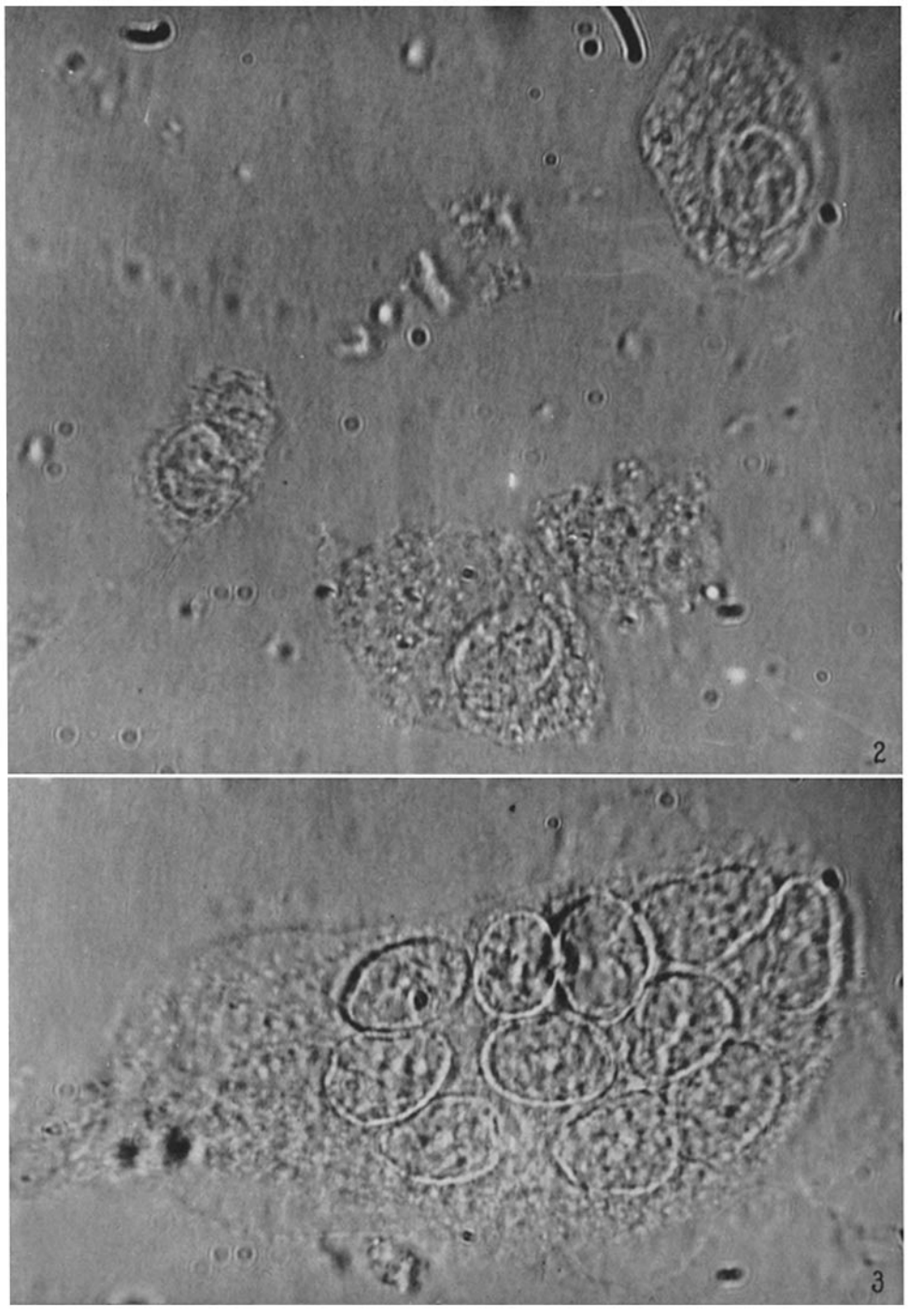
PLATE 30

FIG. 2. Microphotograph of a collection of cells of the type which predominated in the scrapings from subcutaneous nodules. In the group at the bottom of the figure one of the cells is superimposed upon another. Stained supravitally with neutral red and Janus green. × 1,700.

FIG. 3. Microphotograph similar to that in Fig. 2, but showing a giant cell containing eleven nuclei. The granular cytoplasm, nucleoli, vague cell boundary, and very distinct nuclear membranes are particularly well shown in this photograph. × 1,700.



(McEwen: Cytologic studies on rheumatic fever. I)



Photographed by Louis Schmidt

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