A COMPARATIVE STUDY OF SUBCUTANEOUS NODULES IN RHEUMATIC FEVER AND RHEUMATOID ARTHRITIS*

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PLATES 50 TO 55

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Since the original observations of Meynet (1) and Barlow and Warner (2) on the occurrence of subcutaneous nodules in rheumatic fever, numerous studies on these lesions have appeared. It is now well recognized that subcutaneous nodules are a frequent manifestation of the disease rheumatic fever and that these lesions present a highly characteristic histological structure. Occasional reference (3) has also been made to the presence of subcutaneous nodules in rheumatoid arthritis but, until recent years, detailed pathological descriptions of the lesions in this disease have not been presented. In the last few years, however, communications have appeared (4–7), which have shown that subcutaneous nodules are of not infrequent occurrence in rheumatoid arthritis and that these lesions also possess a highly characteristic histological structure. These observations have led to a comparative study of the nodules in the two diseases and to a consideration of the relationship between the clinical entities, rheumatic fever and rheumatoid arthritis (3).

In the present communication there is presented a detailed study of the subcutaneous nodules in the two diseases. This study has

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† The term rheumatoid arthritis is used synonymously with the terms chronic infectious and atrophic arthritis.
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shown that the nodules in the two conditions present striking similarities and the hypothesis is advanced that the lesions are manifestations of the same, fundamental, pathological process. A clinical study on the relationship between rheumatic fever and rheumatoid arthritis will form the subject of a succeeding communication.

Gross Appearance and Clinical Characteristics of Subcutaneous Nodules in Rheumatic Fever and Rheumatoid Arthritis

The essential features of the subcutaneous nodules which occur in rheumatic fever are so well known that a detailed description of their gross appearance and clinical characteristics is scarcely necessary. Findlay (8) has recently given a complete description of these lesions. The more important clinical features of the nodular lesions in this disease are tabulated below in comparison with those of rheumatoid arthritis as we have observed them.

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<th>Rheumatic Fever</th>
<th>Rheumatoid Arthritis</th>
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<tr>
<td><strong>Frequency</strong></td>
<td>Various authors state that the frequency of nodules in rheumatic fever varies between 10 per cent and 25–50 per cent.</td>
<td>Frequency.—In the Arthritis Clinic of the Presbyterian Hospital, 245 patients suffering from rheumatoid arthritis have been examined for the presence of nodules. They were found in 66 patients, an incidence of 25 per cent.</td>
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<td><strong>Situation</strong></td>
<td>In a series of 73 cases Findlay gives the distribution of nodules as follows: Elbows .................... 56 Knees ..................... 37 Ankles ..................... 16 Occiput .................... 16 Knuckles .................. 14 Spine of vertebrae ........ 4 Spine of scapulae .......... 3</td>
<td>Situation.—The nodules in rheumatoid arthritis occur in the same situations as those observed in rheumatic fever, except that they show a relatively greater predilection for the region of the elbows. The distribution in 66 cases was as follows: Elbows .................... 60 Knees ..................... 8 Ankles ..................... 6 Occiput .................... 2 Knuckles .................. 6 Spine of vertebrae (sacral region) .................. 3 Spine of scapulae ........ 3</td>
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<td><strong>Size</strong></td>
<td>The nodules are usually about 5 mm. in diameter, but occasionally they</td>
<td>As in rheumatic fever, the nodules may occur in several locations in the same patient and not infrequently present a symmetrical, bilateral distribution.</td>
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<td>are considerably larger than those observed in</td>
<td>Size.—As a rule the nodules are considerably larger than those observed in</td>
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Rheumatic Fever

attain considerably larger dimensions. In our experience the size of the nodules bears some relation to the period of their duration and to the age of the patient.

Duration.—As a rule the nodules persist for a matter of weeks only, but several cases have been observed in which they remained for many months.

Type of Case and Prognosis.—The appearance of nodules is generally associated with a severe form of the disease and usually is indicative of cardiac damage.

Other Characteristics.—The nodules are located in the subcutaneous tissue and show no evidence of attachment to the overlying skin. Not infrequently they appear to be attached to the sheaths of the underlying tendons and occasionally to the periostem of the underlying bone. The skin is freely movable over them and palpation of the lesion frequently conveys the sense of a hard foreign body. They are not associated with pain except when their situation exposes them to undue pressure.

From the foregoing description it is apparent that the gross appearance and clinical characteristics of the nodules in the two conditions, rheumatic fever and rheumatoid arthritis, are strikingly similar. In the following section, a comparison of the microscopic appearance of the lesions in the two diseases is presented.
Microscopic Appearance of Nodules in Rheumatic Fever

The microscopic appearance of the subcutaneous nodules in rheumatic fever has been carefully described by numerous investigators. It is here proposed to review that description only as it bears upon the histogenesis and evolution of the lesion in relation to the nodules which occur in rheumatoid arthritis.

The various stages in the evolution of the rheumatic granuloma as it occurs in various parts of the body, including the myocardium, have recently been carefully described by Klinge (9) and Gross (10). A comparison of the subcutaneous nodule with these lesions reveals a remarkable similarity and it is now recognized by almost all pathologists that the two are "morphologically and genetically essentially the same" (11).

The histological appearance of the rheumatic subcutaneous nodule is in some measure determined by the size of the lesion and the length of time for which it has been present. In this study particular attention has been paid to those nodules in rheumatic fever which are larger in size and which have persisted for some considerable time. Brief reference will also be made to the appearance of the earlier and more acute lesions.

In Fig. 5 there is shown a low power magnification of a rheumatic nodule from a patient 10 years of age who suffered from rheumatic carditis. The nodule had been present over the external malleolus for 2½ months at the time of excision. With the aid of Masson’s trichrome stain, which is particularly well adapted to the study of collagen changes, it is seen that the lesion consists of multiple, conglomerate areas of varying sizes and shapes. Each individual area is composed of three more or less well defined zones: an area of central necrosis, a surrounding cellular zone and an enclosing zone of well vascularized, fibrous, connective tissue.

The essential features of these lesions are familiar to all investigators and have been well described by Fahr (12), Swift (13) and numerous others. In its early stages the lesion is composed of a small area of focal necrosis with well marked inflammatory cell infiltration (Fig. 7). Early in the development of the lesion collagen bundles become involved in a peculiar type of fibrinoid swelling and degeneration. It was formerly held that fibrin deposition constituted a prominent feature of the central portion of the nodule but the distribution and staining reactions of the material have led us to prefer Klinge’s term “fibrinoid swelling.” With hematoxylin-eosin the central area stains more or less uniformly pink, but with Masson’s trichrome it presents a fibrillar structure which stains a brilliant red (Fig. 1). Occasional leucocytes are scattered throughout. The margin of the necrotic area is composed of a richly cellular zone, the cells of which show a definite tendency to arrange themselves in radial fashion. The characteristics of these cells have been referred to by numerous observers (11), and it is not proposed at this time to present any detailed description of them (Fig. 13). Mention should
be made of the fact, however, that mitotic figures not infrequently appear in considerable numbers. The tendency of these cells to fuse together and form multinucleated giant cells is well known.

The course and evolution of the nodules is further understood by a consideration of the larger and probably older lesions. Microphotographs of such nodules appear in Figs. 9 and 11. In Fig. 9 is shown a rheumatic nodule with a larger area of central necrosis but otherwise presenting all the characteristic features of the early lesions. In occasional instances the center of a large nodule undergoes cystic degeneration. In Fig. 11 is shown a section at the margin of the area of cystic degeneration with hyperplastic vilus-like structures projecting into the lumen. In Fig. 15 the appearance of numerous multinucleated giant cells is well shown. These cells present the characteristics of the foreign body type and one gathers the impression that their appearance is associated with the removal of necrotic tissue fragments.

The terminal stages in the evolution of the rheumatic nodule appear to consist in the formation of scar tissue without distinctive features.

This brief review of the histogenesis of the rheumatic nodule serves to show that various stages in the development of the lesions are characterized by certain morphological distinctions, but that the essential features are the same throughout.

**Microscopic Appearance of Subcutaneous Nodules in Rheumatoid Arthritis**

The study of the subcutaneous nodules in rheumatoid arthritis has revealed that the histological structure of these lesions presents a uniform and highly characteristic appearance which is closely related to, if not identical with, that observed in rheumatic fever.

In Fig. 6 is presented a low power magnification of a typical nodule from a case of rheumatoid arthritis in a man of 50 years. This nodule was situated over the olecranon process and had been present for 2 years at the time of excision. It is seen that, as in rheumatic fever, the lesion consists of multiple conglomerate areas of varying sizes and shapes. Each individual area is composed of three more or less well defined zones which closely resemble those described in the rheumatic fever lesions. These zones consist of (1) a large and irregular area of central degeneration, (2) a surrounding richly cellular tissue, the cells of which are disposed in characteristic radial fashion, and (3) an enclosing area of rather dense and avascular fibrous connective tissue.

The character of the area of central necrosis presents great variation in different nodules. Its appearance is in part determined by the size of the area involved and in part by the duration of the process. In the smaller and apparently earlier
lesions there is a small and not well defined area of focal necrosis characterized by edematous swelling and disintegration of individual collagen bundles. Such early areas of necrosis may show well marked inflammatory cell infiltration chiefly by small round cells and large mononuclear cells although polymorphonuclear leucocytes are not infrequently seen in considerable numbers. The necrotic central areas present the same staining characteristics as those which have been described in rheumatic fever nodules (Fig. 2). The margin of the area of necrosis is again formed by a richly cellular zone, the cells of which are arranged in characteristic radial fashion. The tendency of the cells to be oriented with their long axes perpendicular to the necrotic area contributes to the distinctive appearance of the lesion. In the rheumatoid arthritis nodules this zone appears even richer in cellular elements than in the rheumatic fever nodules and the radial distribution of the cells is more pronounced (Fig. 10). In other respects, however, the cells present an almost identical picture. At this stage of their evolution it is frequently impossible to distinguish the lesions in the two diseases. For the purposes of adequate comparison a more detailed description of the rheumatoid arthritis nodules is here presented.

1. The Zone of Central Necrosis.—The appearance of the area of central degeneration in the earlier and smaller lesions has already been described. In the larger and older nodules the character of this area may be considerably altered. The necrotic areas may be extensive and as a rule are irregular in shape. They may be round or irregularly oval, but are more frequently elongated and even branching. For the most part the degenerated area is dense and homogeneous, staining bright to pale pink with eosin, yellow with picric acid in Van Gieson preparations, reddish brown with phosphotungstic acid-hematoxylin, brilliant red in Masson’s trichrome and greyish blue or purple in Mallory’s orange and aniline blue fuchsin stain.

In other and apparently older nodules, however, the character of the necrotic material has undergone considerable alteration both in structure and staining properties. In some sections the uniform homogeneous character of the necrotic material has been completely replaced by a granular or loose, reticulated, fibrillar structure. In other nodules a process of liquefaction necrosis appears to be in progress, and large, round or oval masses of necrobiotic tissue stand out from the background. These masses appear to represent remains of dense, fused, collagen bundles. At the center of many of the larger nodules a process of cystic degeneration is apparent and amorphous clumps of necrotic and necrobiotic tissue lie free in the center of large, cystic cavities (Fig. 12).

In addition to the disintegrating clumps of collagenous material the remains of other tissue elements can be observed in some of the necrotic areas. Occasionally scattered throughout these areas, but more frequently toward the periphery, are the chromatic remains of disintegrating cells. In some instances these are definitely the remains of polymorphonuclear leucocytes but others appear to be disintegrating, large, mononuclear cells. Occasionally, also, larger and smaller, branching, elastic fibers can be seen.
In many sections the margin of the necrotic area is well defined but in other sections it gradually merges with the surrounding tissue and in many such instances this tissue appears to be progressively involved in the necrobiotic process.

In the case of some of the larger nodules the necrotic material has undergone further alterations. It has lost its homogeneous appearance and is characterized by the deposition of numerous, large, rhomboidal crystals. These crystals are apparently composed of cholesterol. In none of the lesions which we have had the opportunity of studying has calcium deposition or osteoid tissue formation been observed, but such an appearance has been described by others.

Further details of the nature of the area of central necrosis are brought out by the aid of Laidlaw’s silver impregnation stain. These preparations reveal that the reticular framework underlying the area of fibrinoid swelling is relatively well preserved and participates in the radial character of the lesion. With this stain identical pictures are observed in the nodules from rheumatic fever and rheumatoid arthritis. Typical sections are presented in Figs. 3 and 4.

2. The Cellular Zone.—Surrounding the central necrotic area is a zone of cellular tissue, the elements of which tend to be characteristically arranged in radial fashion (Figs. 10 and 12). In their general appearance the cells of this tissue suggest epithelioid cells at the margin of tubercles. The cells have a fusiform or polygonal shape and frequently the cytoplasm is prolonged into one or several slender processes. Often the cell outlines are indefinite and fusion into multinucleate elements with two or several nuclei is frequently observed. The nuclei are large, oval or lobate with a distinct nuclear membrane and one or several conspicuous nucleoli; the chromatin is abundant and diffusely distributed. Although the cell outlines are frequently indistinct, each element is surrounded by a wavy, pink-staining, reticular fibril. Characteristically disposed in radial fashion, these epithelioid cells are often heaped up in a curious, palisade fashion several cells deep. In some places at the margin of the necrotic area the cells surround clumps of disintegrating material, forming large foreign body giant cells (Fig. 16). One gathers the impression that this change occurs only in those nodules in which the activity of the process has ceased and the foreign material is being resorbed.

The intercellular substance consists of fibrillar stroma composed of delicate reticular fibers. The coarse fibers stain red in Van Gieson preparations; the more tenuous ones are well seen in aniline blue preparations.

Varying greatly in different sections there occurs throughout this area an inflammatory cell infiltration chiefly consisting of lymphocytes and monocytes. In some sections considerable numbers of polymorphonuclear leucocytes are also seen and among these scattered eosinophiles.

For the most part the elements of the cellular zone appear to be in active stages of proliferation and mitotic figures are frequently seen. In some of those nodules in which the central area has undergone cystic degeneration the marginal cellular wall displays evidence of active hyperplasia and in many places projects in papillary fashion into the cyst-like cavities (Fig. 12).
3. Peripheral Area.—Surrounding the cellular zone is a wide area of rather dense connective tissue. The connective tissue tends to be arranged circumferentially and consists of thick bundles of collagen fibers and more or less mature fibrocytes. Occasional, small, round cells are scattered throughout. It is this zone which apparently is largely responsible for the firm nodular character of the lesion in the gross and accounts for the relative ease with which the nodules may be removed. External to the zone of dense and mature scar tissue the lesion presents the more or less normal appearance of loose subcutaneous tissue.

Vascular Lesions of Subcutaneous Nodules in Rheumatoid Arthritis

In the peripheral areas of the nodules and in the surrounding connective tissue the blood vessels frequently show significant changes. These changes affect both the arterioles and capillaries although all the vessels in any one section are not uniformly involved.

The appearance of the affected vessels is again largely determined by the stage of the inflammatory process. The early and acute lesions present a picture which is strikingly similar to, if not identical with, that described by Von Glahn and Pappenheimer (14) as characteristic of the vascular lesions in rheumatic fever. A typical early vascular lesion from rheumatoid arthritis is shown in Fig. 17. In Fig. 17 it appears that the wall of the vessel is thickened in comparison with the caliber of the lumen. In this particular section the endothelium appears intact, but the intima is involved in the same type of peculiar fibrinoid swelling which constitutes such a prominent feature in the nodules already described. This fibrinoid material takes the usual fibrin stains, but its character and distribution, especially as seen in Masson preparations, tend to cast doubt on its true fibrin nature. A considerable portion of the material appears to consist of partially degenerated collagen. External to the area of fibrinoid swelling is a cellular tissue having a distinctive and peculiar character. Its appearance is well described in the article by Von Glahn and Pappenheimer on vascular lesions in rheumatic fever:

"External to the necrotic wall of the vessel is a cellular tissue having a very distinctive and peculiar appearance. It is composed of a loose fibrillar stroma, in part fibrinous, in which are many nuclei. One may distinguish (1) lobed nuclei of polymorphonuclear neutrophiles, many of them pyknotic and fragmented, especially those nearest the vessel wall; (2) larger vesicular nuclei, staining less intensely than those of the polymorphonuclears and often distorted or compressed into bizarre elongate or club-shaped forms. They tend to be arranged radially. Still further out is a loose infiltration of lymphoid and plasma cells, occasional eosinophiles and young connective tissue cells."

In other vessels the intima is greatly thickened by a proliferation of subendothelial cells. This process may involve the vessel wall in the whole of its circumference or only a portion of the wall may be affected leading to the formation of small projections into the lumen (Fig. 18). That this process, however, is not con-
fined to the intima is frequently shown by the presence of a well developed layer of elastic fibers extending into such verrucous projections (Fig. 20). In other sections splitting of the elastica has occurred and, in a few instances, an entirely new elastic membrane has been formed. In some vessels clefts or spaces, lined with endothelium and containing red blood cells, appear in the hyperplastic intima. This secondary vascularization of the intima presents a picture very similar to that described by VonGlahn and Pappenheimer in the vascular lesions of rheumatic fever.

The adventitia of many vessels shows a well marked perivascular cell infiltration by monocytic cells, small round cells and scattered plasma and mast cells. In addition to this infiltration by wandering cells there is frequently a definite hyperplasia of histiocytic cells which apparently take their origin from the adventitia. These cells appear in all respects similar to the epithelioid cells which occur at the margin of the necrotic areas of the nodules. For the most part they are disposed in concentric fashion and frequently envelop the vessel in a mantle several cells deep. In some instances, zones of capillary congestion occur about the affected vessels.

Occasional vessels are seen with old and thickened walls in which the various coats cannot be readily distinguished. Such vessels probably represent the terminal stages of the vascular lesions.

**Bacteriological Investigations on Subcutaneous Nodules in Rheumatoid Arthritis**

The results of bacteriological studies on subcutaneous nodules in rheumatoid arthritis have been reported elsewhere (15). Attempts to culture bacteria from these lesions have been uniformly unsuccessful. In addition, efforts to demonstrate the presence of bacteria in sections of the nodules have met with consistent failure.

**DISCUSSION**

In order that conclusions can be drawn as to the significance of characteristic lesions in any particular disease, it is first necessary to show that such lesions occur only in the particular disease in question. In the case of the subcutaneous nodules in rheumatoid arthritis and rheumatic fever, it cannot be claimed that such lesions, as judged by their gross appearance alone, are in any way specific for these diseases. It is well known that subcutaneous nodular lesions are not infrequently observed in other conditions such as syphilis, yaws, gout, tuberculosis and acrodermatitis chronica atrophicans (16, 17). However, as McEwen (11) has recently pointed out, it is most improbable that such
nodules would be mistaken for rheumatic lesions. In the case of rheumatoid arthritis, the gross appearance of the nodular lesions more closely resembles those observed in syphilis and yaws and it becomes necessary to resort to histological studies to demonstrate significant differences. Through the courtesy of Dr. H. Hanford Hopkins and Dr. L. A. Brunsting, we have had the opportunity to study sections of several of the so-called juxta-articular nodules in syphilis. Although the material at our disposal has been somewhat limited, it can be stated that the histological appearance of the nodular lesions in syphilis is not at all that of the characteristic lesions in rheumatoid arthritis. Crouzon and Bertrand (18) have recently reported similar conclusions. It is true that one of Hopkins' preparations presented the characteristic picture of a rheumatoid arthritis nodule, but this patient, in addition to suffering from syphilis, was also a victim of rheumatoid arthritis. In another of Hopkins' sections, from a patient with syphilis, there was present one area of focal necrosis surrounded by a zone of inflammatory cell infiltration. This area showed some resemblance to the lesions seen in rheumatoid arthritis, but the character of the cellular reaction was quite different. In particular the characteristic palisade formation of large mononuclear cells was conspicuously absent. Further distinctions between such gummatous lesions and the lesions observed in rheumatoid arthritis have recently been detailed by Schosnig (19). The appearance of the nodules in yaws, as described in the Harvard African Expedition (20), is so distinct as to leave no room for confusion. The opportunity has not presented itself for the examination of the lesions in acrodermatitis chronica atrophicans, but the recorded photographs of such lesions show few of the characteristic features of the lesions in rheumatoid arthritis. The nodular lesions so frequently seen in gout present such distinct characteristics that it is unnecessary to enter into any discussion of their appearance.

In our experience subcutaneous nodules of the type described have only been observed in cases of rheumatoid arthritis. Careful search for similar lesions has been made in several hundred cases of osteo-(hypertrophic, degenerative) arthritis and none has been found. It is believed that this observation lends support to the contention that this form of chronic multiple arthritis represents a separate and distinct
disease entity (21). In a search for similar manifestations in other conditions nodular lesions have been examined whenever they could be found in patients suffering from a variety of other diseases. Four such nodules were excised from patients suffering from various conditions. One of these proved to be a so called giant cell sarcoma of a tendon sheath, another a xanthoma, a third a lipoma and the fourth a fibromyxoma. On the other hand, it should be pointed out that Findlay (8) has recently reported the presence of a characteristic rheumatic nodule in a child in whom no other stigmata of the rheumatic infection could be observed. Furthermore, in certain other acute infections, Holsti (22) has described vascular lesions which resemble those seen in rheumatic fever. Further investigation is therefore necessary before the lesions which have been described can be considered as absolutely specific for rheumatic fever and rheumatoid arthritis. In the present state of knowledge it would be more correct to regard both the nodular and vascular lesions as highly characteristic of these respective diseases.

SUMMARY

The foregoing comparative study on the subcutaneous nodules in rheumatic fever and rheumatoid arthritis is presented as part of an investigation which has been conducted in this clinic on the relationship of the two clinical entities, rheumatic fever and rheumatoid arthritis. It is believed that the present study has shown that these lesions are highly characteristic of the two diseases and that they represent different phases of the same, fundamental, pathological process. However, it should be pointed out that the presence of closely related or even identical lesions in two, separate, clinical entities cannot be considered as valid evidence in support of the hypothesis that the two diseases are etiologically related. Comparative clinical studies on the relationship of rheumatic fever and rheumatoid arthritis will be presented in a succeeding communication. These studies, as well as serological investigations on the two diseases which have been reported elsewhere (23, 24), lend further support to the conception that rheumatic fever and rheumatoid arthritis are intimately related and possibly different responses of affected individuals to the same etiological agent.
The author wishes to express his thanks to Professor A. M. Pappenheimer of the Department of Pathology of the College of Physicians and Surgeons, Columbia University, for his kind assistance in this study.

Addendum.—While the foregoing investigation was being carried out, there appeared an extensive pathological study of tissue changes in rheumatic fever and rheumatoid arthritis by Klinge and Grzimek (Virchows Arch. path. Anat., 1932, 284, 646). These authors state:

"So we are able to explain without difficulty on the basis of our material the close relationship of chronic polyarthritis, infectious arthritis, polyarthritis lenta with acute febrile rheumatism (acute joint rheumatism) as a continuous sequence of one disease process with different phases and with different clinical and anatomical manifestations in each individual phase."

BIBLIOGRAPHY


EXPLANATION OF PLATES

PLATE 50

**Fig. 1.** Rheumatic fever nodule. Area of focal necrosis surrounded by large mononuclear cells which tend to be arranged in radial fashion. The necrotic material appears to be composed largely of degenerated bundles of collagen which stain a brilliant red. The normal collagen at the periphery accepts a vivid green stain. Note mitotic figure near left border. Masson’s trichrome stain. × 280.

**Fig. 2.** Rheumatoid arthritis nodule. Area of focal necrosis surrounded by large mononuclear cells. This is a very early lesion and is shown for comparison with the rheumatic fever nodule, the description of which applies equally well to this section. The appearance of larger and older lesions is shown in subsequent illustrations. Masson’s trichrome stain. × 280.

PLATE 51

**Fig. 3.** Rheumatic fever nodule. Radiating reticular structure throughout area of focal necrosis. Laidlaw’s silver impregnation stain. × 80.

**Fig. 4.** Rheumatoid arthritis nodule. Radiating reticular structure throughout area of focal necrosis. Reticulum is more dense than in rheumatic fever nodule but otherwise similar. Laidlaw’s silver impregnation stain. × 80.

PLATE 52

**Fig. 5.** Rheumatic fever nodule. Multiple areas of focal necrosis surrounded by cellular zones and enclosed by fibrous connective tissue. Masson's trichrome stain. × 30.

**Fig. 6.** Rheumatoid arthritis nodule. Larger and more definite areas of focal necrosis surrounded by dense fibrous connective tissue. Masson’s trichrome stain. × 18.

**Fig. 7.** Rheumatic fever nodule. A small area of focal necrosis surrounded by large mononuclear cells. The necrotic material is composed of degenerating bundles of collagen. Masson’s trichrome stain. × 280.

**Fig. 8.** Rheumatoid arthritis nodule. A small area of focal necrosis surrounded by large mononuclear cells. Note similarity to Fig. 7. Masson’s trichrome stain. × 280.
PLATE 53

FIG. 9. Rheumatic fever nodule. Area of focal necrosis which involves collagen bundles in a peculiar hyalin degeneration. Hematoxylin and eosin stain. × 280.

FIG. 10. Rheumatoid arthritis nodule. Area of focal necrosis showing a similar type of hyalin degeneration of collagen. Note the characteristic radial distribution of the large mononuclear cells. Hematoxylin and eosin stain. × 280.


FIG. 12. Rheumatoid arthritis nodule. Note that description of Fig. 11 applies equally well to this section. × 80.

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FIG. 13. Rheumatic fever nodule. Large mononuclear cells at margin of area of necrosis. Hematoxylin and eosin stain. × 630.

FIG. 14. Rheumatoid arthritis nodule. Large mononuclear cells at margin of area of necrosis. Hematoxylin and eosin stain. × 630.

FIG. 15. Rheumatic fever nodule. Multinucleated giant cells at margin of area of necrosis. These cells appear to surround fragments of degenerated collagen. Masson's trichrome stain. × 400.

FIG. 16. Rheumatoid arthritis nodule. Multinucleated giant cells at margin of area of necrosis. Compare with Fig. 15. Masson's trichrome stain. × 400.

PLATE 55

Vascular lesions of subcutaneous nodules in rheumatoid arthritis.

FIG. 17. Acute vascular lesion. Note necrosis of vessel wall and type of inflammatory tissue surrounding the vessel. Hematoxylin and eosin. × 280.

FIG. 18. Intimal hyperplasia; splitting of elastica. Elastic tissue stain. × 280.


FIG. 20. Arteritis verrucosa; polypoid projection into lumen of vessel. Elastic tissue stain. × 280.
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