LESIONS IN MUSCLE IN ARTHRITIS

BY

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Recent pathological studies suggest that rheumatoid arthritis may be a disease with widespread involvement of tissues other than the joints. Curtis and Pollard (1940) were the first to describe a non-articular histological lesion which was common to all cases of rheumatoid arthritis—their cases including four with Felty's syndrome. In every one of 11 cases these authors found small perivascular infiltrations with lymphocytes in the corium of the skin and in the muscles. They regarded these perivascular accumulations of cells as evidence of a generalized disease process and as indicating that Felty's syndrome is not essentially different from classical rheumatoid arthritis. Freund *et al.* (1942) found characteristic pathological lesions in the peripheral nerves of 3 out of 5 cases of rheumatoid arthritis. The lesions were located in the perineurium, and in their most typical form presented 3 zones: (1) a central acellular zone composed of homogeneous coagulated material occasionally showing nuclear debris; (2) an intermediate zone of cells with large hypochromatic nuclei with more or less definite nucleoli; and (3) a peripheral outer zone containing numerous lymphocytes and plasma cells. The lesion was sharply differentiated from the surrounding tissue, and they regarded it as in some respects similar to the subcutaneous nodule of rheumatoid arthritis.

Nerves examined included the femoral, tibial, sciatic, and axillary; and the concentration of lesions differed widely in different nerves and different parts of the same nerve. All were perineural except one nodule which was situated in the epineural fatty tissue. The authors regarded these lesions as specific for rheumatism, and they recalled the finding by Koeppen (1932) of perivascular lymphocytic infiltrations in the sciatic nerve in 2 out of 8 cases of active acute and subacute rheumatism. They suggested that the nerve lesions might be related to pain, paraesthesia, vasomotor, secretory, and trophic disorders in the disease.

In following up the nerve lesions in the small nerve branches in muscle, the same authors, Freund *et al.* (1945), noted the presence of inflammatory lesions in the muscle itself, unassociated with nerve fibrils. There were compact accumulations of lymphocytes, plasma cells in small numbers, and occasional eosinophil and epithelioid cells. Few reticulin fibres were found in the lesions, but there was an increase of collagenous connective tissue in the endomysium and perimysium between the inflammatory cells. The lesions varied in size from 20 lymphocytes to a nodule which, in a stained section, was visible to the naked eye. Such focal lesions were found in all of 14 patients with rheumatoid arthritis on whom muscle biopsy was performed. The deltoid, triceps, and gastrocnemius were the muscles examined. The authors drew attention to the importance of the finding of such nodules in a random sample of skeletal muscle not exceeding 5 g. in weight. Associated changes in muscle fibres included a hydropic degeneration, oedema, loss of striation with marked swelling, or shrinkage and atrophy of the fibres.

Steiner, Freund, *et al.* (1946) extended and confirmed their previous observations. Focal lesions of the same kind were found in 9 more cases of rheumatoid arthritis; and a series of 196 control observations were made, including examination of muscle from cases of various nervous and muscular diseases. The control material failed to show any lesions comparable to those in rheumatoid muscle. Additional points of interest in their second series were the finding of: (1) vascular lesions consisting of adventitial and periadventitial lymphocytic infiltration—less frequently intramural lesions were found —and (2) small inflammatory foci where a muscle fibre, surrounded by cell infiltration, showed early evidence of degeneration, indicating clearly that muscle degeneration was a consequence of the inflammatory lesions.

In the course of a systematic study of pathological material from various types of rheumatic disease, specimens of muscle tissue from 11 cases of generalized arthritis have been examined.

Methods

The muscle was removed under general anaesthesia if this were required for other reasons, e.g. manipulation or synovectomy. Otherwise a local anaesthetic was used. Tissue was fixed in 10% formol-saline, and paraffin sections were made. Staining in every case was by haematoxylin and eosin and by Masson's trichrome stain. In certain cases Foot's reticulin stain and Van Giesen were also applied.

The sedimentation rate and haematocrit estimations were by the method of Collins *et al.* (1939). The corrected suspension stability (C.S.S.) is the percentage volume of red cells which it is calculated would have been found after one hour if the haematocrit reading had been 42%. Normal results are 85% or more. A fall below 60% is considered maximal.

Case Summaries

CASE 1

A woman, aged 48, with typical rheumatoid arthritis, gave a history of 20 years' involvement of all joints except the spine, hips, and shoulders. The condition

had recently become less active, the rapid loss in weight had ceased, and the corrected sedimentation stability test (C.S.S.) had improved from 79 to 88%. There was still anaemia—haematocrit 35%—and the blood uric acid was normal. *X*-ray films were typical of rheumatoid arthritis with superimposed osteoarthritic changes. The patient had had five courses of gold therapy, the last being two years ago, and was in the process of having a sixth. There were no complicating factors or other points of particular interest.

Pathology.—Muscle was removed from the right deltoid under general anaesthesia. The size of the stained section was 16 × 8 mm. Three small foci of lymphocytes were seen: (1) a very small cluster of 18 lymphocytes and 2 large epithelioid cells situated near a small vessel, the lymphocytes extending in a short row between nearby muscle fibres; (2) in the perimysium 2 perivascular nodules of small size were seen. One contained 2 histocytes with ingested pigment. A muscle fibre involved in this nodule showed swelling, basophil staining, and loss of striation (Fig. 1); (3) a small nodule of 23 lymphocytes in close proximity to a small vessel. Patchy degeneration of muscle was shown by proliferation of muscle nuclei, which were sometimes enlarged and elongated, hyperchromatic, and situated within the fibre rather than at its edge, as described by Steiner *et al.* (1946).

CASE 2

A man, aged 54, had rheumatoid arthritis with a 14 years' history of joint involvement, all joints except those of the spine being affected. The disease was quiescent, and the man, having lost much weight, was now beginning to put it on again. The C.S.S. had improved from 50 to 55%, the anaemia from 34 to 40% haematocrit; and the plasma uric acid was 3·4 mgm. per 100 c.cm. *X*-ray films were typical of rheumatoid arthritis. The patient had had many courses of gold, the last a year ago. There was a nodule on the left elbow, but no other special features.

Pathology.—Muscle biopsy was from the left vastus externus and the section was 9 × 5 mm. in size. Histologically 1 small nodule was seen containing 24 lymphocytes, 3 polymorphs, and a number of epithelioid cells, in close proximity to a small vessel. The muscle fibres were separated by a general increase of fibrous tissue, and vascular lesions were conspicuous, many of the arterioles having thickened walls and in some cases the lumen was almost obliterated.

CASE 3

A woman, aged 33, had suffered from arthritis of the knees for 4 years, beginning directly after a "blitz." Latterly, swelling had been confined to the right knee only. The only ascertainable focus of infection was one tooth which had been removed. There had been no loss of weight, and the general condition was good. The C.S.S. was still rather rapid, but had risen from 62 to 75%. The haematocrit was 41%. No gold had been administered.

Pathology.—Muscle biopsy from the right vastus internus. The tissue was a fusiform fragment 17 mm. long × 5 mm. broad at its widest part. Two small foci of perivascular lymphocytic reaction were present, but the striking feature of this slide was what appeared to be a rounded scar (Fig. 2). Dense fibrous tissue enclosed a few scattered muscle fibres which were shrunken in size. The area was not near either of the two lymphocytic foci found. As in the previous case, a general increase of fibrous tissue was also present, with evidence of muscle degeneration in the form of proliferation of nuclei and basophil staining of individual fibres.

CASE 4

A woman, aged 45, had had 3 attacks of rheumatic fever at the ages of 10, 21, and 30. The heart was not involved. Soon after the third attack she noticed deformity of her fingers and gradual stiffening of her wrists, elbows, shoulders, and knees. When admitted to hospital in 1946 she showed the picture of a typical rheumatoid arthritis, with marked muscle wasting and symmetrical involvement of all joints except the spine and hips. The knees were flexed to 100° with a range of 30°.

The haematocrit was 33%, the C.S.S. 67%. *X*-ray films were typical of rheumatoid arthritis with secondary osteoarthritic changes. On admission she was recovering from a recent attack of herpes zoster of the right leg. There was no history of rheumatism in the family.

Pathology.—Muscle biopsy was from the right deltoid. The size of the stained section was 14 × 10 mm. This was histologically the most striking case of the series. Large fusiform masses of cells were found which were visible to the naked eye in sections stained by haemotoxylin and eosin. They were perivascular in relation to thin-walled vessels running between muscle fibres.

Lymphocytes, plasma cells, eosinophils, and larger cells of epithelioid type with oval vesicular nuclei and a fine chromatin network were present. In this section eosinophils were a striking feature, and in some of the areas they were the predominant cell (Fig. 3). At the periphery of the nodule, strands of lymphocytes were seen penetrating between individual muscle fibres. Evidence of muscle degeneration as described in Case 1 was present, and there was an increase of interstitial fibrous tissue. This case, with numbers 6 and 7, formed a group in which the foci were endomysial in location, as compared with the remainder, in which they were situated in the supporting connective tissues of the muscle.

CASE 5

A miner, aged 63, gave a history of 9 years of rheumatoid arthritis, involving the knees and elbows particularly. The muscle wasting was not marked, and there had been no recent loss of weight.

On admission in Jan., 1946, the knees were very painful with flexion deformity and slight bilateral effusion. The C.S.S. was markedly raised (59%). The haematocrit was normal (44%) and the blood uric acid 3·1 mgm. per 100 c.cm. The *X* rays showed changes of rheumatoid type with secondary osteoarthritis. He had had two courses of gold therapy with good response, and also deep *x*-ray therapy to the knees. There was nothing else of interest in the past or family histories.

Pathology.—Muscle biopsy was from the vastus internus. The tissue was very loose in texture, and the stained section was 10 × 4 mm. There were few satisfactory fields. The muscle itself was free from infiltration; but an adjoining fragment of fibrous tissue, detached from the main mass in the section examined, contained a cluster of 43 lymphocytes. No definite evidence of muscle degeneration was seen. This is regarded as a doubtful example of muscle involvement.

CASE 6

A housewife, aged 52, had a history of gradual onset of pain, stiffness, and swelling of both knees and fingers of 8 years' duration. There was no gross loss of weight, and her main symptoms were a villous arthritis of the knees. The haematocrit and C.S.S. were normal. She

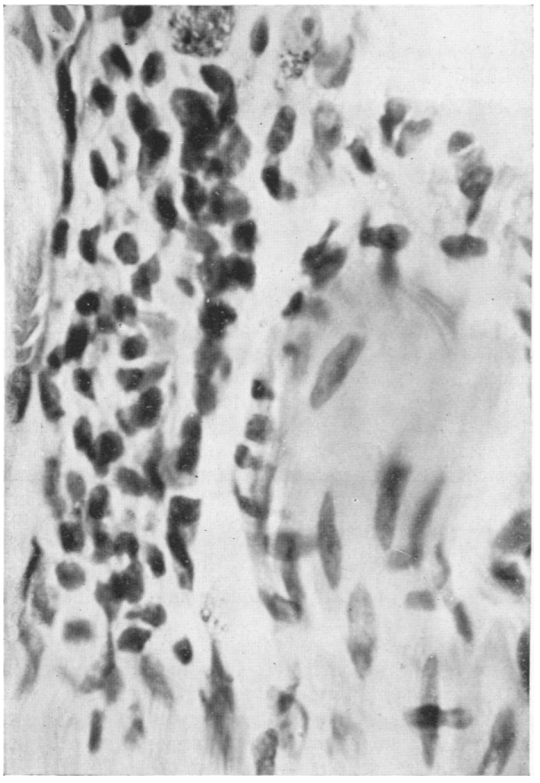

FIG. 1.—Nodule from muscle of Case 1. Between the fibres is seen a collection of lymphocytes and plasma cells with 2 phagocytic histocytes containing pigment. The muscle fibre adjacent is swollen and somewhat basophil in staining reaction, and contains many elongate nuclei. (H. and E. × 400.)

FIG. 3.—Deltoid muscle from Case 4 to show endomysial focus between muscle fibres. Eosinophils were a striking feature in this case. Lymphocytes and plasma cells are also present. (H. and E. × 100.)

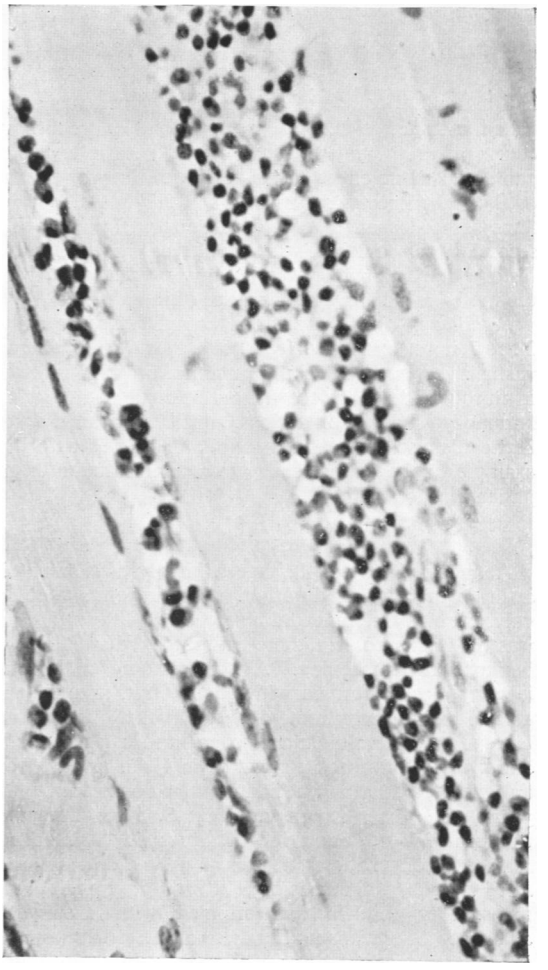

FIG. 3.

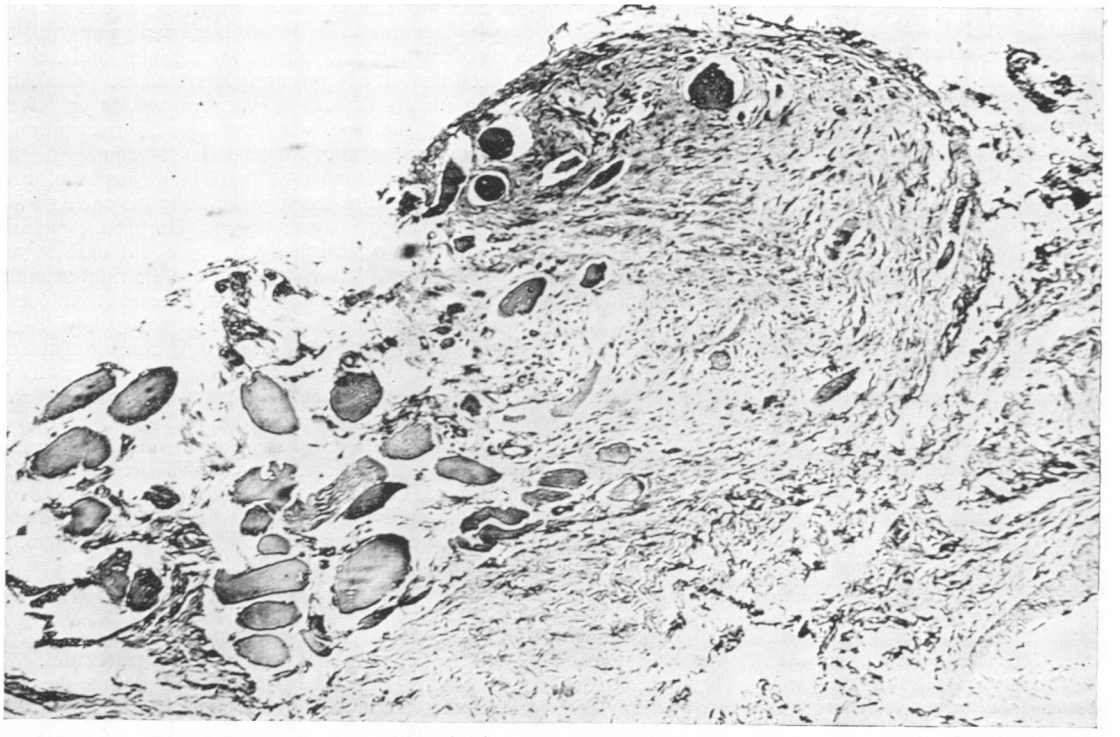

FIG. 2.—Right vastus externus from Case 3. A rounded mass of fibrous tissue is present in which fragments of degenerate muscle fibres are embedded. (Masson's Trichrome Stain × 100.)

had had a full course of gold therapy which was completed in Jan., 1946, with no appreciable benefit. A course of deep *x*-ray therapy to her knees relieved the pain, but had no effect on the swelling. A synovectomy of the right knee was performed in July, 1946. *X*-ray films showed changes of old rheumatoid arthritis with secondary osteoarthritis of the knees. There was a history of rheumatoid arthritis in the grandmother on the mother's side, but nothing else of interest.

Pathology.—Biopsy was from the right vastus internus, 22 × 7 mm., and the left deltoid, 8 × 4 mm. In the vastus 2 very small nodules were seen near vessels situated in fibrous tissue. In the deltoid 1 small nodule of 27 lymphocytes closely investing a small thin-walled vessel between muscle fibres was found. This was a further example of the endomysial perivascular reaction exemplified in Cases 4 and 7.

CASE 7

A housewife, aged 43, gave a history of rheumatoid arthritis of 7 years' duration. All the joints were involved except the spine and hips. In 1944 the right knee was the main problem, there being marked swelling and periarticular thickening. A synovectomy and patellectomy was performed with good result, and she was able to resume light home duties. In 1945 the left knee became very painful and swollen, and a patellectomy and synovectomy was performed in 1946. Apart from an initial loss, her weight had remained constant for five years. The haematocrit and C.S.S. have fluctuated between 38–41% and 62–66% respectively. *X*-ray films showed changes of typical rheumatoid arthritis. She had had two courses of gold without great improvement. Her mother was crippled with rheumatoid arthritis. There was nothing else of interest to note.

Pathology.—Biopsy was of the right deltoid, 8 × 5 mm., and right vastus internus, 13 × 9 mm. In the deltoid 6 small nodules were found. Four surrounded small vessels of capillary dimensions and were closely invested by muscle fibres. They tended to be spindle-shaped, recalling the structure seen in Case 4. The remaining 2 were in the perimysium and were situated near small arterioles.

In the vastus internus there was 1 small nodule only, encircling a vessel in fibrous tissue. Muscle showed marked degeneration of type similar to that seen in Case 10. Muscle nuclei were very numerous, irregular in size and shape, and with many hyperchromatic forms.

CASE 8

A male, aged 56, had had typical rheumatoid arthritis for seven years. The onset was insidious with gradual symmetrical involvement of all joints except the shoulders, hips, and spine. There was marked muscle wasting and flexion deformity of elbows and knees. The epitroclear glands were enlarged. The C.S.S. was 72%, the haematocrit 37%, and the blood uric acid 3·1 mgm. %. *X* rays showed changes of rheumatoid type with secondary osteoarthritic changes in the knees. There was great loss of articular cartilage, with several cystic areas in the femoral condyles and upper ends of the tibiae. There was no history of rheumatic fever. The man had suffered from a discharging right ear in the past which was dry at the time of examination.

Pathology.—Muscle was removed from the right vastus externus at the time of synovectomy of the right knee. The size of the section was 12 × 8 mm. Five foci of lymphocytic infiltration were seen. They were situated in close relation to vessels, but not perivascularly (see Fig. 4). There was considerable increase of fibrous tissue and marked thickening of vessel walls, affecting the intima. This was similar to the changes found in the arterioles of subcutaneous nodules and synovial membrane of rheumatoid arthritis. Some of the muscle fibres were shrunken, and in this section showed an appearance of vacuolation; but degenerative changes were not striking.

CASE 9

A housewife, aged 41, gave a history of rheumatoid arthritis of 10 years' duration. There was marked muscle wasting, with symmetrical involvement of wrists, fingers, knees, shoulders, and feet. There had been an appreciable loss of weight, and recently flexion deformity of knees had developed, necessitating gradual straightening with serial plasters and eventually manipulation under a general anaesthetic. The C.S.S. was 86%, the haematocrit 31%. She had had two courses of vaccine, in 1926 and 1943, but no gold. *X*-ray films of hands showed typical changes of rheumatoid arthritis. There was no past history of rheumatic fever and no history of rheumatism in the family.

Pathology.—Muscle was taken from the right deltoid, 15 × 5 mm. Two small lymphocytic foci were present. In each case some 12 to 20 lymphocytes were seen beside a small vessel. Degenerative changes in muscle were confined to a patchy increase in number of muscle nuclei and slight irregularity in staining of the fibres. The smaller arterioles showed thickened walls, as noted in previous cases.

CASE 10

A male Civil Servant, aged 48, gave a history of rheumatoid arthritis of 9 years' duration. Three phases could be distinguished in the evolution of the articular lesions in this case: Firstly, an oligoarticular phase of relatively short duration, during which the wrists were mainly involved; secondly, a longer articular phase affecting all the joints, which showed the typical rheumatoid arthritic changes; and, thirdly, a phase of articular disorganization and subluxation affecting nearly all the joints of the hands, the right shoulder joint, and the joint between the 3rd and 4th cervical vertebrae. The hands were markedly deformed, with stunted fingers of the achondroplastic type. The extensive disorganization of the metacarpo-phalangeal and inter-phalangeal joints allowed abnormal movements of the fingers in all directions. This picture was very similar to the one described and illustrated by Layani (1939). During the phase of articular disorganization a swelling about the size of a large plum appeared in the region of the right shoulder, and this was subsequently shown at necropsy to consist of an encysted mass containing thick yellowish-grey material very rich in cholesterol. As a result of the disorganization and dislocation of the joint between the 3rd and 4th cervical vertebrae, a classical picture of compression of the cord developed at that level. During the course of the illness there was a variable degree of secondary microcytic anaemia, the haematocrit varying between 34 and 41%. The C.S.S. was consistently lowered, ranging between 59 and 64%. The highest figure recorded for the blood uric acid was 3·1 mgm. per 100 c.cm. At necropsy, in addition to the lesions observed ante-mortem, both peri- and endocarditis and fibrinous pleurisy were found.

Pathology.—Muscle was taken from the right biceps, 22 × 10 mm., and the right rectus, 18 × 11 mm. The specimen from the biceps showed an extreme degree of muscle degeneration, fibrosis, and round cell infiltration (Fig. 5). The muscle fibres were shrunken, convoluted,

and vacuolated, and showed nuclear changes as described by Steiner *et al.* (1946). Muscle nuclei in some areas were very large, elongated, and hyperchromatic, while others showed an aggregation of nuclei giving an appearance like giant cells. The cell infiltration was predominantly lymphocytic. No eosinophils or plasma cells were seen. Some of the foci were perivascular and elongated, as seen in Case 4; others were rounded, diffuse, and paravascular. The right rectus muscle was free of any marked evidence of disease. A few scattered lymphocytes in fibrous tissue near vessels were the only sign of involvement.

CASE 11

A male, aged 48, gave a history of rheumatoid arthritis of 6 years' duration. The onset was sudden, involving all the joints except the hips and spine. At the time of his last admission in 1946 the activity had decreased, judging by the recent gain in weight. C.S.S. rose from 50 to 67%, and haematocrit from 35 to 40%. The patient had had five courses of gold therapy, the last completed in March, 1945. *X*-ray films showed changes of rheumatoid type, with secondary osteoarthritic changes.

Pathology.—Muscle was taken from the right vastus internus, 22×10 mm. The muscle showed a general increase of fibrous tissue, and there were 4 lymphocytic nodules in the perimysium. In each case they were somewhat diffuse and were situated near a thick-walled arteriole, but not strictly in perivascular relation to it. Near one of the foci there was an increase of dense fibrous tissue enclosing shrunken and degenerate muscle fibres. The appearance was that of scar tissue as seen in Case 3 (Fig. 6). In Masson-stained sections there was no evidence of fibrinoid change in this fibrous area.

Summary of Findings

Biopsies were performed on 10 typical cases of rheumatoid arthritis and one doubtful case. There were 5 men and 6 women, of ages varying from 33 to 63, and with symptoms of 2 to 20 years' duration. The C.S.S. at the time of biopsy ranged from a borderline normal of 88% to a maximal decrease of 55%. In all cases flocculation tests for syphilis were negative.

Case 3 was not typical, in that only the knees were involved; the patient had not lost weight, there was no anaemia, and the C.S.S. was only 75%. Cases 1, 6, and 11 were clinically quiescent, had been gaining weight, and the C.S.S. was improving. Cases 3, 4, 8, and 9 were the only ones in which gold had not been administered at some stage in their treatment. In Case 4 there was a strong past history of rheumatic fever shortly before the first onset of typical rheumatoid symptoms. Case 10 is of special interest in that a post-mortem examination was available.

Provisionally, 2 histological types have been classified.

(1) *Perivascular Location in the Muscle Itself.*—This gave an elongate or fusiform nodule closely invested by the muscle fibres. The vessel, of capillary dimension, in this case showed no change. The inflammatory cells, lymphocytes, plasma cells and eosinophils, were closely packed and tended to overflow into fissures between neighbouring fibres. These are the endomysial lesions of Steiner *et al.* (1946), and were seen in Cases 4, 6, and 7.

(2) *Paravascular Lesions in the Fibrous or Fatty Stroma of the Muscle.*—The vessels often showed thickening of the wall; and the cell infiltration, almost entirely lymphocytic in type, appeared to begin in the adventitia and to spread away from the vessel. The nodule formed was of loose texture and not sharply defined. It resembled closely the smaller accumulations in synovial membrane, in synovial fat, and in the perineurium. This type of lesion, classified by Steiner *et al.* (1946) as perimysial, was found in Cases 1, 2, 3, 4, 5, 8, 9, 10, and 11.

The difference between the two types is not merely one of location, but also of histological make-up and relation to the vessel involved, in the first group a dilated capillary, in the second a sclerotic arteriole.

MUSCLE CHANGES

In a few cases gross evidence of degeneration was present. The fibres were shrivelled and tortuous, with marked proliferation of nuclei, which showed rounded, oval, and sausage-shaped forms, often with hyperchromatism and loss of their vesicular form. In these cases they were sometimes found heaped together as in a giant cell. As also noted by Steiner *et al.* (1946), we frequently observed less marked degeneration of individual fibres, remote from lymphocytic foci, in which there was loss of transverse striation, longitudinal fissuring, and, in some cases, vacuolation. Elsewhere muscle degeneration was found adjacent to cellular infiltrations. The three pathological processes — viz. lymphocytic foci, arterial thickening, and muscle degeneration—varied considerably in their relative proportions in different specimens, and did not appear to be entirely interdependent.

In general the pathological findings agreed closely with those of Freund *et al.* (1946), with 2 further observations. (1) Eosinophils were found in great profusion in one case (No. 4). They are suggestive, in view of the work of Rich and Gregory (1943), Levinthal (1939), and others, who have put forward a theory of the aetiology of rheumatism involving anaphylactic hypersensitivity. (2) The finding of scar tissue enclosing degenerated shrunken muscle fibres has not previously been reported so far as we are aware. It was seen in Cases 3 and 11.

All examinations of muscle specimens from controls, including some cases of ankylosing spondylitis, have so far been negative, but investigation of biopsy material from other " rheumatic " and toxic conditions are being continued. A piece of muscle from a case of acute fibrositis with extremely tender muscles and slight periarticular swelling, but no loss of weight, wasting, decreased sedimentation stability, or anaemia, showed no inflammatory cell reaction, but some swelling of muscle fibres, staining deficiency, and loss of striation, with an increase in muscle nuclei.

LESIONS OF SIMILAR HISTOLOGY IN NON-MUSCULAR TISSUES

While our studies were chiefly concerned with muscle, lesions of comparable type in other tissues in cases of rheumatic disease may be mentioned.

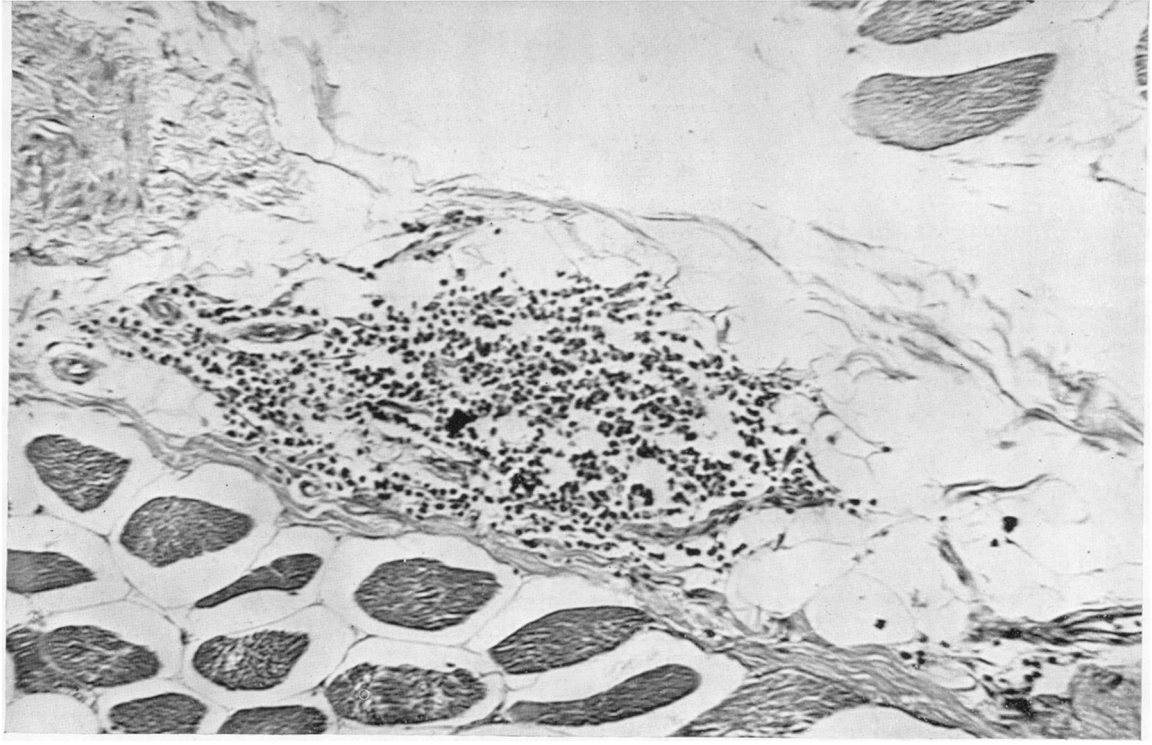

FIG. 4.

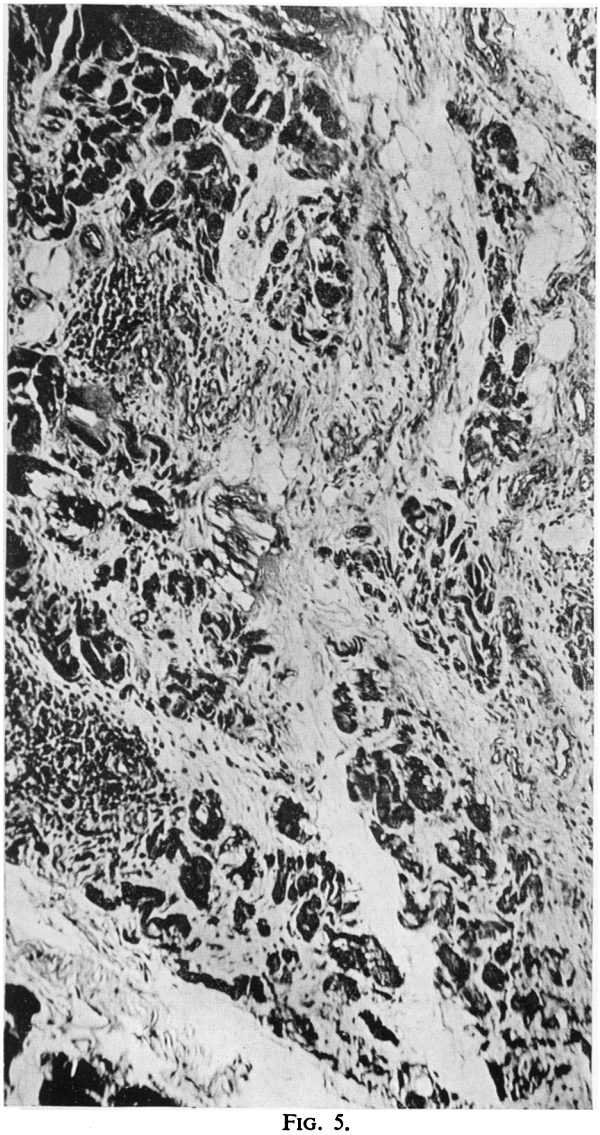

FIG. 5.

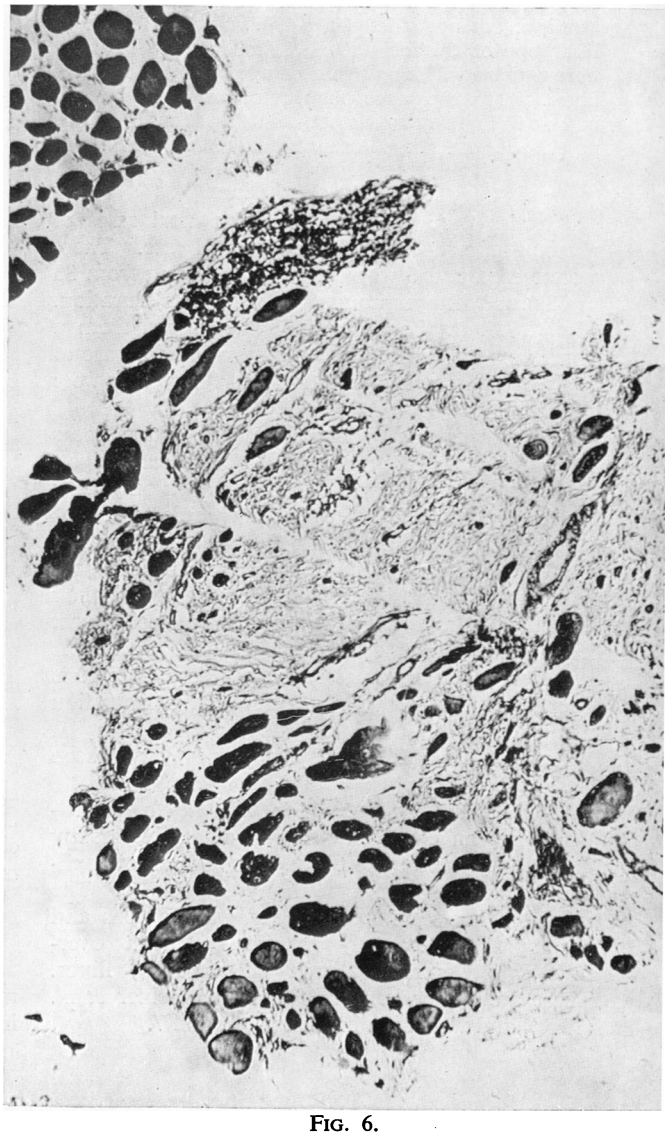

FIG. 6.

FIG. 4.—Right vastus externus of Case 8. A diffuse lymphocytic focus in the perimysium. Three small vessels are seen towards one end of the nodule. Infiltration between muscle fibres has not occurred. (H. and E. × 100.)

FIG. 5.—Right deltoid from Case 10. This shows the most extreme degree of muscle degeneration, fibrosis and lymphocytic infiltration which has been observed in this series. (Masson's Trichrome × 100.)

FIG. 6.—Right vastus externus of Case 11, to show replacement of muscle by fibrous tissue. Within the scar tissue are seen the shrunken remnants of muscle fibres A lymphocytic focus is present at the margin of the area of fibrosis. (Masson's Trichrome × 100.)

FIG. 7.—Radial nerve from Case 10. An arteriole with marked thickening of its wall is seen within the perineurium. Its adventitia is infiltrated with lymphocytes which extend diffusely into the adjacent connective tissue. Numerous capillary vessels are present within the focus. (H. and E. × 200.)

FIG. 8.—Fat from knee joint of Case 6. A paravascular lymphoid focus of very similar structure to that shown in Fig. 7 is present. (Masson's Trichrome × 200.)

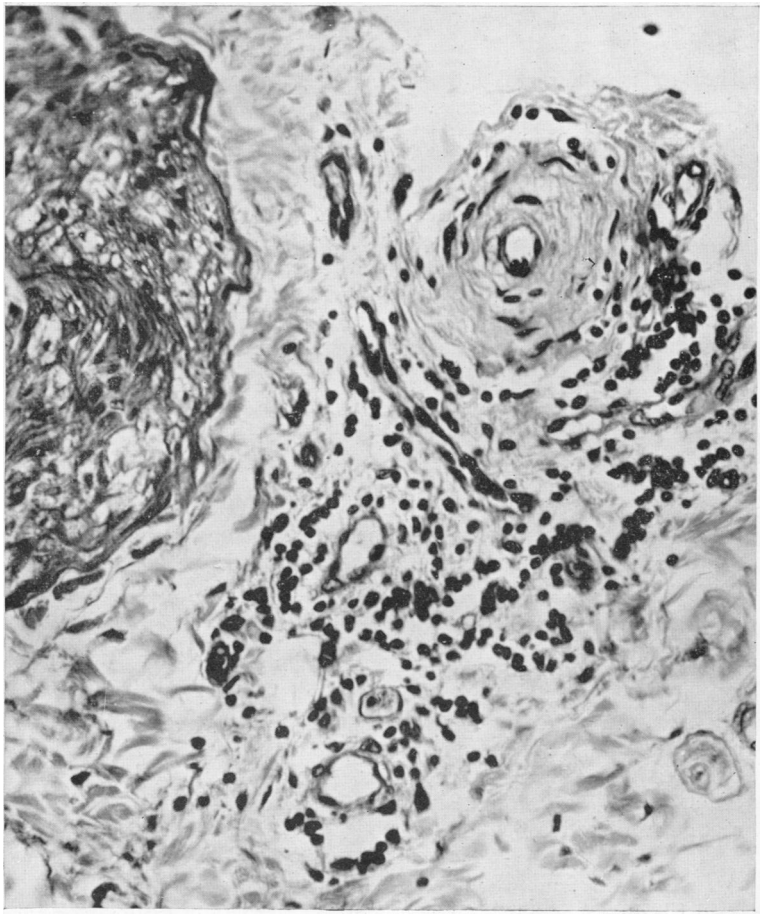

FIG. 7.

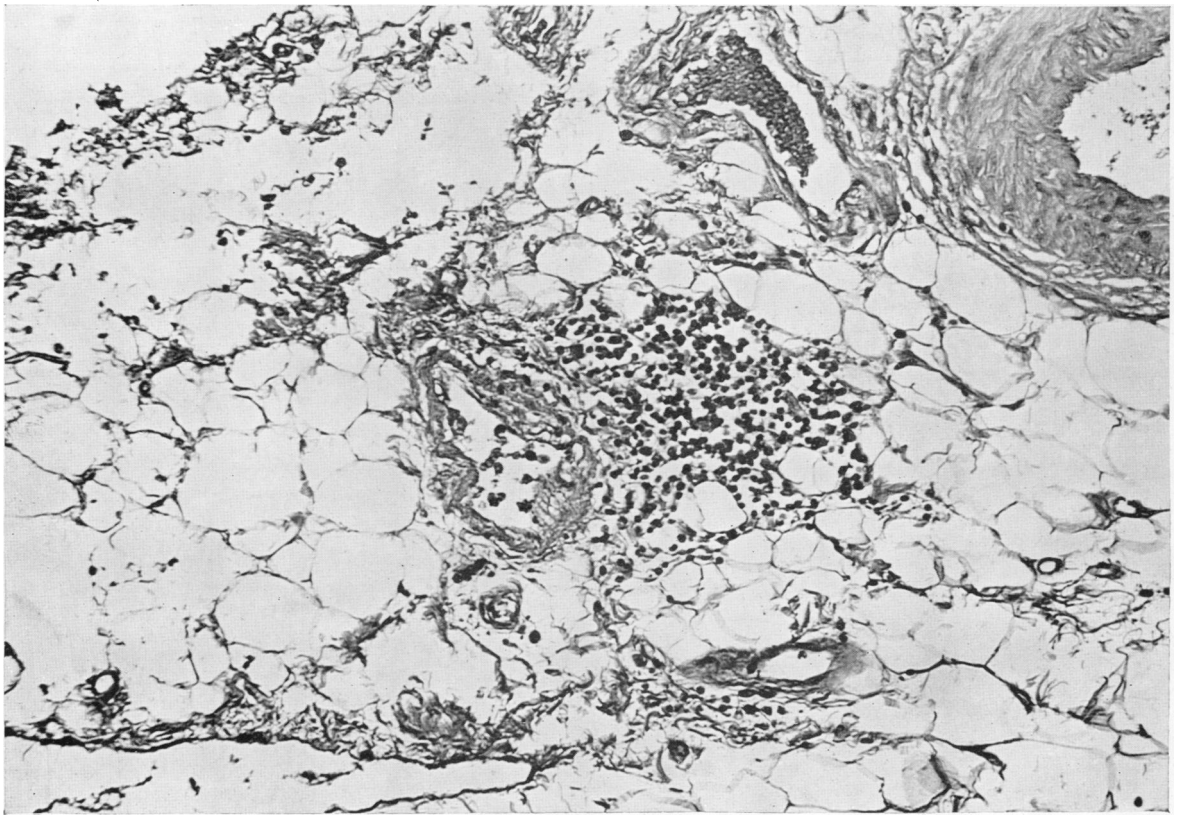

FIG. 8.

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The first is a lesion found in the radial nerve of Case 10 of the present series. In the first block—selected quite at random—in which the nerve was cut transversely, 2 lymphoid foci were seen in the supporting fibrous tissue. They were in close relation to arterioles, with thickened walls. In each case lymphocytes were present at one point in the adventitia, and extended diffusely into the adjacent fibrous tissue (Fig. 7). The findings were in keeping with those of Freund *et al.* (1942), in the condition described by them as nodulous rheumarthritic perineuritis.

The second instance was seen in fatty tissue removed with synovial membrane from the knee joint of Case 6. As seen in Fig. 8, it is entirely within the adipose tissue. A small arteriole is involved, part of the wall showing adventitial lymphoid infiltration which extends away from the vessel. In the synovial membrane in this case the lymphocytic accumulations of Allison and Ghormley (1931) were large, abundant, and highly characteristic in their structure. The finding of histological evidence of involvement of fat is not without interest in view of the finding by Collins (1940) that 3 out of 7 painful nodules in fibrositis were fatty in nature, and that of Copeman and Ackerman (1944) that the trigger points in lumbar fibrositis corresponded exactly with the basic fat pattern of the region. These findings require further investigation.

Discussion and Summary

In specimens of biopsy material taken from the muscles of 10 typical cases of rheumatoid arthritis, and of one with some atypical features, a characteristic histopathology was found, thus confirming the work of Freund, Steiner, and Leichtentritt. The lesions consisted of perivascular cellular reactions in the muscles themselves, and paravascular lesions in the fibrous and fatty supporting connective tissue.

The relationship to blood vessels suggests that the noxious agent is a blood-borne irritant, but throws no light on whether or not it is infective in origin. All affected tissues were of mesodermal origin. The fact that lesions were found in specimens removed at biopsy from muscles selected at random indicates the very widespread nature of the condition. Similar changes were found in active and quiescent cases, whether or not they had been treated by gold.

The same histopathology has not so far been seen in any control material examined, but the histology of muscle from patients suffering from non-rheumatic conditions and rheumatic cases other than rheumatoid arthritis is still undergoing investigation.

The diagnostic value of biopsy in the pre-arthritic state, when wasting and pain precede definite joint changes, is a matter requiring further study, as the arthritis may possibly prove to be secondary to soft-tissue involvement.

We wish to express our indebtedness to the Physicians of the Royal National Hospital for Rheumatic Diseases, Bath, for permission to obtain biopsy material from patients under their care; and to the Sydney Robinson Research Fund, for defraying the expenses of photography.

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