HISTOPATHOLOGY OF THE INTRINSIC MUSCLES OF THE HAND IN RHEUMATOID ARTHRITIS : A CLINICO-PATHOLOGICAL STUDY

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Since 1944 the author has systematically removed specimens from the intrinsic muscles of the hand whenever there was an occasion to reconstruct the painful arthritic hand (Kestler, 1946). This study is based upon eleven cases in which the intrinsic apparatus of the hand was studied under the microscope. In nine cases other tissues, including muscles, were examined from various regions of the skeletal system. Four controls were used who had been operated upon for traumatic lesions of their hands. It seems that sufficient data have been collected to report the findings.

The purpose of this article is to describe the pathologic changes found by the author in hands that were affected by rheumatoid arthritis in various stages of the disease. The impression is conveyed that rheumatoid arthritis is primarily a disease of the soft structures, the connective tissues proper. With the pathologic findings at hand the author's theory about the mechanism of specific deformity of rheumatoid hands will be advanced. The author is not aware of similar findings in the literature. Studies pertaining to the pathology of the intrinsic muscles of the hand in rheumatoid arthritis could not be found in a survey of the medical literature.

Literature

Koeppen (1932) appears to be the first to have found perivascular lymphocytic infiltration in the sciatic nerve in two cases out of eight which were examined. These were cases of acute or subacute rheumatism.

Curtis and Pollard (1940) described perivascular lymphatic infiltration in the skin and in skeletal muscles other than discussed in this paper. However, they called attention to the fact that these changes should be evidence of a generalized process.

In 1942 Freund and others reported lesions in the peripheral nerves in cases of rheumatoid arthritis, In a further study by the same authors (1945). inflammatory lesions were noted in the deltoid, triceps, and gastrocnemius muscles in fourteen patients with rheumatoid arthritis. These changes were unassociated with nerve fibrils.

Steiner and others (1946) confirmed their findings in a subsequent publication in 1946. Triceps, deltoid, pectoralis major, rectus abdominis, iliopsoas, gastrocnemius, and other unidentified muscles of the legs were examined at this time.

Gibson and others (1946) studied muscle material in eleven patients with generalized arthritis. These authors studied biopsy specimens from the deltoid, vastus externus and internus, and in one case from the biceps.

Aim of Study

When the author performed his first operation for a painful arthritic hand he was struck by the acuteness of the pathologic findings in spite of the very active so-called anti-rheumatoid therapy the patient had gone through, not only for years, but until shortly before surgery was undertaken. Besides several courses of gold therapy, this patient received the following treatments over a period of four years: antistreptococcus toxin, intravenous cinchophen, a non-specific vaccine, foreign protein, vitamin E, large doses of vitamin D, oral and parenteral salicylates, sodium iodide, and local and intravenous histamine. And yet the subcutaneous tissues were oedematous and inflamed. The capsule of the metacarpo-phalangeal joints was thickened and when it was opened a creamy greyish fluid escaped. The lining of the capsule had a dark red velvety appearance and consisted of enlarged villous tissue. Similar findings were encountered in practically every other case where the above structure was operated upon. The muscle bellies of the interossei, lumbricales, and those of the intrinsic

muscles of thumb and little finger, conversely, presented a normal gross appearance.

Another point of interest was that the characteristic deformity of the rheumatoid hand—the atrophy of the interossei, the ulnar deviation of the fingers in about 50 per cent. of the cases, the various fixed deformities of the phalanges—could not be entirely explained on the basis of disuse atrophy and gravity.

Material and Methods

Eleven patients with rheumatoid polyarthritis were operated upon. Different procedures were carried out, a great number of which were concerned with the metacarpo-phalangeal joints (Kestler, 1946 and in the press). The following structures were examined by biopsy: subcutaneous tissues, fascia, aponeurosis, extensor apparatus, para-articular and peri-articular tissues, capsule of metacarpo-phalangeal joints, capsule of interphalangeal joints, tendon sheaths, interosseous muscles, lumbricales, lateral bands. Tissues were excised under general anaesthesia and fixed in formalin. Blocks were cut in the normal way and paraffin embedding was used. Staining in every case was by haematoxylin and eosin; in some instances Van Gieson's and Weigert's methods were also used.

Case Reports

Since all these cases represented the characteristic lesions of rheumatoid polyarthritis, four will be described in detail.

Case 1

A housewife, 45 years old, had typical rheumatoid polyarthritis. With the exception of the spine and hip joints, every joint was involved over a period of nine years. The onset was gradual. Hands, elbows, and ankles were the areas of chief complaint when this patient was seen first in November 1943. Her general condition was fair. She was walking with a considerable limp due to the painful lesion in both ankle joints and in the tarsal and subtalar joints. Temporo-mandibular joints were subsequently involved, and shoulders, elbows, and wrists were restricted in their motions. There was a painful bursitis in both olecranon bursae, with fluid and thickening. Hip and knee movements were free and painless. Swelling and pain of both hands and feet were the principal complaints, and it was this latter condition for which the patient received several courses of gold therapy during the previous two years without any lasting effect.

It is of interest that this patient's ankles (the talar and subtalar joints) showed a most satisfactory and lasting response to histamine iontophoresis. The hands and more specifically the finger joints became increasingly painful. While every finger joint was painful and swollen, it was the proximal finger joint of each finger that was the centre of the complaints. When the pain became incessant the patient was hospitalized.

Examination of Hands.—A painful deformity of the metacarpo-phalangeal joints dominated the picture. These proximal finger joints were in 15° of flexion, from which active flexion was possible to 25°. Passively and with great pain this could be increased by 5°. The para- and periarticular tissues were enlarged and oedematous; the creases about the proximal finger joints were stretched. The middle finger joints of each finger were enlarged, and were held in moderate flexion. Motion in these joints was limited actively as well as passively. The distal finger joints were the least affected. The patient could not make a fist; pinching with the thumb and index finger and between thumb and mid-finger was weak. There was a moderate interosseous type of atrophy with ulnar deviation of th fingers on both hands. There was subluxation of all proximal finger joints.

Radiographs revealed the usual picture of atrophic changes with marked subluxations of the proximal phalanges in the proximal finger joints. The subluxation increased in degree from the index to the little finger.

The Wassermann reaction was negative; the blood sedimentation rate was 90 mm. in one hour (Westergren). There was an increase of serum globulin with the albumin-globulin ratio slightly reversed. There was moderate anaemia present. Blood uric acid was 3·8 mg. per 100 c.cm. Cholesterol and free cholesterin was normal. Kidney function was not impaired.

The excision of the metacarpal heads was performed as reported elsewhere (Kestler, 1946).

Gross Pathology.—Subcutaneous tissues were oedematous and injected. The extensor assembly was thickened, dark red, and the extensor tendons were found to be injected with a network of minute vessels; this was more marked at the periphery of the tendon. The extensor aponeurosis was dark red and thickened and, in spite of the pneumatic tourniquet, there was considerable ooze. The cut surface of the aponeurosis was enlarged in places. The articular capsule was greatly thickened and dark red. Upon incision of the joint, greyish material escaped from it. The synovia and articular surface of the joint capsule were bulging like a turned out sleeve, with an enormous villous thickening. The villi and the capsule were dark red. The articular cartilage was preserved, though injected, and there was a spotty pannus erosion throughout, particularly on the fourth and fifth metacarpal heads. This pannus erosion was limited to the periphery of the cartilaginous head. The interosseous muscles were normal in their gross appearance. The lumbricales were not inspected in their entirety, specimens being removed only after the metacarpal heads were excised. The lateral bands were dissected out on the index and mid-fingers. They were found to be injected and a thin film of inflammatory membrane was seen on them. This thin film of material could be seen on the extensor aponeurosis also.

The following tissues were examined: subcutaneous tissue, dorsal aponeurosis or extensor assembly, joint capsule, synovial membrane, cartilage cup, metacarpal head, dorsal interosseous muscles, lateral bands of intrinsic muscles, lumbricales.

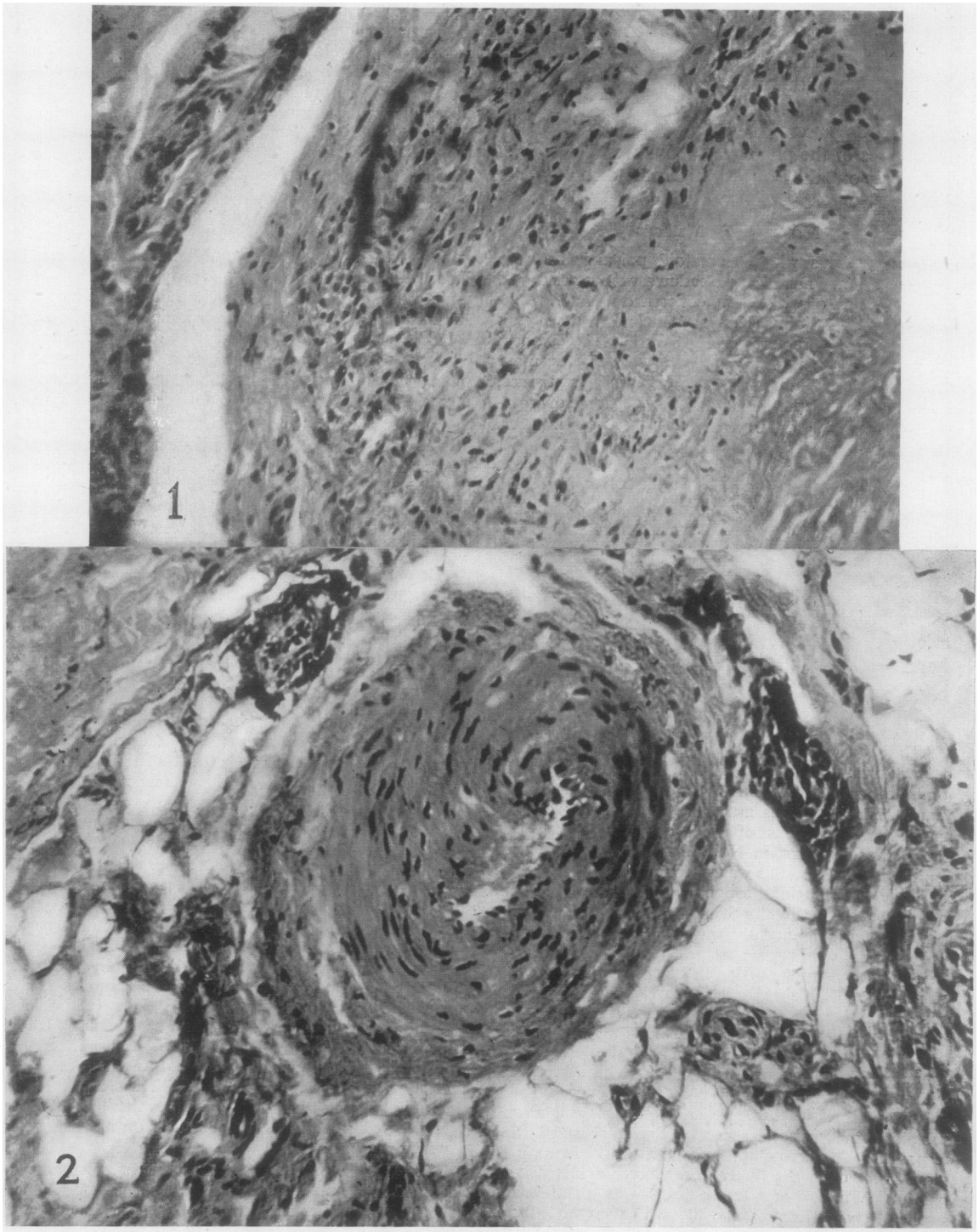


FIG. 1.—From extensor assembly, Case 1. Left long finger area showing the histology of a rheumatoid node. ×100.
FIG. 2.—From tissue removed with the capsule of proximal finger joint. This shows an extremely thickened arteriole, the lumen almost completely obstructed. In the right upper corner there is a circumscribed area of round-cell infiltration and above the vessel there is a more scattered round-cell infiltration. Both these are rather para-adventitially located. The fibro-collagenous tissue is abundant. ×400.

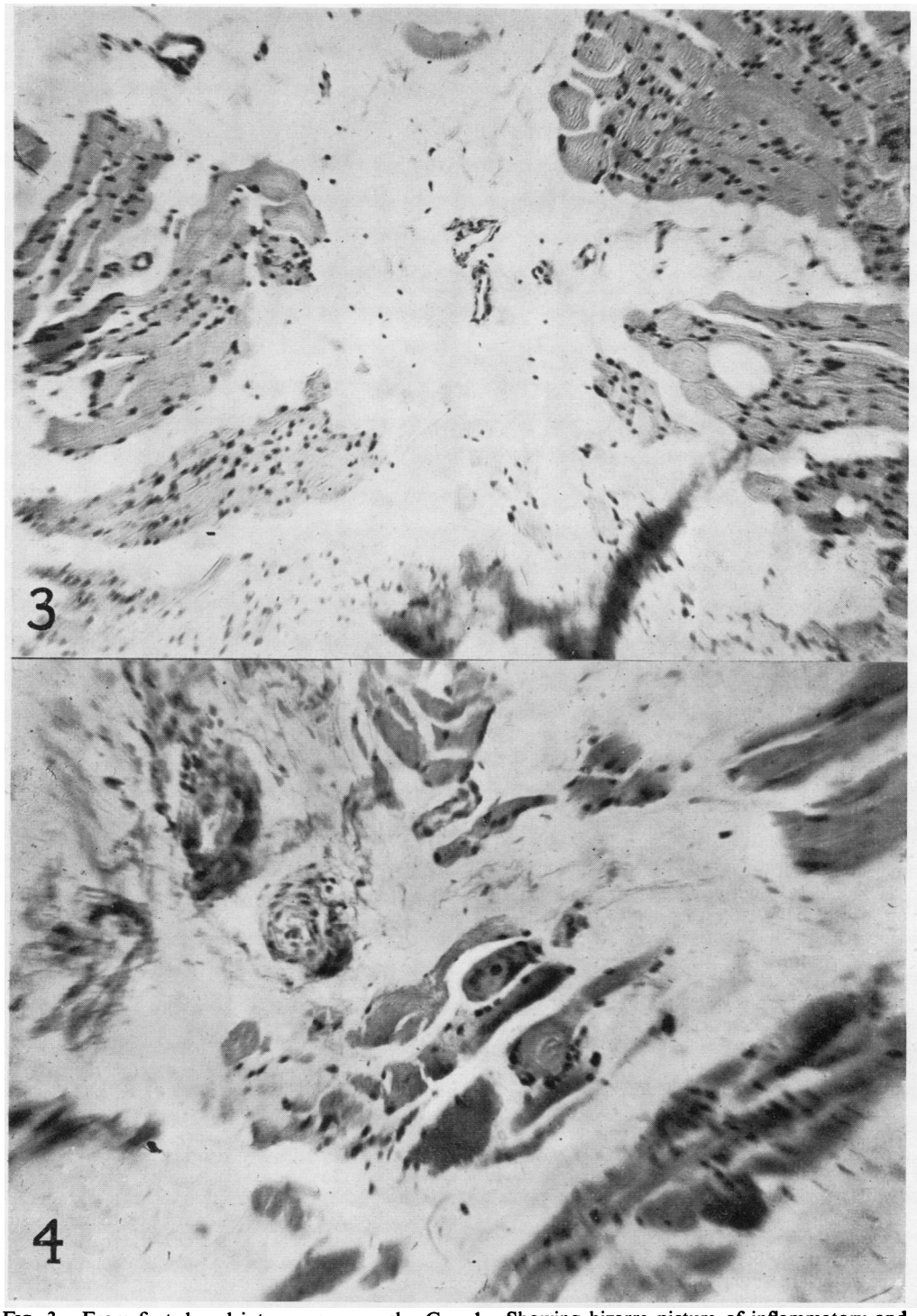


FIG. 3.—From first dorsal interosseous muscle, Case 1. Showing bizarre picture of inflammatory and degenerative changes. Increased amount of nuclei, scattered infiltration by round cells, cross striations in muscle fibres, shrinkage of muscle fibres. Connective-tissue mesh surrounding the areas where muscle tissue used to be. ×100.

FIG. 4.—From the second dorsal interosseous muscle, Case 1. Extreme stages of shrinkage of muscle fibres and scattered round-cell infiltration. Replacement of muscle tissue by collagenous fibres. Arterial changes within the muscle tissue and inflammatory changes in the blood vessel. On the left upper corner disintegrating muscle bundles are being replaced by connective tissues. ×250.

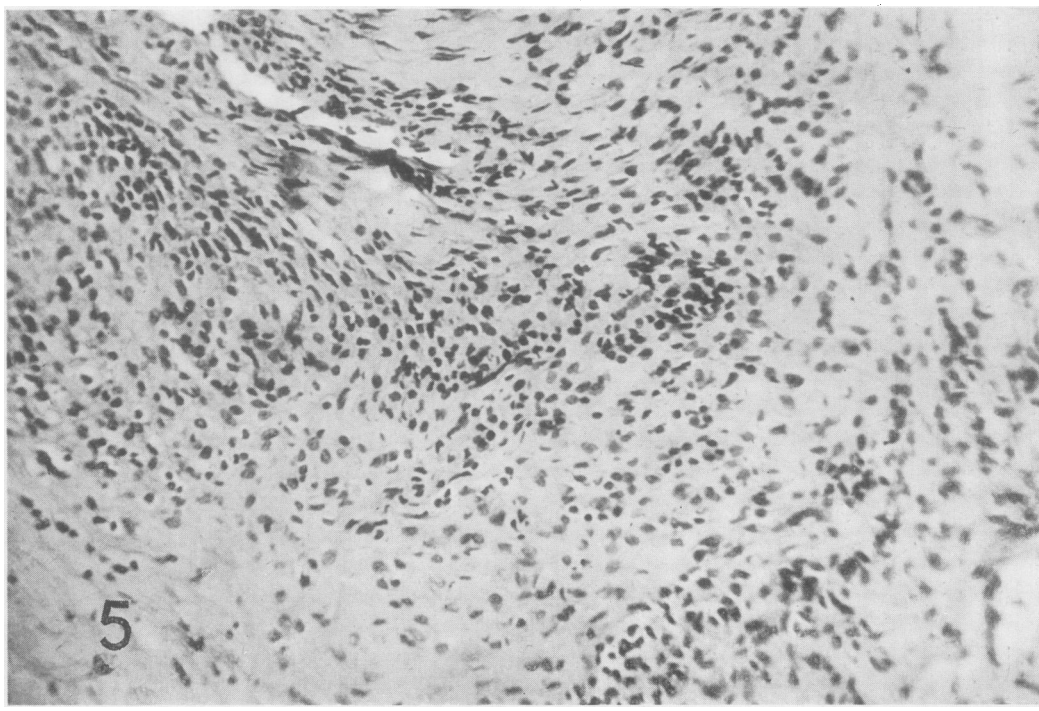


FIG. 5.—From the lateral band of the left index finger, Case 1. Showing histologic picture in a field from a lateral band. Diffuse infiltration by lymphocytes, epitheloid, and plasma cells in an abundant connective-tissue stroma. ×100.

Histological Findings

Subcutaneous Tissue.—In the subcutaneous tissue a scattered round-cell infiltration was found consisting mostly of lymphocytes. This round-cell infiltration occasionally showed a nodular appearance. Plasma cells were seldom seen in these areas; eosinophils were also few in number. Thickened arterioles and venules were seen occasionally and there was a round-cell infiltration occasionally observed para-adventitially.

Extensor Apparatus.—In the extensor apparatus diffuse infiltration with so-called rheumatoid pannus was found with epitheloid cells, plasma cells, and an increased amount of connective tissue. Numerous areas were found giving the picture of a rheumatoid node as seen in the subcutaneous nodes of rheumatoid individuals: a homogenous central area representing a necrotic field. This necrotic area showed different staining qualities. It consisted of necrotic connective tissue and was surrounded by epitheloid cells lying in a connective tissue stroma. These epitheloid cells were scattered with lymphocytes and plasma cells throughout (Fig. 1).

Joint Capsule.—The joint capsule showed a typical picture of a thoroughly homogenous rheumatoid granulation tissue with large numbers of lymphocytes and a great many plasma and epitheloid cells. The fibro-collagenous tissues were abundant. A small number of eosinophils were seen occasionally. Vascular changes were most interesting here. They consisted of extreme thickening of arterioles in places, with almost complete obliteration of the lumen (Fig. 2). There was a round-cell infiltration in the adventitia of these vessels.

The appearance of some of these arterioles showed a striking resemblance to findings in periarteritis nodosa. While there was no sign of cell infiltration of the intima or intramural tissue, the increase of collagenous tissue rich in cells was quite impressive.

Synovial.—Excessive villous hypertrophy with nodular inflammatory changes consisting of lymphocytes and plasma cells mostly, but there were also eosinophils. In the subsynovial tissues the blood vessels were increased and their wall was thickened. Inflammatory foci, nodular or diffuse in form, of scattered round cells were seen in numerous fields.

Cartilage Cup.—Grossly the cartilage cups were not very much affected. The centre of the head was intact; at the periphery there was pannus erosion in places. Microscopically it was seen that the metacarpal head was actually invaded by pannus and the cartilaginous surface eroded. In these eroded areas the cartilage matrix was loose; it showed signs of disintegration and the cartilage cells were fragmented and the nuclei had disappeared. The connective tissue, infiltrated throughout with cells, was invading the cartilage from outside and

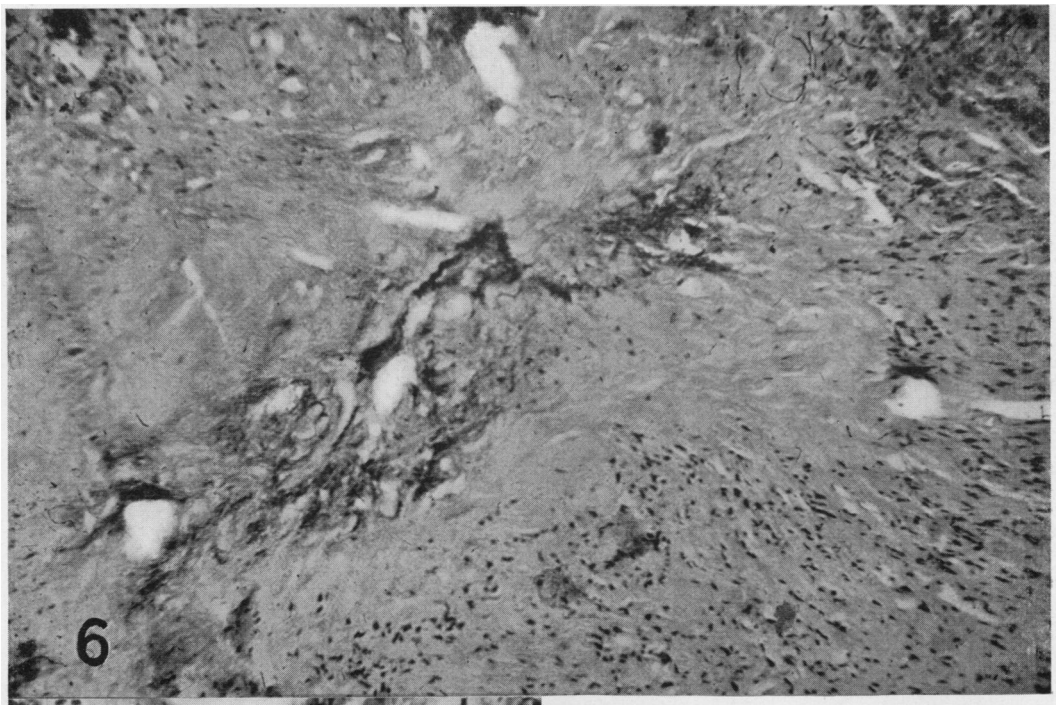


FIG. 6.—From the lateral band of the right index finger, Case 2. Showing central area of necrosis surrounded by epitheloid cells and lymphocytes (plasma cells). Great increase in connective tissue. ×100.

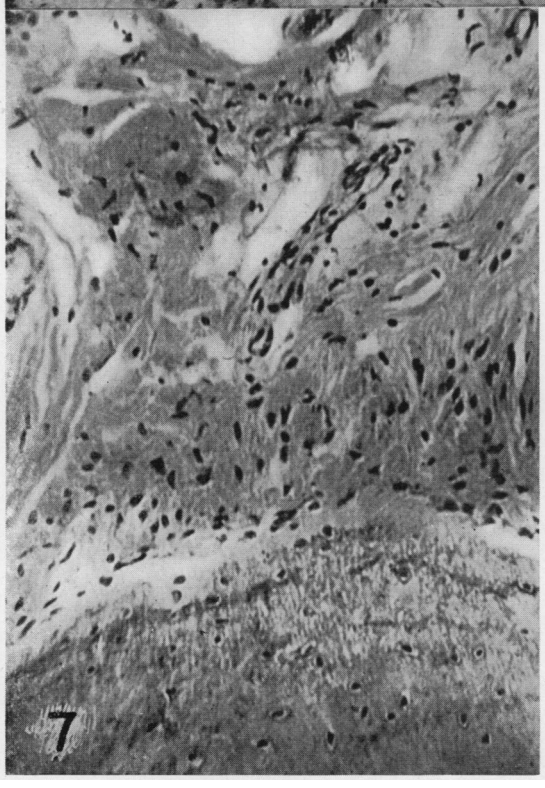


FIG. 7.—Section from the metacarpal head of the right mid-finger, Case 2. Pannus consisting of connective-tissue that is swollen in place and sclerotic in other areas, speckled by epitheloid cells and lymphocytes are invading the cartilaginous surface of the metacarpal head. This section is taken from the periphery of the cartilage cup near to the neck of the metacarpal bone. The cartilage itself shows signs of disintegration. ×100.

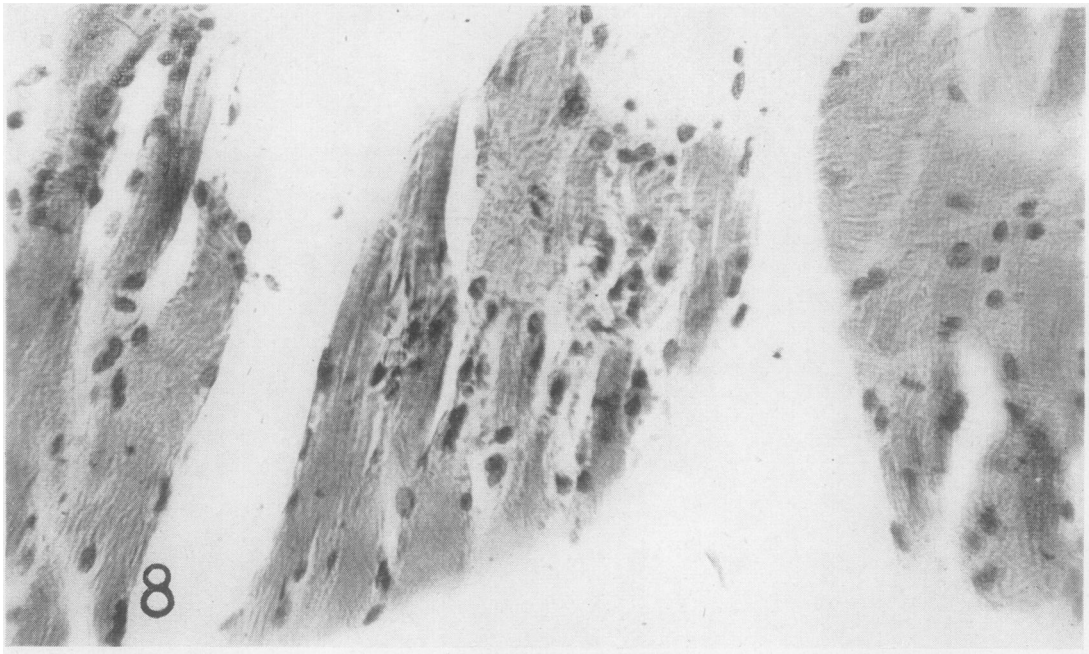


FIG. 8.—From interosseous muscle, Case 3. Extensive degenerative and inflammatory changes in the interosseous muscle. Approx. × 400.

finally eroded it. In this connective tissue a large number of minute capillaries were seen with their walls greatly thickened. A small number of lymphocytes were seen in their adventitia and not infrequently in their lumen. In the cartilage itself the following changes were seen. In the matrix there were areas of different staining. This was not due to the inequality of the slide in thickness. This we believe is a degenerative change which shows the following variations: thickening and fibrillation of the matrix as it goes into decomposition; the cartilage cells increase in number, their nucleus becomes large and plump; there is usually one nucleus; in areas where the number of cartilage cells is large they have lost their hyaline cartilage cell character, showing the structure of fibrocartilage; as the cartilaginous layer is thinning out it shows a longitudinal waving line staining dark blue.

Metacarpal Head.—The cortex was thinned out, the trabeculae were narrowed. In the marrow spaces, collections of lymphocytes and plasma cells were observed. These were frequently seen around blood vessels. One gained the impression that these changes destroyed the cartilage from within: the cartilage being pressed from the outside and from within the bone marrow by the granulation tissue. Similar observations were made by Bennett (1941) in other joints.

Muscles: Interossei and Lumbricales.—The most striking picture that was encountered by us in the study of the intrinsic apparatus of the hands was the diffuse involvement of the muscle tissue proper by inflammatory and degenerative changes.

An endomysial and perimysial round-cell infiltration was present, scattered all over in the various fields of slides. In places this was nodular in character as described by Steiner and others; however, there were many fields seen where these inflammatory lesions presented a more diffuse infiltration. The cells were mostly lymphocytes and epitheloid cells in this case. Plasma cells, mononuclears, and eosinophils were comparatively few. The shape of the nodules was various, spindle-shaped and elongated forms representing the majority. Most of the nodules seen in this area were not packed with cells but were rather interwoven by collagenous fibres. Quite interesting blood-vessel changes were found in the connective tissue between the muscle bundles, consisting of arterioles and capillaries with greatly thickened walls and with inflammatory cells in or near the adventitia (Fig. 4).

The muscle nuclei were greatly increased, their shape was elliptical or round and enlarged. The muscle fibres showed unusual shapes: wavy, crumbled, broken fibres mingling with normal ones. Abnormal transverse striations were seen in places, scattered holes in others. In some fields the transversely cut muscle bundles were missing and a fibrous mesh surrounded the shells of previous muscle tissue, representing fatty degeneration (Fig. 3). In other fields the disintegration and dissolution of muscle fibres could be observed and their replacement by collagenous tissue (Fig. 4). Perinuclear vacuolization was very frequent.

Lateral Bands.—Small specimens were removed from the lateral bands of the intrinsic muscles. There were

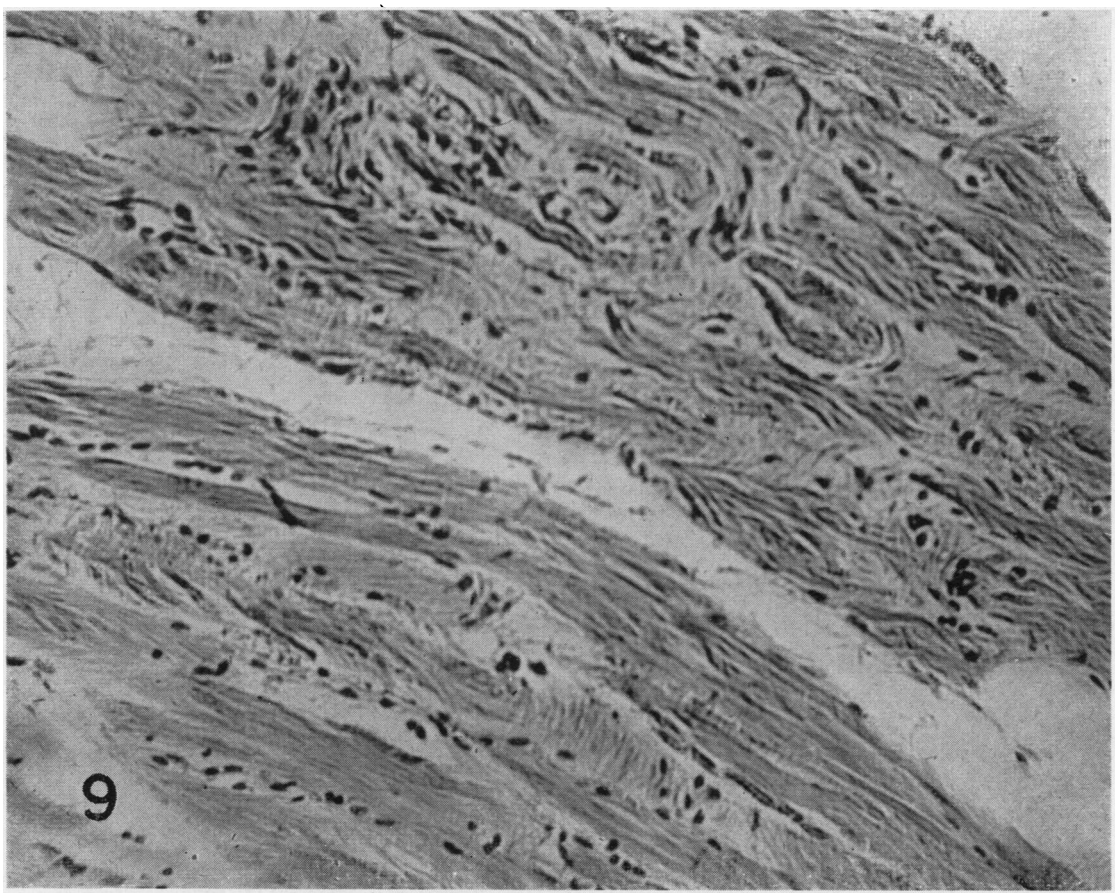


FIG. 9.—Section from lumbricalis muscle (second lumbricalis left hand), Case 4. Inflammatory and degenerative changes in the muscle tissue proper. ×100.

numerous fields infiltrated by epitheloid cells, lymphocytes, and plasma cells in a homogenous connective-tissue stroma. In places this infiltration has a nodular form (Fig. 5). There were fields that showed the characteristic appearance of the rheumatoid node.

CASE 2

A housewife, 42 years old, had suffered from rheumatoid polyarthritis for the past twelve years. Every joint of the body was involved, from the temporo-mandibular to the first metacarpo-phalangeal. There was extensive involvement of both hips with almost complete ankylosis. When she was seen at first, early in 1946, the sites of the patient's chief complaints were, in the following order: metacarpo-phalangeal joints of both index fingers, mid-finger joints of both mid-fingers, both hips, and both shoulders. The patient had been previously subjected to the usual anti-rheumatic treatments, including salicylates, bee venom, gold (three courses), vitamin D in large doses, and diathermy.

Right Hand.—There was moderate atrophy of the intrinsic muscles, with no deviation of the fingers in any direction. There was moderate swelling of the metacarpo-phalangeal joints of the index fingers only. Active extension of the metacarpo-phalangeal joint was possible to 170° with pain at this limit, and active flexion to 130°. Ten more degrees could be obtained by force, however, with great pain. No subluxation was present. Mid- and distal finger joints were intact. There was a similar condition of the left hand. The third fingers were practically intact. There was painful flexion deformity of mid-finger joints of both ring fingers with subluxation of the proximal portion of the mid phalanx.

The proximal finger joints of the index fingers being the centre of complaint, they were operated upon first (June 1, 1946). The metacarpal heads were excised as reported elsewhere (Kestler, 1946). Several biopsies were secured. Biopsy of lumbrical muscles was usually taken after the metacarpal head had been excised.

The Wassermann reaction was negative. The sedimentation rate was 45 mm. in one hour (Westergren).

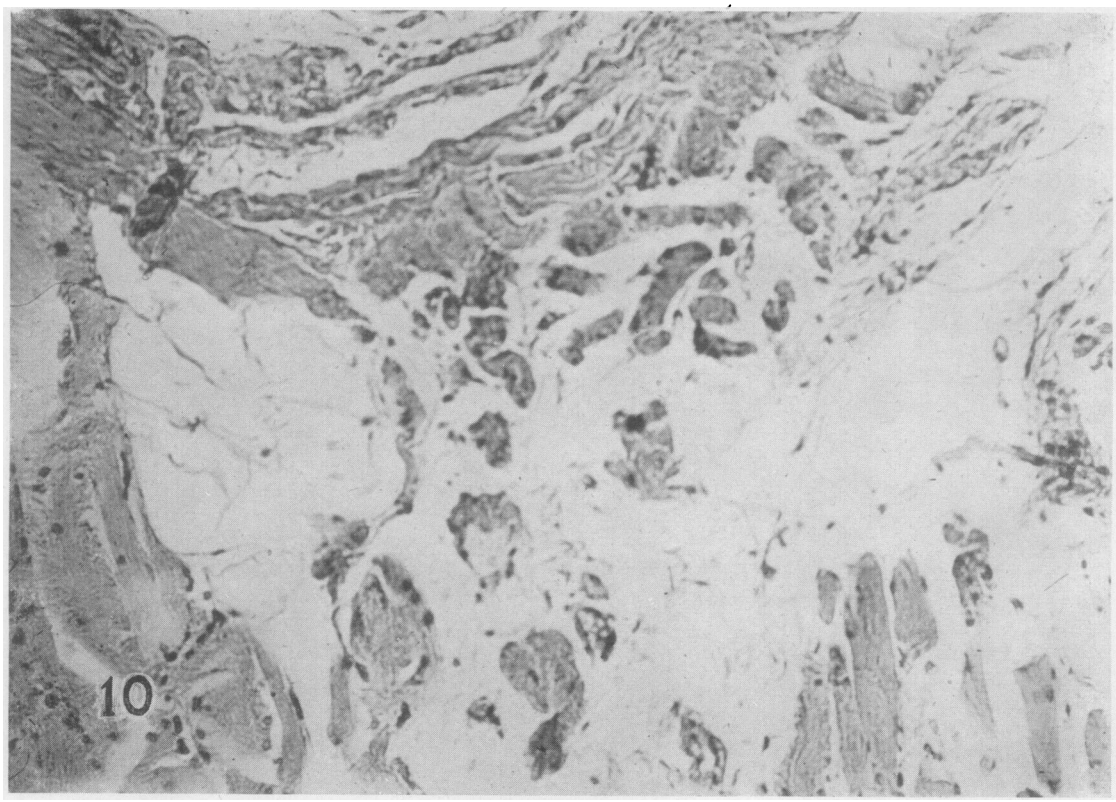


FIG. 10.—Section from the third dorsal interosseous of the right hand, Case 5. Inflammatory and extreme degenerative changes in interosseous muscle. ×100.

Except for moderate increase in serum globulin and moderate secondary anaemia, the rest of the findings were negative.

Radiographs revealed diffuse osteoporosis of the metacarpal bones and phalanges. There was no subluxation in any of the proximal finger joints.

Microscopic Findings.—Specimens of the tissues, as in Case 1, were examined and the results were about the same. The muscle involvement was less extensive, consisting only of spotty areas of inflammatory changes and similar degenerate changes. The interesting finding in this case was that sections taken from the lateral band of the intrinsic muscle of the left index finger showed the typical appearance of a rheumatoid node with an area of necrosis surrounded by epitheloid cells, plasma cells, and lymphocytes (Fig. 6).

While the radiographs did not reveal extensive bony changes and there was no subluxation, it is interesting to stress that, even in a case with mild clinical findings, tissue pathology was quite extensive. There was a visible thickening of the synovial membrane, mostly at the periphery of the cartilage cup; it showed a villous hypertrophy. In some places there was pannus erosion of the cartilage at the periphery.

This was considered a mild case both from clinical and pathological points of view. The follow-up confirmed this, inasmuch as two years after the operation there has been no recurrence of pain or swelling in the fingers that were operated upon, and there is the maximum functional result one can expect from this operation: active extension to 170° and full range of flexion in the proximal finger joint of the index finger. The pinching power of the index finger and thumb is good enough for most of the functional requirements.

CASE 3

A housewife, 34 years old, had had rheumatoid polyarthritis for nine years. The habitus was one frequently seen in patients suffering from this disease. Her family and past histories were not significant. The patient received most of the accepted anti-rheumatic treatments, including several courses of gold therapy to which she responded fairly well. The last course of chrysotherapy was given in 1946. Examination showed a fairly well-developed white female. Her general appearance was that of a chronically ill patient. Her weight was 118 lb. and her height 5 ft. 4 in. From the temporo-mandibular joints to the ankles, every joint was involved to a greater or less degree. The joints most

severely affected were both wrists and the periarticular and articular structures of both hands. While the lower extremities were involved, fairly good function was preserved.

The sedimentation rate was 28 mm. in one hour (Westergren). Red blood cells numbered 3,900,000 and white cells 7,400 per c.mm. of blood, and Hb was 75 per cent. Serum albumin was 3·8 per cent., serum globulin 2·9 per cent., and serum calcium 10·5 mg. per 100 c.cm. of blood. Alkaline phosphatase measured 3·9 Bodansky units. Serum phosphorus was 3·6 mg. and blood uric acid 3·1 mg. per 100 c.cm. of blood.

Right Hand.—This showed atrophy of the interossei to a very great extent. No ulnar deviation of the fingers was noticed. The thumb was markedly deformed, the distal phalanx was in the position of extreme hyperextension due to subluxation, and so was the proximal phalanx. There was painful limitation in the motion of the metacarpo-phalangeal joints; each had a different range, the fourth and fifth being the most painful. Each proximal phalanx was subluxated under the head of the respective metacarpal bone. There was an average of 20° flexion contracture in the metacarpo-phalangeal joints; active flexion from that point was possible to 35°. The patient was not able to make a fist.

Index Finger.—The middle finger joint was rigid in slight hyperextension. The distal finger joint of the index finger could be actively flexed from its normal extended position approximately 15°.

Mid-finger.—The middle finger joint was in about 15° of hyperextension with no active or passive flexion in this joint. The distal finger joint was not in flexion contracture but rather in the position of 10° of flexion from which passive extension was full and active flexion restricted.

Fourth and Fifth Fingers.—Changes in the fourth and fifth fingers were restricted mostly to the metacarpo-phalangeal joints with extensive subluxation and a considerable amount of pain in these joints. The deformity in the other finger joints of the fourth and fifth fingers was only moderate.

Tissue Pathology.—Subcutaneous tissues appeared to be normal in colour and thickness. The aponeurosis of the extensor apparatus as well as that of the intrinsic muscles was found to be thickened. Upon incision of the capsule of the proximal finger joints small amounts of light-greyish, thick fluid escaped. The lining of the capsule was oedematous and thick, and villous tissue was facing the joint cavity. The villi were enlarged and pinkish in colour. The articular cartilage of the second and third metacarpal bones was practically normal, which means that it was intact and had a shiny appearance but at the periphery of the cartilage cup the synovial membrane was thickened and red. These findings were very interesting in view of the fact that this patient had had a number of courses of gold therapy shortly before surgery. This finding was in accordance with findings we had in other cases that had had gold therapy and also in accordance with the findings of authors like Gibson and others. Specimens were removed from all the tissues encountered; then the interosseous muscles were carefully dissected out. They were normal in appearance, and somewhat pale. However, this may be due to the fact that a tourniquet was used. Specimens 0·5 cm. in length and 3 mm. in width were removed from two interossei, namely, those of the index and ring fingers. More advanced changes were found at the heads of the fourth and fifth metacarpals including their para- and periarticular tissues; the thickening was greater, the villi were larger, the subluxation more extensive, and the metacarpal heads were destroyed; the cartilage had disappeared and there were marginal exostoses at the epiarticular area.

Microscopic Findings.—The most striking findings in this case were the colourful variations of stages in muscle tissue proper, showing the wide variety of inflammatory changes and degenerative changes as described above (Fig. 8). Inflammatory changes about the blood vessels were also noticed within the mucle tissue. The findings were very much the same as in Cases 1 and 2 already described in detail.

The middle finger joint of the right mid-finger was also operated upon in this patient. Specimens from the joint capsule and ligaments as well as of the extensor expansions showed lesions similar to those in the proximal finger joints.

Case 4

A man, aged 44, had rheumatoid polyarthritis with an eleven-year history. All his joints were involved. The disease was in a quiescent stage with the exception of the finger joints of both hands. His sedimentation rate was 48 mm. (Westergren). He was anaemic. His albumin-globulin ratio was moderately reversed. Blood uric acid was 3·8 mg. per 100 c.cm. He had had many courses of gold therapy, the last three months ago. There was a response to gold therapy at the beginning but subsequently he had no improvement. He was seeking relief for painful limitation of the proximal finger joints on both hands.

Hands.—The neutral position of both hands was accentuated by an extensive ulnar deviation of the fingers. The area of the proximal finger joints was swollen; they were held in 15° of flexion; from this position there was about 10° of flexion possible with pain. All proximal phalanges were subluxated. The mid-finger joints were held in extension, and with the exception of the fourth and fifth fingers on both hands they could not be flexed. There was 15° flexion deformity of both distal finger joints of both index fingers. Because of extreme pain and limitation of motion, the excision of the metacarpal heads was performed.

Pathology.—The para- and periarticular tissues about the metacarpo-phalangeal joints were oedematous, and thickened. Upon opening the joint capsule a considerable amount of greyish fluid escaped. The lining of the capsule was thick; villous tissue was emerging from the synovial structures, which were dark red. The villi could be seen well by gross examination. The articular cartilages of the metacarpal bones were destroyed. The damage to them was increasingly severe from the index to the fifth finger; in other words, while

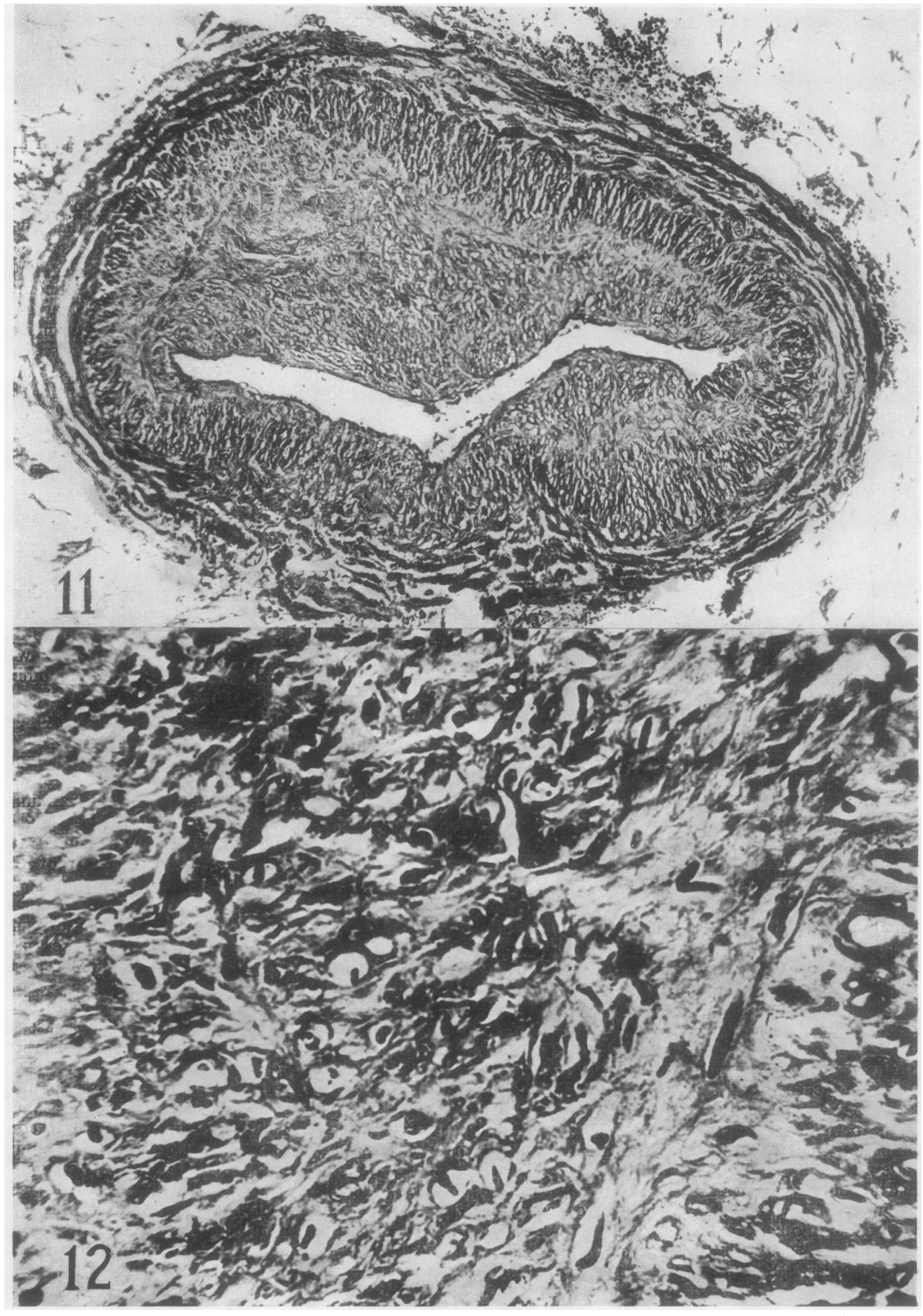
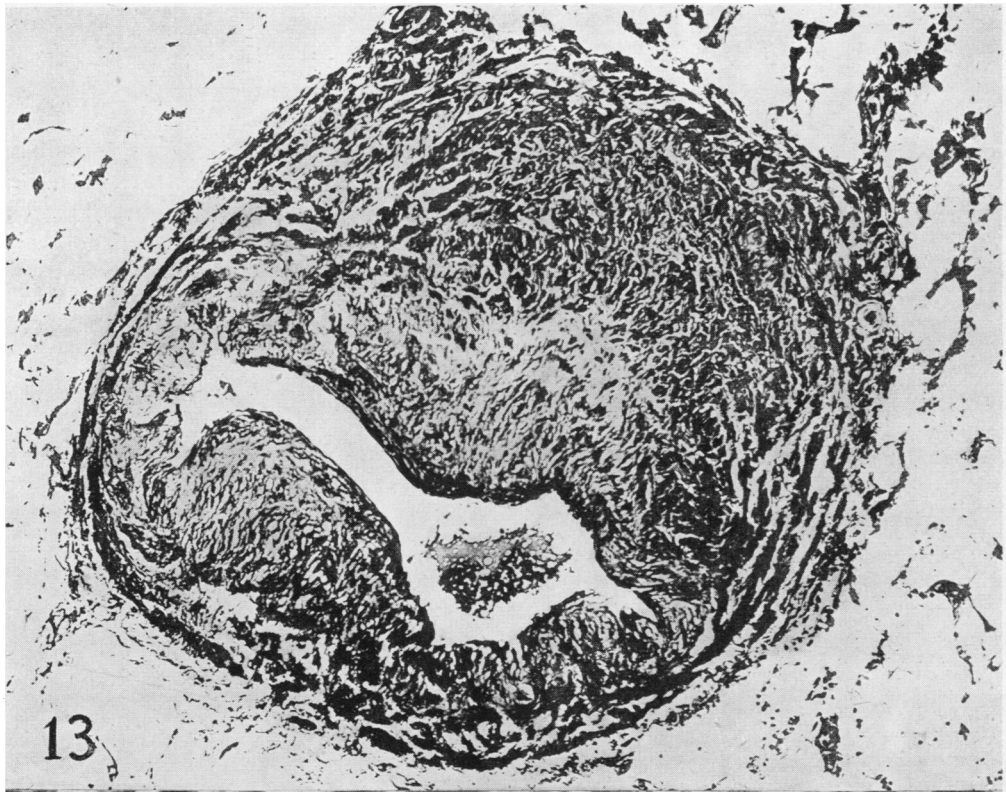


FIG. 11.—Blood vessels from intermuscular septum of left vastus lateralis, Case 5. Showing diffuse perivascular adventitial round-cell infiltration. Extensive obliteration of the vessel is quite striking. ×150.

FIG. 12.—High power view of Fig. 11, showing excessive amount of fibro-collagenous tissues rather rich in cellular elements. Vacuolization of cells seems to be a significant feature. ×372.



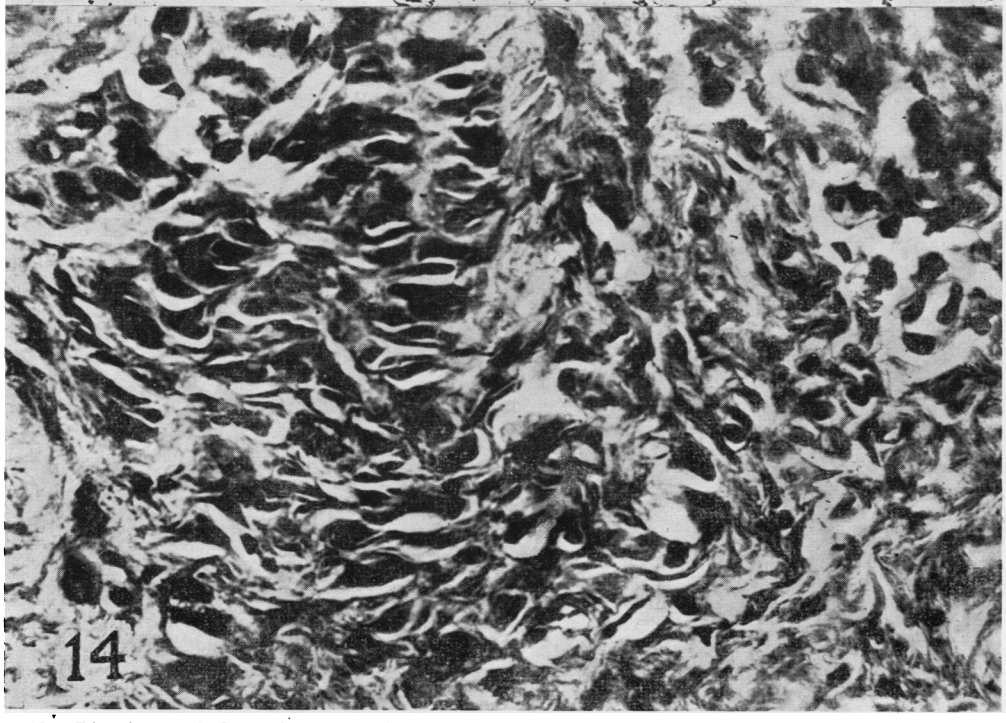


FIG. 13.—Blood vessel from intermuscular septum of right gluteus medius, Case 6. Showing extreme thickening of the blood vessel and scattered round-cell infiltration outside the vessel. ×150.

FIG. 14.—High-power view of Fig. 13. Fibro-collagenous changes similar to those in Fig. 12.

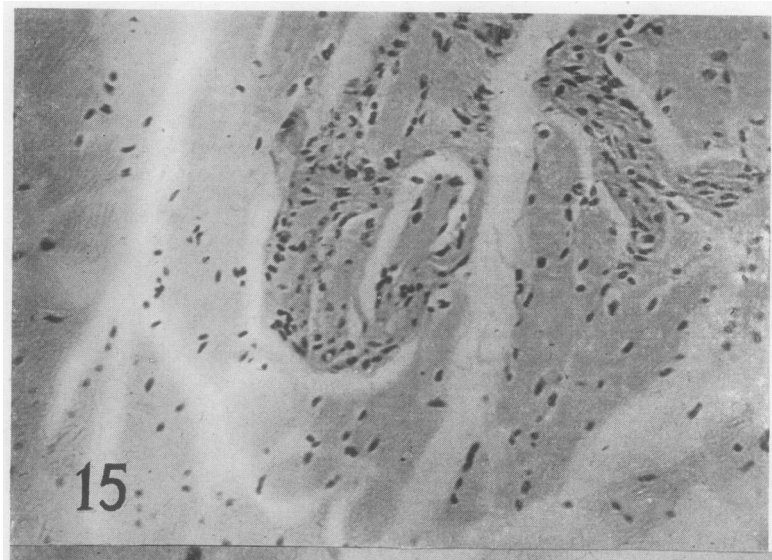


FIG. 15.—Lumbrical muscle, left hand, Case 7. ×250.

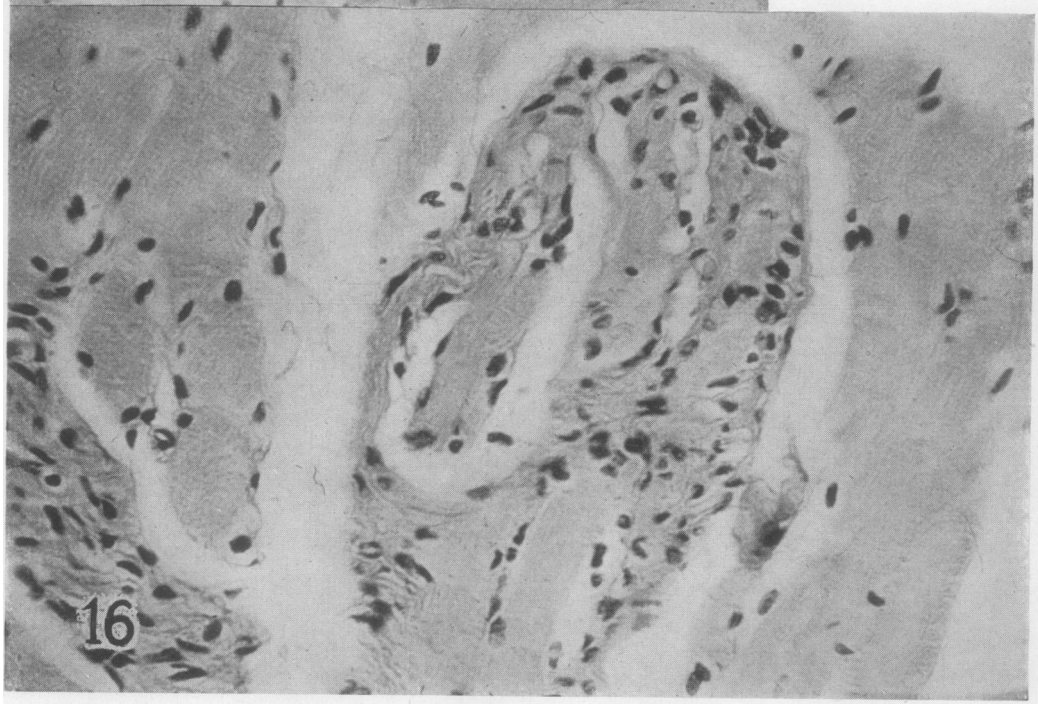


FIG. 16.—Same as Fig. 15. ×400.

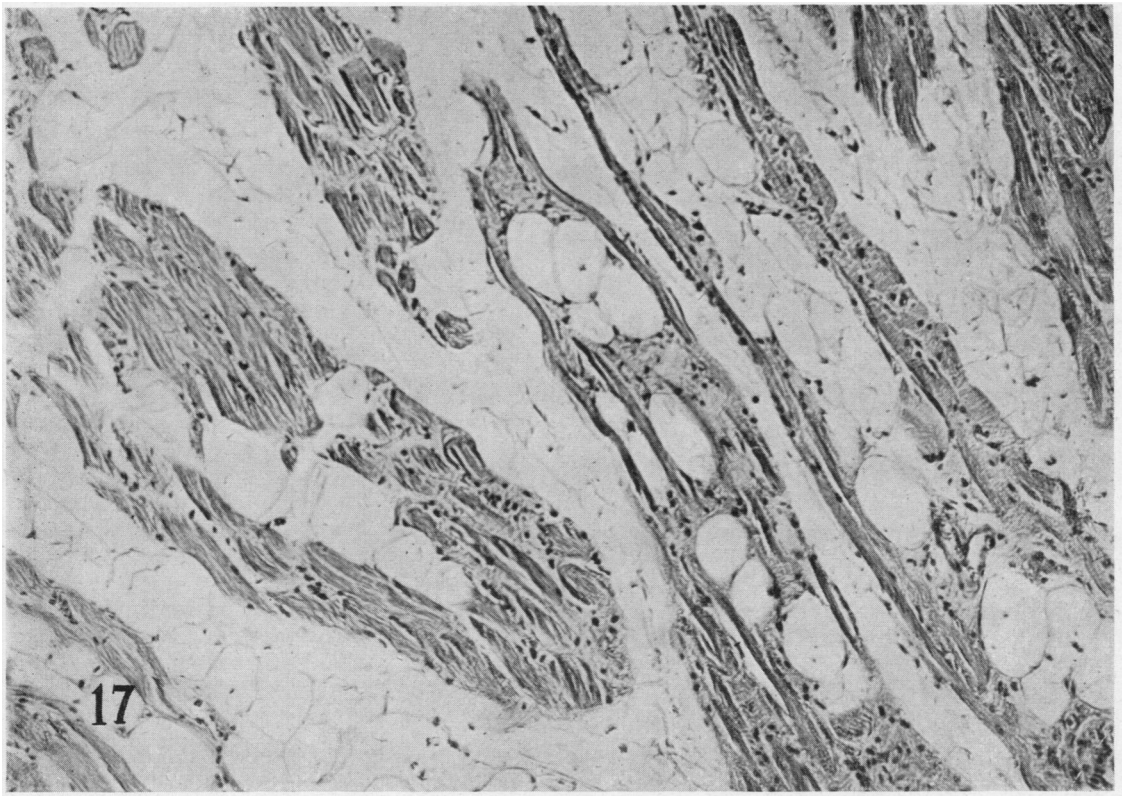


FIG. 17.—Interosseous muscle, Case 8. Extensive inflammatory and degenerative lesions in the muscle tissue proper. ×100.

there were cartilage islands on the second and third metacarpal heads, hardly any remained on the fourth and fifth.

Microscopic examination of tissues was performed by the same routine as in the previous cases. The findings were very similar to those seen in the previous cases (Fig. 9).

CASE 5

A 41-year-old woman with a history of rheumatoid polyarthritis of six years' duration had as the outstanding feature extreme changes in the dorsal third interosseous of the right hand (Fig. 10). Figs. 11 and 12 show significant blood vessel changes in the left vastus lateralis in this case.

CASE 6

A 37-year-old woman had rheumatoid polyarthritis of four years' duration. The details were practically the same as those reported for previous cases. The dorsal interosseous of the mid-finger of the right hand was found to be involved in numerous places, as shown in previous cases described above. Characteristic changes in the blood vessels were found in this case in other skeletal muscles (Figs. 13 and 14).

CASE 7

A 34-year-old man had rheumatoid polyarthritis for four years. Figs. 15 and 16 show change in one of the lumbrical muscles in the left hand.

CASE 8

A 29-year-old woman had rheumatoid polyarthritis of three years' duration. Fig. 17 represents a section from an interosseous muscle of the right hand. A section obtained from the metacarpal head of the right mid-finger revealed pannus eroding the cartilage cup in a similar way to that shown in Fig. 7. There was disintegration of cartilage tissue where the pannus invaded the cartilage.

CASE 9

A 48-year-old woman with rheumatoid polyarthritis of five years' duration showed findings practically identical with the ones previously described.

CASE 10

A 42-year-old man for the past eight years had been suffering from rheumatoid polyarthritis. Tissue changes did not differ from those reported above.

CASE 11

A 41-year-old woman had rheumatoid polyarthritis of six years' duration. The histopathology consisted of lesions similar to those in the previous cases.

Discussion of Tissue Pathology

In summarizing our findings in the intrinsic apparatus of the hand, the most striking feature was the active involvement of the extensor assembly, the muscle tissue proper, and the lateral bands by the rheumatoid process.

In the muscle tissue the lesions observed should be divided in four groups:

1. Inflammatory lesions. These were perimysial and endomysial in character. The cell elements consisted of lymphocytes, plasma cells, epitheloid cells, and much less extensively of mononuclear, eosinophil, and polymorph neutrophil cells. The arrangement of these cells was frequently nodular according to the description of Freund and others (1942) and Steiner and others (1946). However, a scattered infiltrative appearance was not infrequently observed.

2. Degenerative changes of muscle tissue represented by the enlargement of muscle nuclei, increase in number of the nuclei, vacuolization with eccentric position of the flattened nucleus, etc.

The muscle fibres took on a variety of abnormal shapes: winding and bending as a sign of shrinkage was observed. The shrunken muscle fibres were swollen and wavy. Muscle fibres were broken up into small elements: some of them showed a spotty disintegration; others were replaced by fatty or fibrous connective tissue.

3. Changes in the blood vessels were two-fold, thickening of their walls by concentric increase of collagenous tissue and a peri- or para-adventitial round-cell infiltration in these small blood vessels.

4. Collagenous tissue changes consisting of increase of the collagenous tissues and swelling of their ground substance. Fibrinoid changes in the connective tissue and sclerosis of the collagenous substance were observed. Where the degenerative changes in the muscle fibres were extensive, replacement by connective tissues was abundant.

We have already mentioned the concentrically thickened walls in the small blood vessels. It seems that this thickening is not confined to the adventitia only but also extends intramurally. The nodular and diffuse round-cell infiltration about the vessels was also referred to. These changes about the small blood vessels were observed in the extensor aponeurosis, in the subcutaneous tissues, in the joint capsules, and in the connective tissue septa of the muscle tissue proper.

It is not the aim of this paper to discuss similarities in histopathology of cases of rheumatic fever, scleroderma, periarteritis nodosa, and lupus erythematosus (Klemperer, 1947). We merely wish to record these findings in the intrinsic muscles of the hands of patients suffering from rheumatoid polyarthritis.

Structures Other than Muscle Tissue

In the extensor assembly and in the fibrous attachments of the intrinsic muscles like the lateral bands or the structures about these bands, rheumatoid granulation tissues represented by diffusely infiltrated connective tissue, by epitheloid cells, lymphocytes, plasma cells, occasionally by eosinophils, was the routine finding. A feature not described heretofore was the textbook picture of a so-called rheumatoid node right in these extensor expansions. The significant blood-vessel changes were observed in these structures as well.

Aetiology

From these findings we may conclude that rheumatoid arthritis is primarily the disease of the soft tissues, as stated by Gibson and others (1946), among others. A blood-borne infection, most likely an agent from the group that causes infectious granulomas, is invading the mesenchymal tissues. Of these mesenchymal tissues the connective tissues and muscles seem to be involved primarily. As to the articular cartilage, this is being invaded secondarily. Inflammatory changes in the bone marrow were observed by us and by others (Bennett, 1941). Pannus erosion of the articular cartilage is a common finding; it seems, therefore, that the articular cartilage is pounded from within and from outside.

Allergic reaction does not seem to explain, at least to us, the tissue reactions of rheumatoid arthritis. We are in agreement with those who are of the opinion that alterations in the connective tissue as described by us and by others (Klinge, 1933; Rossle, 1933; Schosnig, 1932; Wu, 1937) in different conditions are not necessarily of allergic origin. We know from the work of Schosnig, Wu, Selye and Pentz (1943), and others that fibrinoid collagen changes must not be interpreted invariably as an expression of allergic reaction. It is our unshaken belief that rheumatoid arthritis is not an allergic disease.

Correlation of Tissue Pathology with the Clinical Picture

It was a known fact that tendon sheaths, the synovial membrane, the articular cartilage, and the bone itself about the finger joints became actively

involved with rheumatoid granulation tissue. It was also a generally accepted view that the intrinsic muscles of the hand developed an atrophy of disuse.

Nothing is to be found in the literature, however, dealing with observations regarding the intrinsic apparatus itself: the extensor assembly, the interosseous and lumbrical apparatus, and their extensor expansions or lateral bands. Following the work of Freund and others, and again that of Steiner and others which dealt with what they described as a nodular polymyositis and neuromyositis of rheumatoid arthritis, it became quite possible that changes they found in skeletal muscles depicted at random may be found in muscles all over the body. And yet the active involvement of the intrinsic muscle apparatus in inflammatory lesions and the degenerative changes developing thereon offers an explanation for a number of clinical facts hitherto not appreciated.

It is not within the scope of this paper to elaborate on the evolutionary phases of the deformed arthritic hands. Another study is dealing with this problem in detail (Kestler, in the press). We are confined, therefore, to a few statements based upon the pathological findings as discussed above. While a basic pattern is almost invariably present the rheumatoid hands do not show a uniform deformity. The basic pattern applies to the proximal finger joints, which almost invariably show a flexion deformity. There are numerous variations, however, in the deformities of the middle and distal finger joints.

The basic factor responsible for the deformities is the active inflammatory involvement of the periarticular structures of the finger joints as well as the inflammatory and degenerative lesions of the intrinsic muscle apparatus proper. It is appreciated, however, that these inflamed, painful units of the hand are secondarily subjected to the force of gravity. Due to these inflammatory changes the intricate mechanism so important in maintaining the accurate balance of the intrinsic muscle apparatus is disturbed, and finally, as the condition progresses, completely lost.

Added to this, the inflammatory and degenerative changes in the muscles resulting in shrinkage and loss of muscle substance will shorten the muscles, producing thus an interosseous type of atrophy and an ulnar deviation of the fingers. The degree of this latter deformity seems to be dependent upon the amount of intact muscle tissue that has survived. This muscle tissue will then permit a more or less limited functional activity of the fingers.

The condition could be compared perhaps with the " fibrous contracture of the hand ", a clinical entity only recently described by Bunnell (1948). In this, due to entirely different aetiology, fibrous bands throw the intrinsic muscles out of action. In rheumatoid arthritis of the hands, the active inflammatory disease and the secondary degenerative changes of the muscle tissue itself and the fibrous attachments thereof are inhibiting and eliminating the active function of the intrinsic muscle apparatus.

Conclusions

In eleven cases of chronic rheumatoid polyarthritis which were treated by surgery, biopsy specimens taken during reconstruction of deformed hands revealed inflammatory and degenerative changes in the intrinsic muscles. Inflammatory and degenerative lesions were marked in all these cases.

Almost invariably the characteristic histologic appearance of the subcutaneous rheumatoid node could be observed in the aponeurotic sleeves, the lateral bands, the joint capsules of proximal and middle finger joints, and the tissues thereon. Frequently the inflammatory lesions were found to be nodular in character; however, diffuse infiltration of the tissues was just as frequent.

Significant lesions about the blood vessels are reported, mostly in the small arteries, consisting of concentric accumulation of connective tissues and of peri- and para-adventitial nodular foci. These arterial lesions showed similarities to the ones seen in periarteritis nodosa.

The opinion is expressed that the lesions in the structures described above, including the muscle tissue proper, are the primary ones. The articular cartilage seems to be affected by secondary invasion.

In five of the eleven cases, biopsy specimens were taken from other structures and muscles besides the hand, and similar lesions to those reported here were found.

Chrysotherapy did not seem to influence tissue pathology, regardless of the number of courses given and whether or not there was a favourable response. The time that had elapsed between removal of biopsy specimens and the discontinuance of chrysotherapy did not seem to modify the histopathology. Two cases which according to their histories were not subjected to gold therapy showed identical changes. In view of these findings, while the great value of chrysotherapy if successful is recognized, the conclusion is established that its effect is nothing but palliative. It cannot and does not directly hinder the growth of rheumatoid granulation tissue. It may, however, indirectly delay destruction of articular cartilage by permitting active function, rendering temporary relief in cases where this is done by the drug.

The characteristic deformity of the rheumatoid hand is the result of simultaneous factors, of which the primary and dominating feature is the direct involvement of the intrinsic muscle apparatus proper by the rheumatoid process. The wonderful precision balance of this intrinsic apparatus is disturbed through this, establishing the first link in a chain of pathological sequences.

According to our observations, active use of the hands and their finger joints seems to delay or even prevent destruction of these non-weight-bearing articulations.

It was observed that the amount of subluxation in the proximal finger joints increases from index to little finger. The destruction of the articular cartilage was found to be increased in the same manner.

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Histopathologie des Muscles Propres de la main dans l'Arthrite Rhumatismale; Étude Anatomo-clinique

Conclusions

Dans onze cas de polyarthrite rhumatismale chronique traités chirurgicalement, la biopsie pratiquée au cours de la reconstitution des mains déformées a révélé des modifications inflammatoires et dégénératives des muscles propres. Ces lésions inflammatoires et dégénératives étaient également marquées chez tous les malades.

On a presque invariablement observé l'apparition de nodules rhumatismaux sous-cutanés à aspect histologique typique, siégeant au niveau des gaines aponévrotiques, des ligaments latéraux, des capsules articulaires des articulations proximales et médiane des phalanges et des parties molles. Les lésions inflammatoires étaient fréquemment de caractère nodulaire; mais l'infiltration diffuse des tissus était tout aussi fréquente.

L'auteur rapporte la présence de lésions périvasculaires marquées, surtout dans les artérioles, et constituées par l'accumulation concentrique du tissu conjonctif et de foyers nodulaires péri- et para-adventitiels. Ces lésions artérielles présentaient des analogies avec celles que l'on observe dans la périartérite noueuse.

L'auteur exprime l'opinion que les lésions dans les structures décrites ci-dessus, y compris les tissus musculaires eux-mêmes, sont des lésions primaires. Le cartilage articulaire semble être affecté par l'invasion secondaire.

On a pratiqué la biopsie d'autres tissus en dehors de la main chez cinq malades sur onze, et l'on a observé des lésions semblables à celles qui viennent d'être décrites.

La chrysothérapie ne semble pas avoir eu une influence sur les lésions tissulaires, indépendemment du nombre des séries de traitements administrées, et quel qu'ait été le résultat clinique. Le temps écoulé entre la biopsie et la cessation du traitement ne semble pas avoir modifié l'aspect histopathologique. Deux malades qui, d'après leurs observations, n'avaient pas reçu de traitement par les sels d'or présentaient les mêmes modifications. Ces résultats amènent à conclure que, malgré sa valeur, la chrysothérapie ne produit qu'un effet palliatif. Elle ne peut pas empêcher directement la développement du tissu granuleux rhumatismal. Mais elle peut retarder indirectement la destruction du cartilage articulaire en permettant l'activité fonctionnelle, et en amenant un soulagement momentané dans les cas où ce résultat est obtenu par la médication.

La déformation caractéristique de la main rhumatismale est due à plusieurs facteurs simultanés qui sont essentiellement caractérisés par l'atteinte directe par le processus rhumatismal de l'appareil musculaire propre. Cette atteinte dérègle l'admirable appareil de précision constitué par les muscles de la main, et forme le premier élément d'une série de modifications pathologiques.

L'activité des articulations des mains et des doigts semble retarder ou même empêcher la destruction de ces articulations qui ne supportent pas de poids.

On a observé que le degré de luxation des articulations digitales augmente en allant de l'index au petit doigt. On a trouvé que la destruction du cartilage articulaire augmente dans le même sens.