A VARIANT OF RHEUMATOID ARTHRITIS CHARACTERIZED BY RECURRENT DIGITAL PAD NODULES AND PALMAR FASCIITIS, CLOSELY RESEMBLING PALINDROMIC RHEUMATISM

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Introduction

Observations culminating in the work of Nichols and Richardson in 1909 clearly differentiated rheumatoid arthritis from degenerative joint disease, a distinction which has been universally accepted and has done more to clarify our ideas on chronic rheumatism than any other single concept. Rheumatoid arthritis itself, however, has tended since then to become an unwieldy nosological hotch-potch, including almost any chronic joint affliction which is not obviously exogenous (for example traumatic or bacterial) in origin. Many have suggested that the term includes a variety of diseases, and attempts have been made to separate out such clinical entities as:

(a) infective arthritis, characterized by the involvement of a few large joints and the presence of a focus of infection, but no recoverable metastatic organism and by a tendency to improve or even to heal following the removal of the focus;

(b) classical rheumatoid arthritis, occurring in middle-aged women and involving, characteristically, multiple finger joints;

(c) psoriatic arthritis, characterized by terminal interphalangeal joint involvement and association of activity with skin exacerbations;

(d) joint disorders associated with ulcerative colitis and other intestinal diseases (for example Whipple's syndrome), characterized by a relatively mild course with remissions and exacerbations dependent on activity of the primary disease;

(e) spondylitis ankylopoietica or, as some prefer to call it, rheumatoid arthritis of the spine, differing in the earlier age and preponderantly male incidence: its peripheral joint manifestations are different neither clinically nor pathologically from those of rheumatoid arthritis "proper";

(f) intermittent hydrarthrosis and palindromic rheumatism (Hench) which are thought by some, but not by Hench, to be variants of the rheumatoid arthritis syndrome; certainly some cases of intermittent hydrarthrosis ultimately develop the same type of permanent joint involvement as in rheumatoid arthritis: see later discussion;

(g) Still's disease. This is rheumatoid arthritis occurring in children and the so-called distinguishing features (for example late radiological involvement) are due only to the increased cartilage protection of epiphyseal bone at this age. Other features, such as pericarditis, enlarged glands, and spleen, are seen in adults as well;

(h) arthritis associated with visceral disseminated lupus erythematosus (see later discussion);

(i) Felty's syndrome with arthritis, splenomegaly, anaemia, leukopenia, and pigmentation of the skin is now generally agreed (for example Talkov and others, 1942), to be rheumatoid arthritis, occasionally complicated by coincident disease such as cirrhosis of the liver: in the classical rheumatoid case, any or rarely all of these extra signs may be present;

(j) Sjögren's syndrome (rheumatoid arthritis with kerato-conjunctivitis sicca).

Thus, we have a number of loosely conceived nosological entities of whose life course we know as yet little and whose pathological changes, still ill-understood, appear superficially to resemble each other very closely. These various syndromes are statistically determined rather than true entities, based on clinical or anatomical data rather than a knowledge of aetiology. The chief reason for distinguishing between them is the practical usefulness of such distinctions for prognosis and treatment. For scientific purposes, the resemblances between these various conditions are, from many angles, more important than their differences; it seems probable that the basic (and unknown) pathological processes are, in all, similar in nature. This means that these conditions may be considered as variants on a basic theme, or from a basic type. Such variants fall into several possible categories. The variation-producing factor may be constitutional (for example, the congenital ductus arteriosus variant of subacute bacterial endocarditis); it may be age of onset (for example, Still's disease); it may be modification by environmental factors, such as nutritional state, etc., or it may be the presence of some other disease producing a pseudovariant (for example, cirrhosis of liver complicating rheumatoid and producing Felty's syndrome). There might be variation in original exogenous stimulus (for example, antigen)—or variation in the type or location of tissue originally stimulated. Of such vagaries we know very little—why some patients with rheumatoid develop eye lesions and others do not, why some psoriatics develop arthritis and others do not—but to "account" for the variant we postulate some extra factor, operative before or after the onset of the main disease, either determined by it or actually determining the main disease.

A further characteristic of such variants is that a gradation exists between the type and its variant. Thus we do not include rheumatic fever as a variant of rheumatoid arthritis because we do not see cases which are pathologically halfway between rheumatic fever and rheumatoid arthritis; our patients turn out ultimately to have either permanent joint or permanent heart disease or neither (in contra-distinction to those of other clinics, for example, Baggenstoss and Rosenberg, 1941; Bayles, 1943; Young and Schwedel, 1944). Thus, to prove a syndrome to be a variant, it is necessary to establish the existence of lesser and variable degrees of variation from type, that is, transitional forms.

It is the object of this paper to detail such a variant. A case will first be described (in full detail since it appears to be unique) which shows the variation at a maximum, so much so that the correct diagnosis was not reached for nine years: following this, other cases will be detailed rather more shortly, showing transition to the more usual type of rheumatoid arthritis.

Case Histories

Case 1

E.P., a man aged 60, on his first admission (Feb. 2, 1943) with no family history or relevant disease, had been in good health until the age of 51, except for a minor degree of silicosis contracted during service as a mining engineer in South Africa, for which he was invalided at the age of 45. He had contracted no tropical disease. The present complaint started in 1934 at the age of 51* following an exposure to damp and cold: the hands became swollen and painful in attacks lasting some two or three days. At this period he had perhaps two attacks every month, affecting only the hands and feet. These are described as swellings and pain in the neighbourhood of the proximal interphalangeal joints, one or two being affected at each incident, and then perhaps others in succeeding incidents. These attacks continued to 1935, being always more frequent during the winter months, but completely absent in a warm climate (South Africa in December 1935 and January 1936) and returning on the voyage home.

In October 1935 the patient saw Consultant I (Medicine) complaining at that time of "superficial painful swellings on the toes, fingers, wrists, knees, and soles of feet, especially marked in cold weather".

* The patient's wife was medically qualified and kept a detailed diary of her husband's condition and copies of the medical reports from the numerous specialists whom he consulted; I am much indebted to her for allowing me to see and use these documents, as well as to the consultants themselves.

Examination showed nothing abnormal except a small oedematous area appearing during examination between the index and middle knuckles of the left hand, which disappeared in a few minutes. In between these attacks the patient was perfectly well. For example:

"*Aug. 2.*—Swelling of right little finger.
Aug. 6.—Finger better.
Aug. 7-8.—Right wrist painful.
Aug. 9.—Wrist free of pain. Got slightly chilled: by evening the right index finger was considerably swollen with clear distal demarcation, swelling covering one inch above and below middle phalangeal joint; middle finger also swollen. Left hand: middle finger swollen and similar to right index. Feet: uncomfortable but not definitely swollen.
Aug. 10.—Swelling of fingers improved.
Aug. 11.—Fingers improved but swelling started over fifth metacarpals on both hands.
Aug. 13.—Hands much improved.
Aug. 15.—Very slight swelling over first metacarpophalangeal joint.
Aug. 17.—Slight trace of swelling remaining.
Aug. 22.—Slight discomfort, but no real swelling.
Sept. 1.—Slight swelling of third left finger.
Sept. 4.—Painful swelling over first metacarpal left hand. Feet painful. Right hand also uncomfortable.
Sept. 5.—Right hand swollen and middle finger very tense. Left hand still swollen: middle finger tense. Feet painful.
Sept. 6.—Most of swelling of right hand improved, but hard swelling appearing under middle and third finger tips. Left hand better. Feet still painful.
Sept. 7.—Left hand worse again, swelling over first knuckles, middle finger tense. Right hand and fingertips improved; feet extremely painful with hard swellings under heads of metatarsals.
Sept. 9.—Both hands much swollen and feet painful. Contraction of fourth finger of right hand owing to swelling over tendon. Hard swelling over olecranon. Spent day in bed.
Sept. 11.—Saw Consultant II (Physical Medicine). Hands subsided. Fourth finger of right hand contracted.
Sept. 13.—Sufficiently well to play three sets of tennis.
Sept. 15.—Saw Consultant III (Allergy) who after testing for protein reactions pronounced condition to be non-allergic. Swelling almost vanished from hands with exception of fourth finger left hand. Right fourth finger still contracted. Fluid in left olecranon bursa.
Sept. 16.—Fourth left finger tense. Wrists both painful.
Sept. 18-22.—Much improved.
Sept. 27.—Still some contracture of tendon of fourth finger right hand and fluid in left olecranon bursa. Generally comfortable in the morning, but in the afternoon the right foot was painful with very tender spot below right outer malleolus.
Sept. 29.—Both hands and all fingers tense and swollen. Feet painful." (Extracted from diary.)

In October 1936 he was seen by Consultant IV (Medicine). He was complaining at that time of puffy swellings on the back of the hand with tenseness of fingers and wrists, swelling of the soles of the feet, and small shotty nodules in the olecranal bursa which showed effusion and hard nodular swelling on both ulnae. There was a premonitory sensation of tenseness and then swelling arising in two to three hours, sometimes taking days to subside. This was brought on by cold weather but left no permanent change. A tentative diagnosis of gout was made and the patient was treated with aspirin and colchicum. No improvement having followed a holiday in Bermuda in April 1937, he was sent into a private clinic under the care of Consultant V (Gastro-enterology), where the condition was thought to be gout. Blood uric acid was 3·6 and later 3·2 mg. per 100 c.cm. Atophan at first seemed to be helpful, causing the swellings to disappear for a few days, but subsequently it had much less obvious effect. The erythrocyte sedimentation rate was recorded as 62 mm. and 4 mm. per hour (Westergren) one month later. Haemoglobin was 96 per cent., red cell count 4,900,000 and white cell count 10,000 per c.mm. of blood, 70 per cent. polymorphs, and later 7,600, 62 per cent. polymorphs. Consultant VI (Ear, Nose, and Throat) found no nasal or pharyngeal infection. Urine was sterile and normal. Cholecystogram showed no gall-bladder shadow and it was thought that gall-stones were present, but as there was no evidence of cholecystitis it was decided to leave them. Previous to this investigation he had been having about twenty attacks yearly in the preceding three years. These were lasting something like a week.

After the patient left the clinic the diary records much the same pattern as before, of daily stiffnesses and swellings attacking hands, feet, wrists, and shoulders, with painful swellings over the olecranal processes of both ulnae, alternating with periods of freedom permitting a normal life, including golf.

In the following two years, 1938 and 1939, he had very few attacks indeed, none or one or two a year. In 1940, however, he had a few more attacks, something like six per year, each lasting two or three days. At this time he was working very hard. In the summer of 1941 the attacks became more frequent, about twenty per year, and, although atophan was increased in dosage, no benefit was obtained. In October 1941 he saw Consultant VII (Rheumatism) who thought the condition was an angioneurotic oedema possibly due to infection. White blood cells were 10,000 per c.mm. with 3 per cent. eosinophils, 2 per cent. monocytes, 73 per cent. polymorphs, and blood uric acid 2·5 mg. per 100 c.cm. During the active phase the erythrocyte sedimentation rate was 30 mm. in one hour (Westergren) and blood uric acid 3·4 mg. per 100 c.cm. A large gall stone was demonstrated by radiography and removal was recommended.

During November 1941 the diary records daily involvement of one or two joints, fingers, wrist, or forearm, with swelling and pain, often unilateral or alternating, lasting two or three days and then remitting, only to involve fresh joints: para-articular puffy tender swellings over the back of the hand, the size of a brazil nut, were noted together with further shotty nodules along the shaft of the ulna and in the pads of the digits. There was also noted on one occasion tenderness and contraction of the palmar fascia producing a transient contracture of the right middle and ring fingers, as had been seen previously.

Consultant VIII (Medicine) was seen in January 1942.

"Has an attack now, began two days ago. Now has a diffuse though patchy oedema scattered over hands, wrists, forearms. Areas are red, taut, not tender. Joints free. Also periosteal nodes, of which there are now two on ulna. They come quickly but go very slowly. . . . Both legs are now swollen with oedema that will come and go in twenty-four hours. No evidence of food allergy."

Because of radiological involvement the right antrum was operated on and showed some muco-pus growing staphylococcus albus. No finger swellings were seen until three weeks later, the day before discharge. As a *Strep. faecalis* vaccine showed delayed positive skin reaction a course of injections was given but with no result. Transitory two-day swellings continued, affecting both hands, varying fingers, left forearm, both elbows. Atophan produced no improvement. Radiological examination of elbows, knees, showed no abnormal bony change. On June 16, right index finger and left middle finger were swollen and the right olecranon bursa became swollen and painful. Fluid from this bursa showed pus cells and *Staphylococcus aureus*. Radiograph of chest showed silicosis. Blood count (July 2) 100 per cent. Hb. White cell count 6,700 per c.mm. of blood, 61 per cent. polymorphs, 2 per cent. eosinophils, monocytes 6 per cent., lymphocytes 31 per cent. Erythrocyte sedimentation rate (Wintrobe) 16 mm. in one hour. Blood uric acid 3·6 mg. per 100 c.cm."

Consultant IX (Thyroid Surgeon) thought that the oedema of the ankles was due to right-sided cardiac insufficiency associated with silicosis and emphysema. On Sept. 14, 1942, he was seen in conjunction with Consultant X (Rare Diseases) who thought it "belonged to the angioneurotic oedema, Raynaud group. The swelling of the hand which had come up quite quickly today showed a large central swelling, blanched, and surrounded by another area almost cyanotically red. The bony prominences disappear like the soft swellings but take longer: the most recent one is over the head of the fibula. These attacks are associated with cold weather. Final opinion, angioneurotic oedema with intermittent hydrarthrosis." (The case has since been briefly recorded by Dr. Parkes Weber (1946) in a discussion of palindromic rheumatism.) Therapeutic suggestions were autohaemotherapy, shock therapy, penicillin, adrenaline, atophan, "opondon" and "testoviron" and pituitary extract. The latter five preparations were tried without improvement.

Recent History obtained from the Patient.—During 1942 he had about fifty attacks, each lasting on the average two or three days, and was never really clear from the condition. Only in the past year had the wrists been affected. The ankles had shown pitting only for the six months before entry to hospital, at which time there were four varieties of lesion complained of: (1) tautness and swelling of the proximal phalangeal joints of the hands and feet with spindling, (2) small intracutaneous lumps mainly in the pads of the fingers and thumbs; these were tender and painful, came up in two days, and lasted for one month or longer, (3) nodules over the olecranon lasting two or three months and sometimes longer; nodules over the hip had been there since October 1942. These larger nodules over bony prominences had been permanently present only for the past year. He had also had (4) some diffuse swelling over the wrist joint and carpus. It was only during the year before entry that the fingers had remained swollen between attacks.

Examination on Feb. 12, 1943.—The pupils were examined and the fundi found to be normal; there was no iritis. Throat and ears were normal. The venous pressure in the neck was not increased. There was emphysema. The heart sounds were faint and regular, with no added sounds. All reflexes were present and normal. Blood pressure was 130/85 mm. Hg. There was a soft mass on the right hypochondriac region of the abdomen (? gall-bladder). The testicles were normal. The glands in the right axilla were enlarged but not tender; in the left axilla, both groins, and right epitrochlear region, they were palpable but not enlarged.

Nodules were seen (1) subcutaneously over the crests of the left and right ulnae (Fig. 1a), over the bony portion of the right hip (greater trochanter), fixed to periosteum, and over the fibula head on the left side. (2) Small nodules were palpable in the top of the finger pads (Fig. 1b). Two of these were present on each of the thumbs, and one had just subsided at the base of one of the fingers on the palmar aspect. They were not very tender.

Joints.—There was free movement of all joints (except an old injury affecting the metacarpo-carpal joint of the right thumb). There was some swelling with tautness and shiny atrophy of the skin (a slight cyanotic appearance also) over the proximal interphalangeal joints of the left second, third, and fifth, and the right hand fifth fingers (Fig. 1b). Two days after the first examination there was some slight swelling noticed over the carpus and wrist on the back of the left hand. The ankles showed pitting oedema. There was some swelling of the phalangeal joints of several toes. The knees, elbows, shoulders, and hips were normal.

Investigations.—The temperature was normal throughout the patient's stay in hospital. The pulse was about 70 per minute.

Urine.—The specific gravity was 10,12-10,16. The urine was acid, with no albumin, sugar, or blood.

Blood Chemistry.—Uric acid was 2·9 mg. per 100 c.cm. of blood during an attack and 2·8 mg. later. Cholesterol was 198 and 174 mg. per 100 c.cm., serum calcium 12 and 10·9 mg., phosphate 3·9 mg., alkaline phosphatase 11 K.A. units, plasma proteins 5·1 g. per 100 c.cm. (albumin, 2·7 g., globulin 2·2 g., fibrin 0·2 g., and the albumin globulin ratio 1·2).

Sedimentation Rate.—This was 9 mm. in one hour (Westergren) in duplicate, and later 15 mm. in one

hour in duplicate. Plasma protein was later 6·7 g. per 100 c.cm.

Heart.—The electrocardiogram showed a right axis shift, P.R. interval 0·24 seconds, ST_2 and $_3$ elevated.

Blood Count.—Haemoglobin was 13·4 g. per cent., the red cells 4·6 million, and the white cells 5,000 per c.mm. of blood (51 per cent. polymorphs, 47 per cent. lymphocytes, 2 per cent. monocytes, no eosinophils).

Radiological Investigation showed, in the feet, some lipping and a small "cystic" area of rarefaction on the medial side of the right first metatarsal head (Fig. 2). The fifth right metatarsal head showed decalcification, loss of the subchondral boundary line, and considerable irregularity of the articular surface. The most remarkable feature of the hands (Fig. 3) was decalcification of the juxta-articular cortex of the left third and fifth proximal phalangeal heads on their radial sides; where the articular surface abuts on this area, slight erosion was seen, with small subchondral areas of rarefaction. Similar subchondral translucent areas were seen in the head of the second left proximal phalanx. In the right hand the fifth proximal phalangeal head showed similar rarefaction and loss of the normal subchondral boundary line; three months later it showed further marked loss of definition and small cystic areas. It will be noticed that these joints are those which were permanently swollen clinically (Fig. 1b). These changes were observed before biopsy was undertaken: they were not visible in radiographs made one year before (April 1942) and therefore coincide with the onset of permanent swelling.

Biopsy was performed on the subcutaneous nodules on the olecranon processes of both sides, on the bone lesion and joint of the third left proximal phalanx, and on one of the small left thumb-pad nodules. The appearance of the olecranon nodules was grossly that of a rheumatoid nodule. When the thumb-pad nodule was incised, a small amount of pus escaped. When incision was made over the bone cyst just proximal to the proximal interphalangeal joint, a small cyst was seen lying on top of the periosteum with its neck towards the joint cavity. This was removed; it was difficult to be certain whether it communicated with the joint. On the periosteum being incised with a gouge, a small gush of pus was noticed from which culture and smears were taken (as also from the thumb-pad node). Smears from both lesions showed mainly monocytes with a blue cytoplasm containing many small vacuoles and sometimes ingested polymorphs. There were also 20 per cent. polymorphs, some of them degenerate, some containing similar small vacuoles. The cultures from both lesions were sterile (blood agar and 5 per cent. serum broth, anaerobic and carbon dioxide-enriched aerobic culture).

Microscopic Examination showed the nodule from the right elbow to consist of old whorled fibrous tissue in which were embedded many small vessels, some of them surrounded by a few lymphocytes and monocytes (non-specific change). The nodule from the left elbow (Fig. 4) consisted of a series of necrotic cavities, some filled with blue-staining debris, some with dense swollen collagen fibres, some with recent fibrin strands. These centres were surrounded by a thick palisade layer of fibroblasts, containing many lymphocytes, monocytes, plasma cells, and polymorphs. The structure was a typical nodule of rheumatoid arthritis. In the tissue from the terminal digital pad of the thumb immediately beneath the epidermis was a structure closely resembling a rheumatoid "necrobiotic" nodule (Fig. 5), but rather more "biotic" than "necrotic". The central area of acute necrosis contained less collagen, but many degenerate cells, many of a monocyte nature, and some fibrin. Some eosinophils were seen in one portion. The superficial portion contained peculiar histiocyte nests, composed of the same cells as took parts in the palisade, but without central necrosis, judged by serial sections and at an earlier stage judged by the finer reticulum network.

The cyst from the third proximal finger showed synovial membrane with marked proliferation and inflammatory changes; at one place strongly eosinophil granules were seen in a small cell nest surrounded by giant cells (Fig. 6); these did not appear to be derived from eosinophil leucocytes, and were possibly derived from collagen degeneration: strips of cartilage were embedded in the granulation tissue.

The bone lesion showed some osteoclastic resorption of spicules and foamy fibrous tissue with a cyst (Fig. 7) containing monocytes similar to those found in the pus smear (Fig. 8).

The following possibilities were considered: palindromic rheumatism (Hench), rheumatoid arthritis, intermittent hydrarthrosis, sarcoidosis, gout, angio-neural arthrosis (Solis-Cohen), and allergic rheumatism (Kahlmeter). The occurrence of bony change, the residual spindling, and the results of biopsy favoured the diagnosis of rheumatoid arthritis, although the very acute character of the lesions and the long recurring course without any serious articular damage argued an atypical case. The early history closely resembled that of palindromic rheumatism, but the low cholesterol was against this diagnosis. The other five possibilities discussed had little to recommend them. There was no heart failure judged by jugular pressure rise, but the presence of silicosis and emphysema warranted caution.

The essential lesion was a recurrent focal necrosis with inflammatory reaction of a rheumatoid nature affecting the tissues in the neighbourhood of joints, bursae, tendon sheaths, and finger pads.

Diagnosis.—A diagnosis was made of rheumatoid arthritis, silicosis, emphysema, and cholelithiasis.

Treatment.—The treatment prescribed was: a full, high-vitamin diet, assisted active exercises following light massage, and no drugs except sodium salicylate, bicarbonate, and ascorbic acid. Deep *x*-ray therapy was also suggested.

After the patient's discharge from hospital (Feb. 18, 1943), painful swellings developed over the heads of the second and third right metatarsals and fifth left metatarsal bones after walking for the first time. Consultant XI (Radiology) reviewing the *x*-ray plates, was "not convinced that there was anything to justify the diagnosis of rheumatoid or even infective arthritis other than

possibly the joint swelling ", and he " considered that the apparent loss of cartilage was an artefact ". (Flakes of cartilage undergoing dissolution were seen lying in the synovial membrane from the excised cysts, as frequently seen in synovial membrane of rheumatoid arthritis. These cysts were undoubtedly herniations from a joint which had been used while still containing increased fluid.) Consultants XII and XIII (Pathology) saw the sections of synovial membrane and suggested that the condition might be sporotrichosis, as the patient had been in a South African mine in 1927 where an outbreak occurred. As iodine offers a cure for sporotrichosis, this suggestion was received enthusiastically, despite the completely atypical clinical story, and in our own opinion the likeness of the nodules to those of rheumatoid arthritis. He was admitted for the second time (April 7, 1943), and a further biopsy of the fifth proximal interphalangeal joint (Fig. 9) merely confirmed the previous findings: another pathological consultant (XIV) said the nodules were identical with those from cases of rheumatoid arthritis. Fresh tissue and swabs of the pus from the synovial membrane and from the finger were examined and were cultured on Sabouraud and numerous other media as well as being injected into rats by ourselves and by Dr. Duncan (Mycology). All these investigations were sterile.

While the patient was in hospital his condition was much as before. He was afebrile, and the sedimentation rate was 12 mm. in one hour (Westergren). He had a troublesome attack of bronchitis which had subsided before the second admission. The electrocardiogram showed, as before, prolonged P.R. interval (0·26 sec.), elevated ST interval in leads II and III, and a right axis shift. A radiograph of the chest showed the left ventricle to be slightly enlarged, the transverse diameter being 5½ inches. There was some slight prominence of the pulmonary artery. Emphysema and small silicotic nodules were seen throughout the lung with some *increased hilar* shadowing. Further investigations were as follows: Brucella agglutinations negative. G.C. fixation test negative. Wassermann and Kahn tests negative. Blood urea 54 mg. per 100 c.cm. of blood; cholesterol 187 and 197 mg.; plasma phosphates 3·6 mg.; plasma protein 7·0 g.; plasma phosphatase 12 K.A. units per 100 c.cm. Hb. 11·0 g. per cent. He was discharged from hospital three days after entry (April 7, 1943) for a therapeutic test with iodine. For one week on placebo he was normal, but he developed pyrexia and general discomfort twelve hours after starting iodine.

His condition improved after stopping the iodine, but later (June 20) there was " no real improvement in the details of his condition. *Hands*: The nodules in his fingers have been very troublesome up to the last few days, but for the moment have somewhat subsided. The joints are still swollen, both the two that were biopsied (proximal interphalangeal joint of left third and right fifth fingers) and the proximal interphalangeal of the fourth right and the terminal joint of the first left finger. Wrists have been swollen, now better. There have been two slight bouts of oedema of dorsum of both hands, that on the left hand still persisting slightly. *Forearms*: Painful nodule middle of shaft left ulna. *Elbows*: left has been swollen and painful, now better. Right has a very painful swelling over ulna. *Shoulders*: Right shoulder has been and still is very painful with a swelling approximately over the acromium process. Also painful over region of insertion of deltoid. Such movements as getting hand into pocket and raising the arm are difficult and painful, and so is lying on that side. Left shoulder not painful except when he has been lying on it. *Feet*: dorsum right foot swollen and movement of big toe joint painful. Walking not good. Oedema of ankles much improved. Still very limited in choice of shoes. *Knees*: very painful, ' set ' after they have been kept in one position and are difficult to get moving again—improve upon movement. Swellings over medial and lateral condyles of femur and over left patella. He is still taking salicylates and vitamin C, and still having massage which, I think, has definitely helped his feet but does not seem to ease his shoulder or his hands much."

Consultant XV (Medicine) suggested lipoidosis. Arrangements were made for the patient to go for a course of spa treatment in addition to diet, massage, exercises, salicylates, and phenobarbitone.

After the patient had had a course of spa treatment, Consultant XVI (Rheumatism) was of the impression that the condition was " a fibrositis of the periarticular type ".

The treatment seemed to do him little good. In October 1943, after radiography of sinuses and examination of post-nasal swab, Consultant XVII decided that infected ethmoidal antra were the fount of infection, as a pure and plentiful growth of *Staphylococcus albus* had been reported. Short-wave therapy was begun in November 1943, and continued with occasional intermissions till the autumn of 1944, but produced no improvement. Then protein shock therapy with *E. coli* was tried, but produced no improvement. Small doses of his own serum given subcutaneously did no good. Since February 1945 he had no particular treatment except " Atophan ", when his feet seemed particularly " gouty ".

One week before the third admission to the Postgraduate Medical School (July 6, 1945) the patient developed dysphagia, tenderness, and swelling beneath the left sternomastoid with fever up to 103° F., and paronychia (July 2) treated with sulphapyridine. Examination showed no throat infection clinically or bacteriologically. There was tenderness and swelling deep to the left sternomastoid. Haemoglobin was 11·4 g. per cent.; white cells numbered 17,000 per c.mm., 75 per cent. polymorphs, blood urea 42 mg. per 100 c.cm., P.R. interval 0·36 seconds. A radiograph showed thickening of the right antrum and backward deviation of trachea in the region of the thyroid. The urine was normal.

Fever, swelling, and leucocytosis disappeared with penicillin, and the sedimentation rate returned to 6 mm. in one hour (Westergren). The cystic mass deep to the sternomastoid, which became palpable with subsidence of the inflammation, itself subsided and the patient was discharged. Six weeks later (Aug. 14, 1945), the lump was scarcely palpable. There was ankle oedema;

the big toe (MTP) joints and the second right (PIP) toe joints were almost fixed. The right forefinger was swollen and tender, the skin shiny and pallid, and the swelling had only come up in the last day or so. There was a healing nodule over the radial side base of the second right MCP shaft (one week old), and small nodules (with central brown depressed area), in the pads of both thumbs and beneath the metatarsal head of the third left toe. There were large subcutaneous nodules on the right ulna (as before), and crops of smaller ones over the elbow region and right knee. Blood uric acid was 3·9 mg. per 100 c.cm. of blood, cholesterol 211 mg. per 100 c.cm., total protein 7·9 g. per 100 c.cm.

Radiological re-examination showed progression of the lesion in the right first metatarsal head, which now showed irregular erosion and complete loss of joint space. The fifth right metatarsal head had recalcified considerably, but showed residual irregularity. The eft first terminal joint now showed a coarse system of translucent spaces involving both proximal and distal phalanges; there was erosion of bone from the margins of the joint affecting both distal and proximal phalanges with destruction of cartilage and complete loss of joint space (Fig. 2). In the hands, destruction of the fifth right proximal interphalangeal joint had occurred. Considerable restitution had occurred in the fifth left PIP joint, which showed only a small area of subcortical rarefaction. The third left PIP joint, however,. had progressed to complete loss of joint space and destruction of cartilage with erosion of the articular surface and the formation of patchy cystic areas of translucency. The medullary cavity of the proximal phalanx also showed complete resorption of the normal coarse cancellous bone. The second left proximal phalangeal head showed no progression.

On Aug. 20, 1945, an acute episode of collapse and pain occurred. He was seen by Consultants XVII (Cardiology) and XV. An electrocardiogram next day showed signs compatible with posterior myocardial infarct. Six days later pain and dyspnoea were less, the temperature was 100·4° F., the pulse 42 per minute, and the blood pressure over 100 mm. Hg. Consultant XVIII (Cardiology) found (Aug. 31, 1945) the blood pressure to be 95/65 mm. Hg., the pulse 64 per minute and regular, and the heart enlarged with soft apical systolic murmur, scattered rales, and impaired percussion note at the right base: the liver was easily palpable, but not tender. A further electrocardiogram confirmed the diagnosis of infarct ($ST_{2,3}$ elevation with $T_{2,3}$ inversion and Q waves. No change in P.R. interval (0·36 seconds)). By Nov. 29, 1945, the patient was oedematous with signs of failure despite mersalyl and digoxin. Rheumatoid nodules on both trochanters and both elbows were continually breaking down. The patient died at home on Dec. 20, 1945. No necropsy was done.

Comment.—It is fortunate that this patient's course was so well documented and that notes were available from so many consultants. (The history, incidentally, illustrates in a way not usually recorded the pilgrimage that chronic illness of an unusual kind in the upper income levels may involve and the variety of diagnoses entertained by distinguished specialists.)

The points that need special emphasis are the transient nature of the joint swellings and of the small intracutaneous nodules of the fingers and toes, and the direct relationship of the latter to pressure, the smaller acute swellings in the region of the tendon sheaths and palmar fascia producing transient finger contraction, and the bursitis. The larger permanent nodules over bony sites differed in no way, histologically or clinically, from those seen in rheumatoid arthritis.

Radiological changes were long delayed and atypical. They were attributed to pressure atrophy of bone and herniation of synovial contents into the bone ends as is so frequent in rheumatoid arthritis, but only rarely confined for so long to the non-articulating joint surface as here. I have seen only one other patient with a similar appearance in the proximal phalanx, thought to have rheumatoid arthritis. In the feet the rarefaction of the first distal phalanx can probably be ascribed to a similar process.

The terminal episode was thought to have been coronary ischaemia leading to infarction and failure. The previously prolonged P.R. interval points in the same direction. Unfortunately, the failure to secure a post-mortem examination makes it impossible to say whether this infarction was due to atherosclerosis and thrombosis, due to arteritis or due to obstruction by granulomatous (nodule) tissue such as has been described rarely in the valve ring region of rheumatoid patients (Bagenstoss and others, 1944). Rheumatoid cases with cardiac nodules (Bennett and others, 1940) usually have very widespread nodule formation.

Case 2

The second case showed the same intracutaneous nodules coming up acutely, due to pressure, and the same transient finger contractions: she was a hospital patient throughout, and radiological changes appearing early facilitated the diagnosis.

M.C., a woman aged 28, was admitted on May 14, 1946, complaining of pain and swelling of joints.

Three years before admission she developed pain and swelling of the proximal interphalangeal joint of the right third finger, spreading to the fingers of both hands, and to the wrists and metatarsal regions. Pain was followed by bluish discoloration of the skin and then by swelling. The condition was migratory but often involved several joints at one time. Two years ago the palms of both hands became bright red and, whenever she did any work involving pressure with the

fingers (such as making pastry or pushing a pram), she developed small painful nodules and blisters at the sites of pressure lasting several weeks.

She married about this time and became pregnant nineteen months before admission; this was accompanied (from the second month until the first week of the puerperium) by complete freedom from pain and swelling of the joints, but the colour of the palms was not affected. At the sixth month her cheeks, normally well coloured, became very red, together with her nose, and these symptoms have persisted since. Despite a history of hypertension during pregnancy, delivery was uneventful, but pain, redness, and swelling returned one week afterwards in the wrists, fingers, knees, feet, ankles, shoulders, and elbows and have become worse since. Periods were normal and bore no relationship to skin colour, joint pain, etc. During the last ten months the elbows have become reddened, painful, and nodular; for the last three weeks she noticed a tender nodule over the sacrum and some pain in the neck. She has marked " jelling " after periods of rest.

The family and previous history were irrelevant; there was no history of sore throat.

Examination showed erythema and telangiectases of the nose and cheeks in a " butterfly " distribution with some slight hyperkeratosis but no horny plugs, and little or no atrophy. The palms were markedly reddened over pressure areas and there were splinter haemorrhages in the nail folds of most fingers. Large nodules were present over both olecranon processes and over the sacrum. The heart was normal; the blood pressure 130/80 mm. Hg. No enlarged spleen and lymph glands were found.

There was slight soft tissue thickening of all proximal interphalangeal joints except that of the right thumb, and swelling of the first, second, and fifth metacarpophalangeal joints of both hands (Fig. 10) of the left wrist joint and of the left knee, which contained a small effusion. The grip was weak.

Radiological Examination.—This showed no abnormality in the chest or sinuses. The hands showed typical rheumatoid changes with general rarefaction and erosions affecting both wrist joints and many metacarpal metatarsal and proximal interphalangeal joints. These progressed until one year later (1947) the following joints were grossly affected: metacarpophalangeal right 1, 2, 3, 4, left 1, 2, 3, 4, 5, proximal interphalangeal right 3, left 3 and 4, metatarso-phalangeal right 1, 2, 3, 5, left 3, and both wrist joints.

Bacteriological Examination.—This showed no abnormal flora in the throat; blood and urine cultures remained sterile. The Wassermann reaction was negative.

Dental Examination.—There was no sepsis or caries and only slight gingivitis; radiographs revealed two retained roots.

Haematological Examination.—The haemoglobin was 14·2 g. per cent. The red cell count was 5·2 million per c.mm. of blood, with anisocytosis, anisochromasia, and polychromasis; the white cell count was 4,000 per c.mm., with 65 per cent. polymorphs. The sedimentation rate (Westergren) was 43 mm. in one hour.

Blood Biochemistry.—Plasma cholesterol was 196 mg. per 100 c.cm. of blood; alkaline phosphatase 11·5 K.A. units; albumin 4·2 g. per 100 c.cm., globulin 3·1 g. (and the same a year later), blood uric acid, 1·4 mg. The urine showed a moderate to small amount of albumin during the first five weeks, disappearing later, but neither pus nor casts.

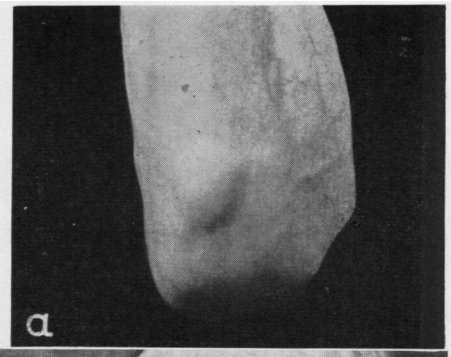
Course.—The day after admission the patient complained of pain in the left shoulder, worse with deep breathing or sitting forward and radiating up the left neck and down the left sternum. Pressure on the chest increased this pain. A pericardial friction rub was heard at all areas, especially at the base, and electrocardiograms showed typical changes. The rub persisted for two weeks and the electrocardiogram changes gradually returned towards normal in five weeks (Fig. 11). A low-grade fever with peaks up to 101° F. persisted during the first two weeks but subsided thereafter together with the pericarditis. Pleuritic pain was noticed a year later but was not associated with a rub, with electrocardiographic, or with *x*-ray abnormalities. Pain consonant with perisplenitis was complained of on several occasions, lasting about three days.

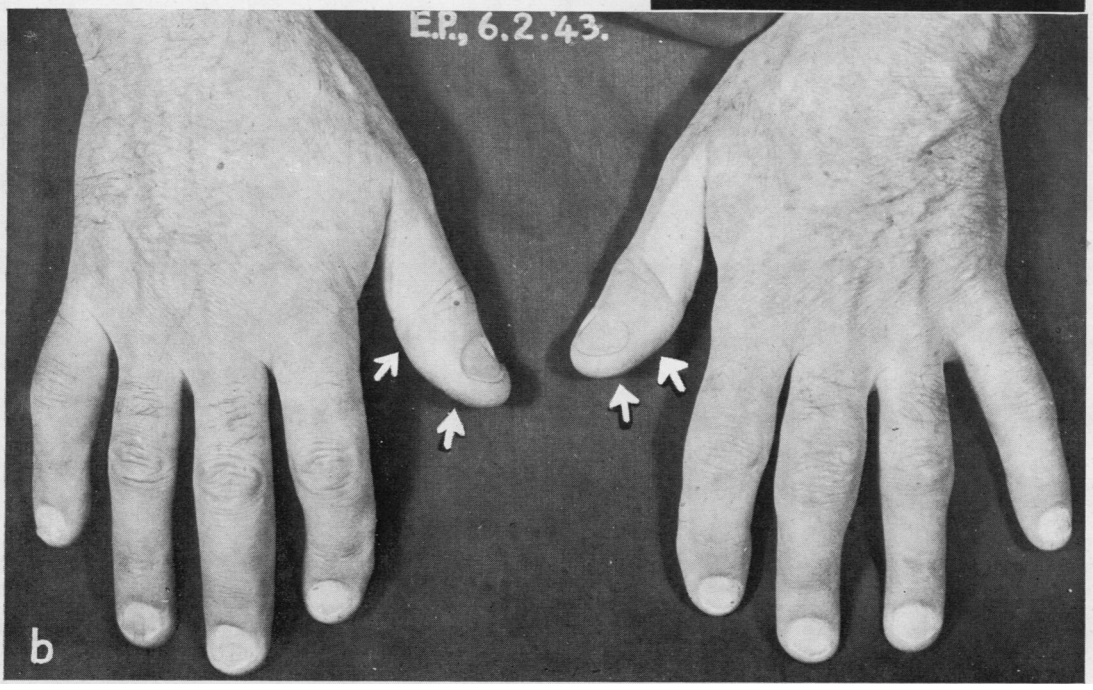
During the next four weeks, while she was under close daily observation in hospital, a remarkable sequence of inflammatory phenomena was observed unaccompanied by any rise in temperature or albuminuria; these phenomena continued without intermission during the following two years* up to the time of writing. They were apparently unaffected by a febrile episode (in August 1946) of cervical adenitis due to tonsillar infection by an undetermined " haemolytic " streptococcus (penicillin-sensitive but not Group A and producing no soluble haemolysin). Rapid cure with penicillin wrought no change in general status; there was no alteration in leucocyte level, from 3-4,000 with 33 per cent. and 53 per cent. polymorphs respectively, and no increase in the already raised blood sedimentation rate.

The most striking of these phenomena were small deep-seated blisters about 2 to 3 mm. in diameter developing mainly in the terminal pads of the fingers but also occurring elsewhere (Fig. 12). They seemed to be initiated by minor traumata; the patient said that the increased incidence in the thumb and index finger at the beginning of the week was related to handling Sunday's hot roast joint. Further, during a period of relative quiescence, a large crop was produced in the left thumb following two attempts to light a cigarette with a new lighter she had been given: within half an hour the thumb became swollen and later developed nodules and deep-seated blisters. We induced one of them within twenty-four hours by firm pressure with a pencil tip. Each blister seemed the end stage of an intracutaneous nodule: it started as a firm, indurated, and palpable swelling about 5 mm. in diameter, paler than the surrounding digital skin, appearing rapidly and gradually disappearing after a few weeks, passing through a stage resembling a small 2 mm. diameter blister in the centre

* The following account is compiled from notes made when the patient was in hospital and at regular out-patient visits, as well as from a daily diary kept by the patient covering a period of three months.

FIG. 1.—Case 1. (a) Left elbow showing subcutaneous nodule. (b) Hands showing swelling of proximal interphalangeal joints (right fifth; left fifth, third, and second), and sites of cutaneous nodules in digital pads of the thumbs (arrows).





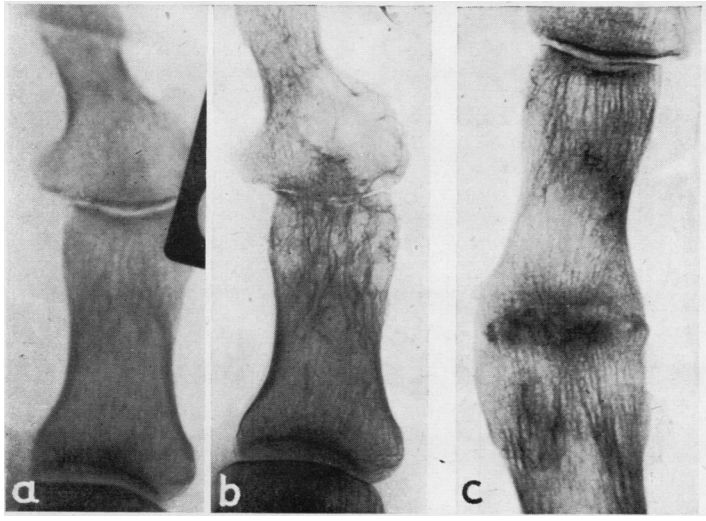
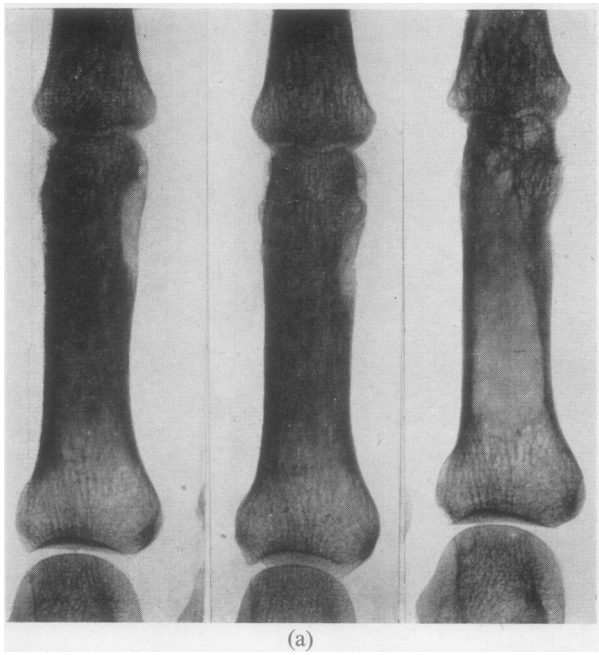
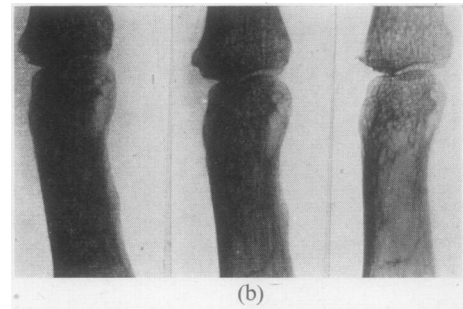


FIG. 2.—Case 1. Radiographs of big toe joints showing development of change between Feb. 8, 1943 (a, right), and July 20, 1945 (b and c, right and left respectively).



(a)



(b)

FIG. 3.—Case 1. Radiographs showing changes in the third (a) and fifth (b) proximal phalangeal heads right hand (compare Fig. 1 (b)). Note progression of lesions from Feb. 8, 1943 (left), to May 15, 1943, and July 20, 1945 (right).

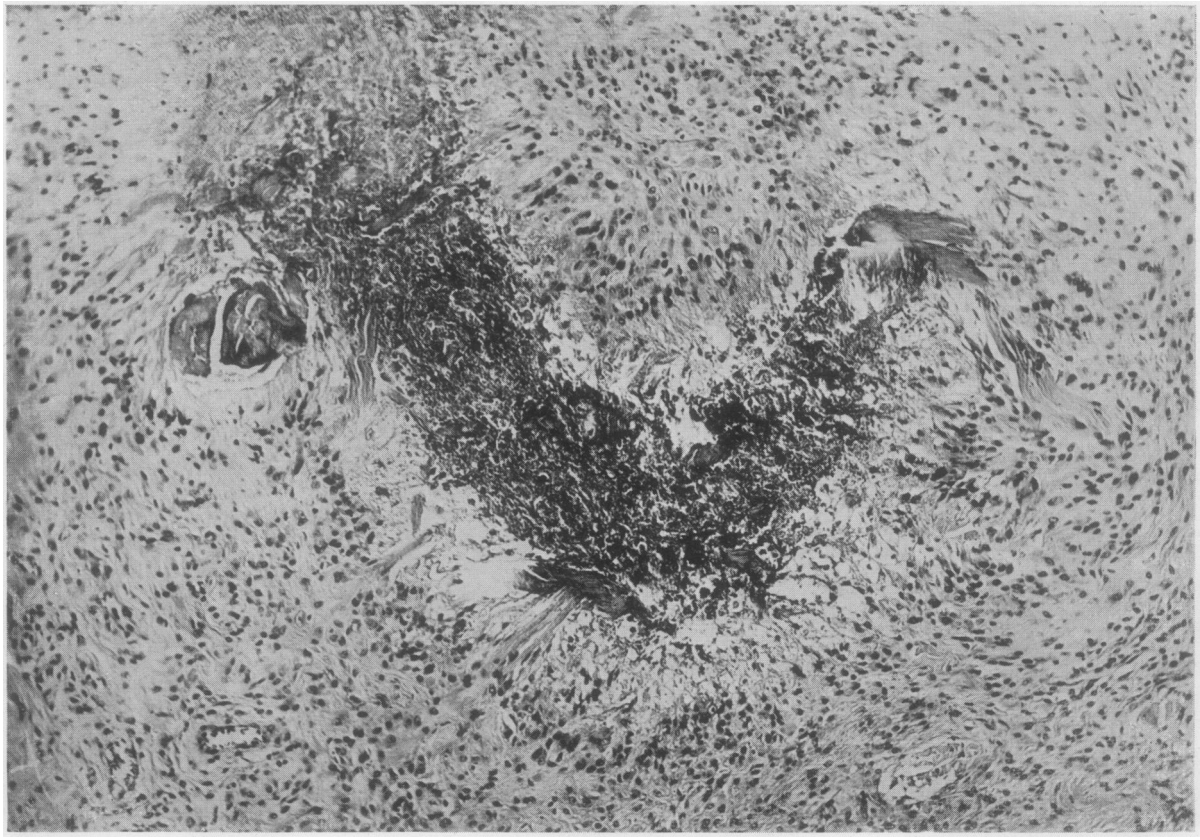


FIG. 4.—Case 1. Subcutaneous nodule from left elbow region (stained haematoxylin and eosin, × 120) showing central necrotic area with altered collagen and surrounding palisade layer undergoing vacuolation centrally.

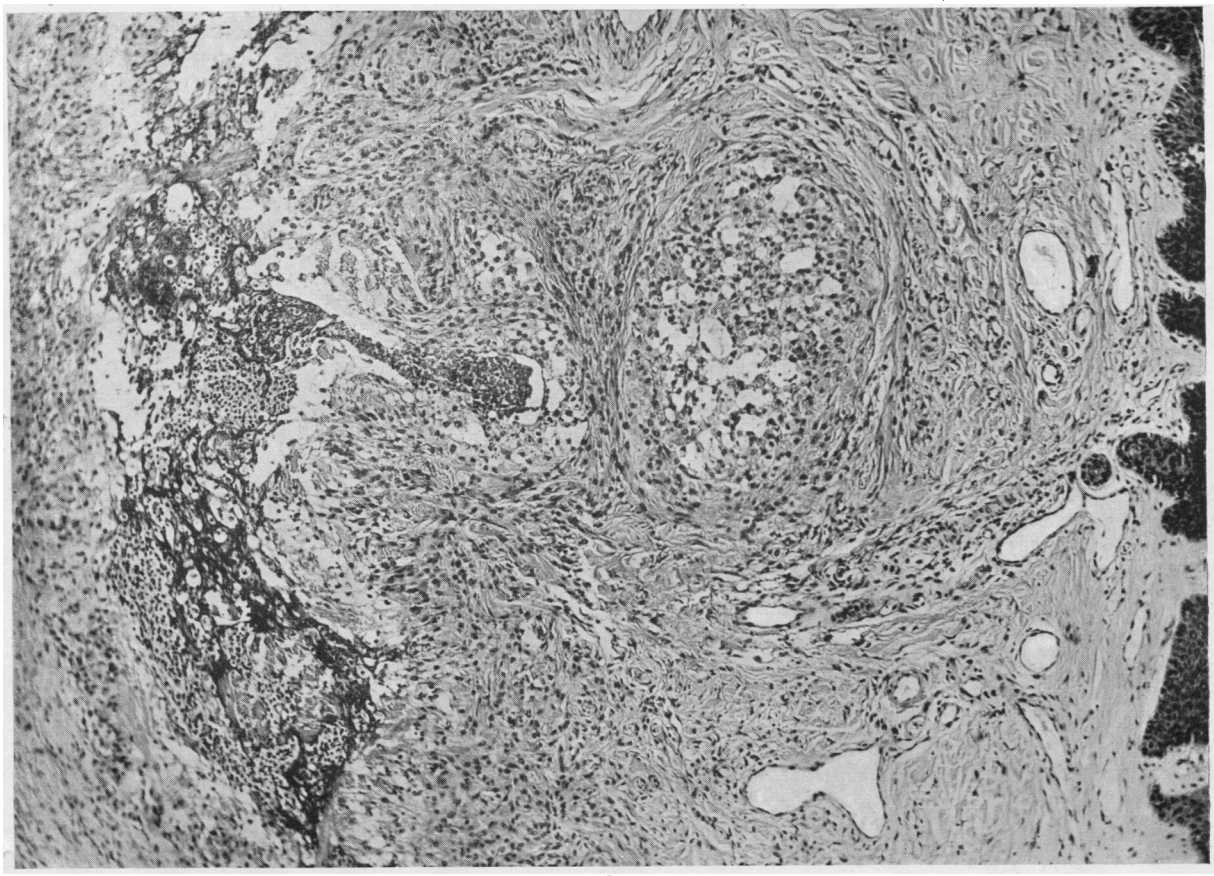


FIG. 5 (above).—Case 1. Cutaneous nodule from thumb pad (stained haematoxylin and eosin, × 90) showing necrotic collagen and fibrinoid material, basophil in character and infiltrated with pyknotic polymorphs, in central necrotic area. This is surrounded by a palisade layer, showing hydropic vacuolation in places. Superficial to this is a histiocyte nest in an earlier stage of development. (Epidermis on the right.)

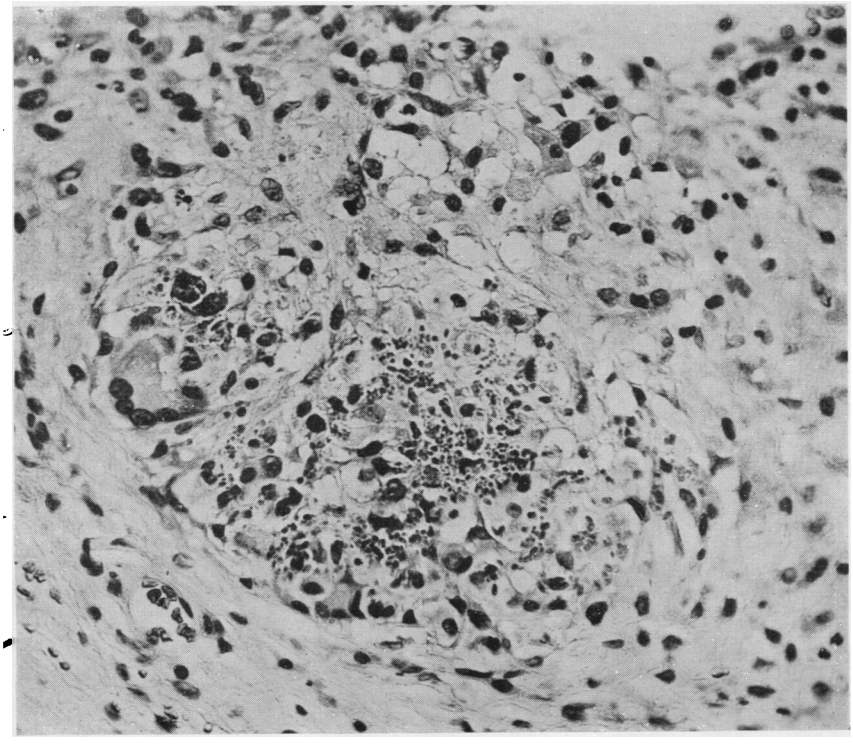


FIG. 6 (left).—Case 1. Synovial membrane from finger cyst (third proximal interphalangeal) (stained haematoxylin and eosin, × 300) showing nest of refractile eosinophil bodies with giant cells of foreign-body type.

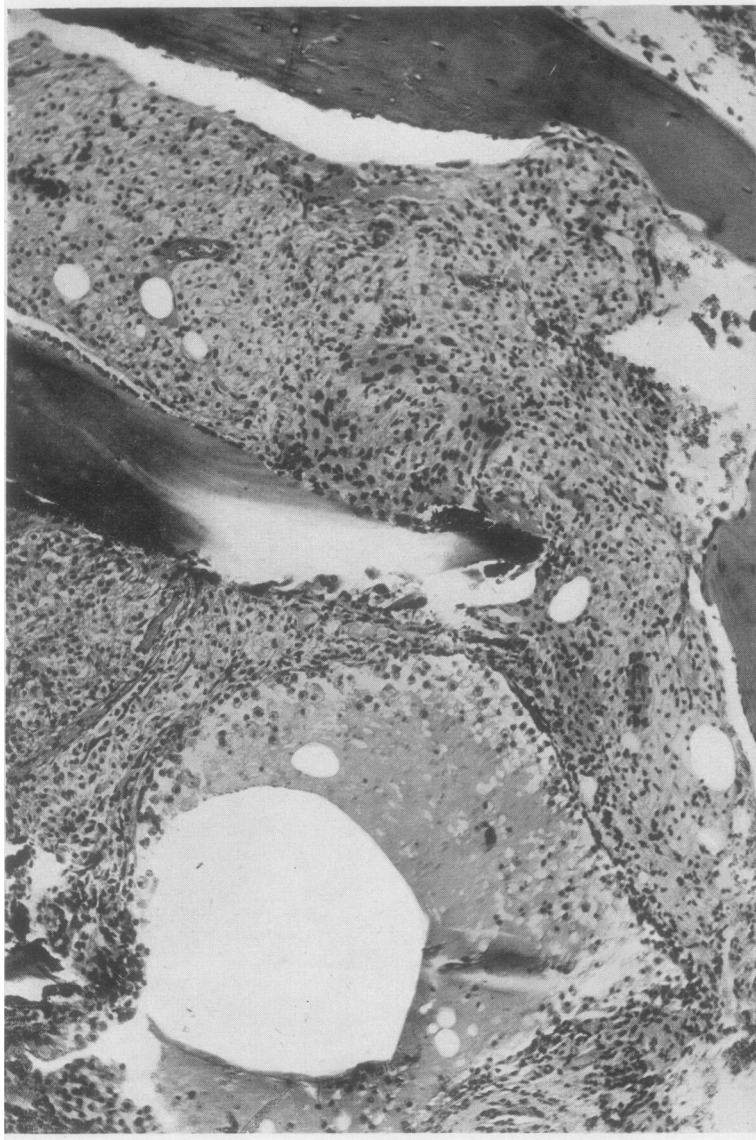


FIG. 7.—Case 1. Bone (stained haematoxylin and eosin, × 115) adjoining third proximal interphalangeal joint showing cyst, replacement of marrow by fibrous tissue, and foam cells with osteoclastic resorption of bone.

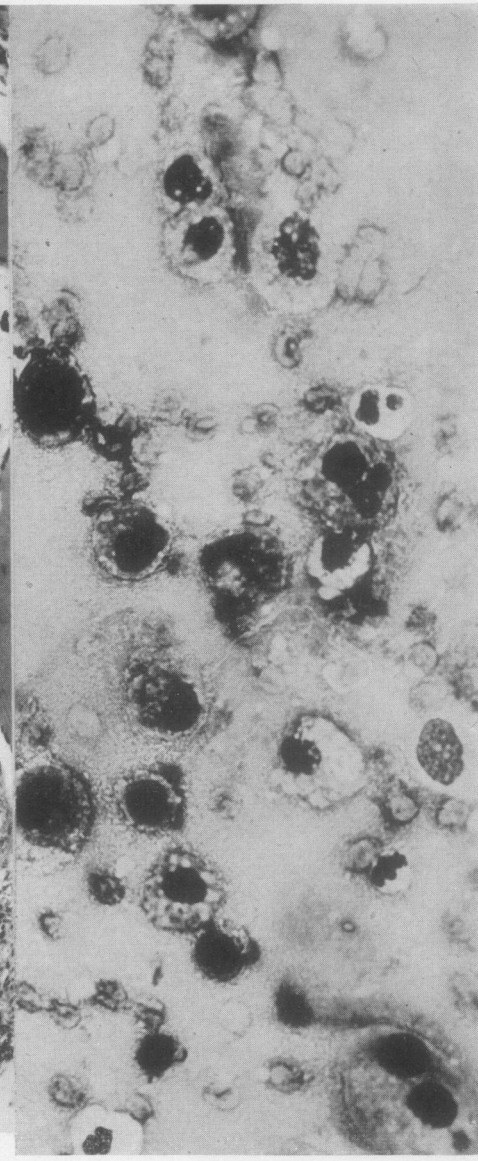


FIG. 8.—Case 1. Exudate (Leishman, × 500) from finger cyst showing macrophages.

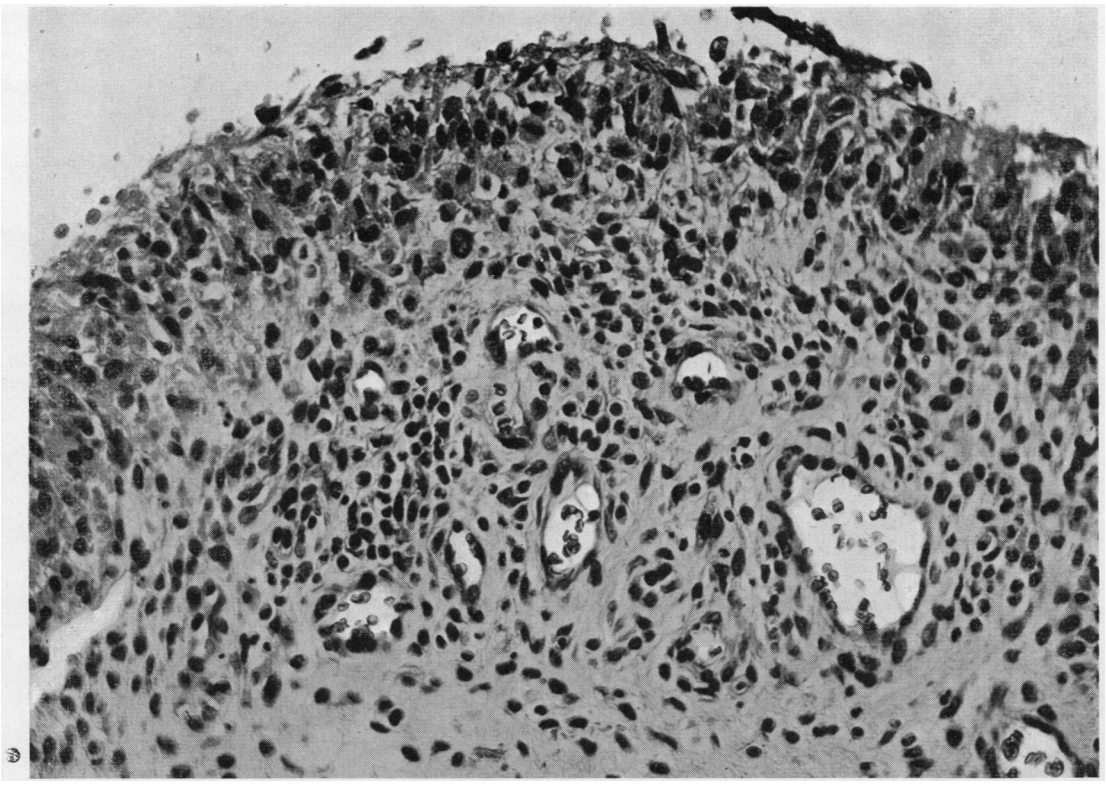


FIG. 9.—Case 1. Synovial membrane (stained haematoxylin and eosin, × 280) from fifth proximal interphalangeal joint showing hypertrophy of lining cells with fibrin exudate and perivascular polymorph infiltration subjacent to that.

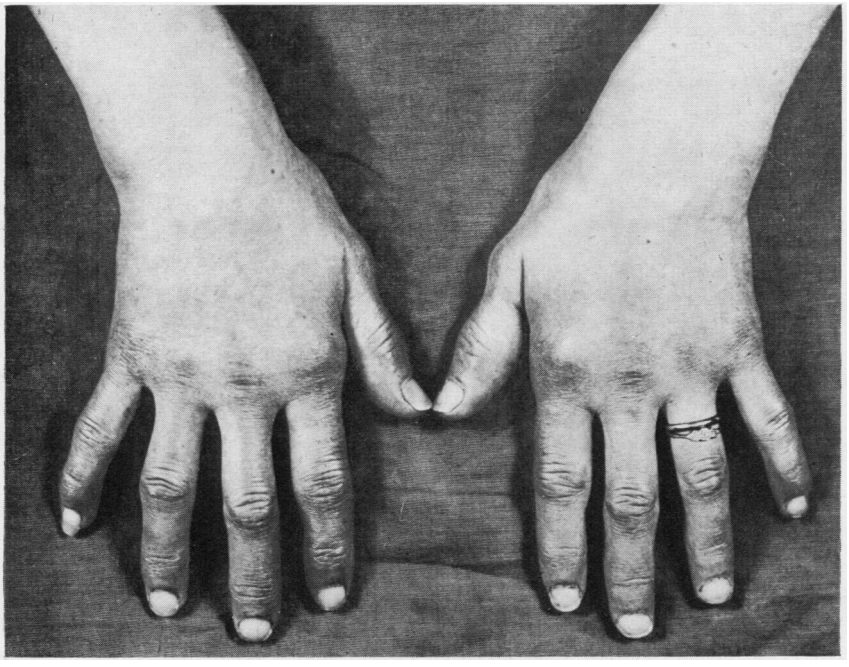


FIG. 10.—Case 2. Dorsal view of hands to show erythema, joint swellings, nail bed thromboses, and cutaneous nodules.

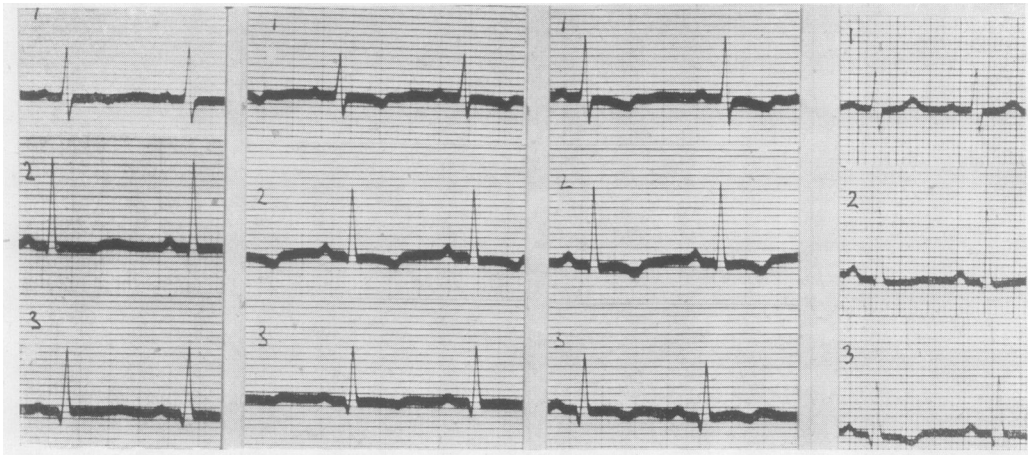


FIG. 11.—Case 2. Electrocardiogram showing pericarditis. The cardiograms were taken, from left to right, on May 17, May 30, and June 8, 1946, and on Feb. 5, 1947.

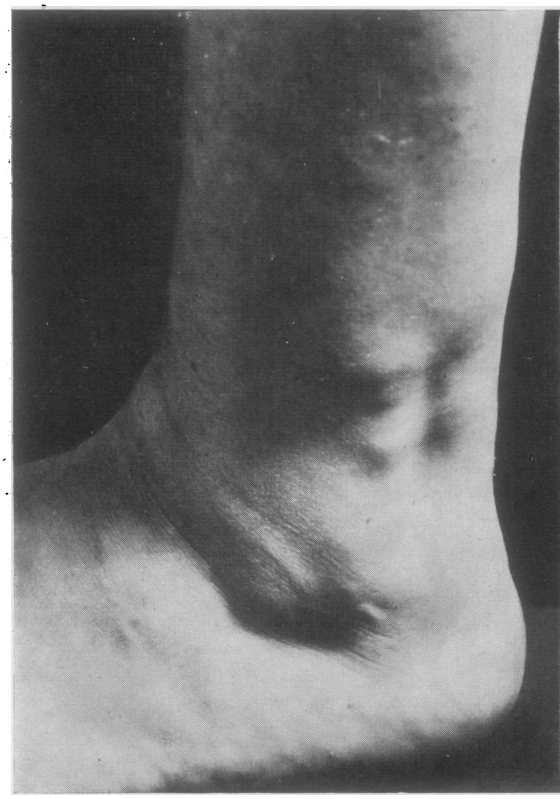


FIG. 13.—Case 2. Subcutaneous nodules over Achilles and peroneal tendons.

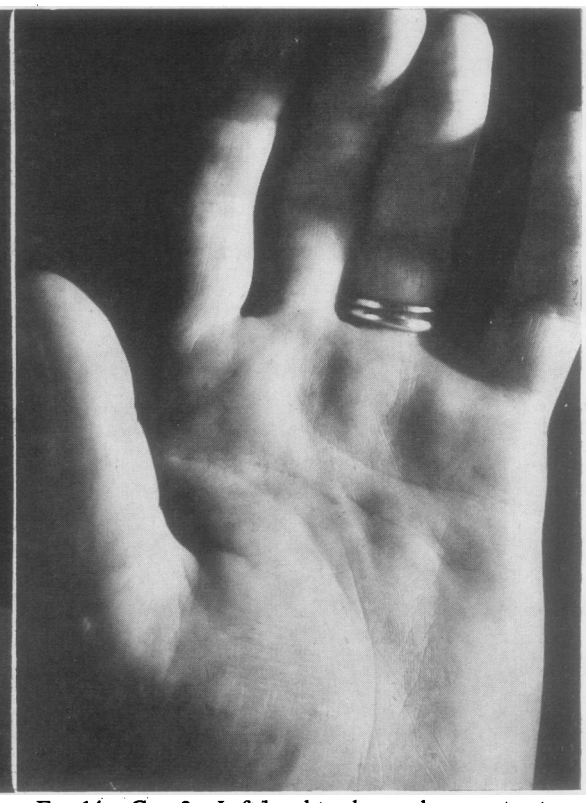


FIG. 14.—Case 2. Left hand to show palmar contracture and flexion of three medial fingers.

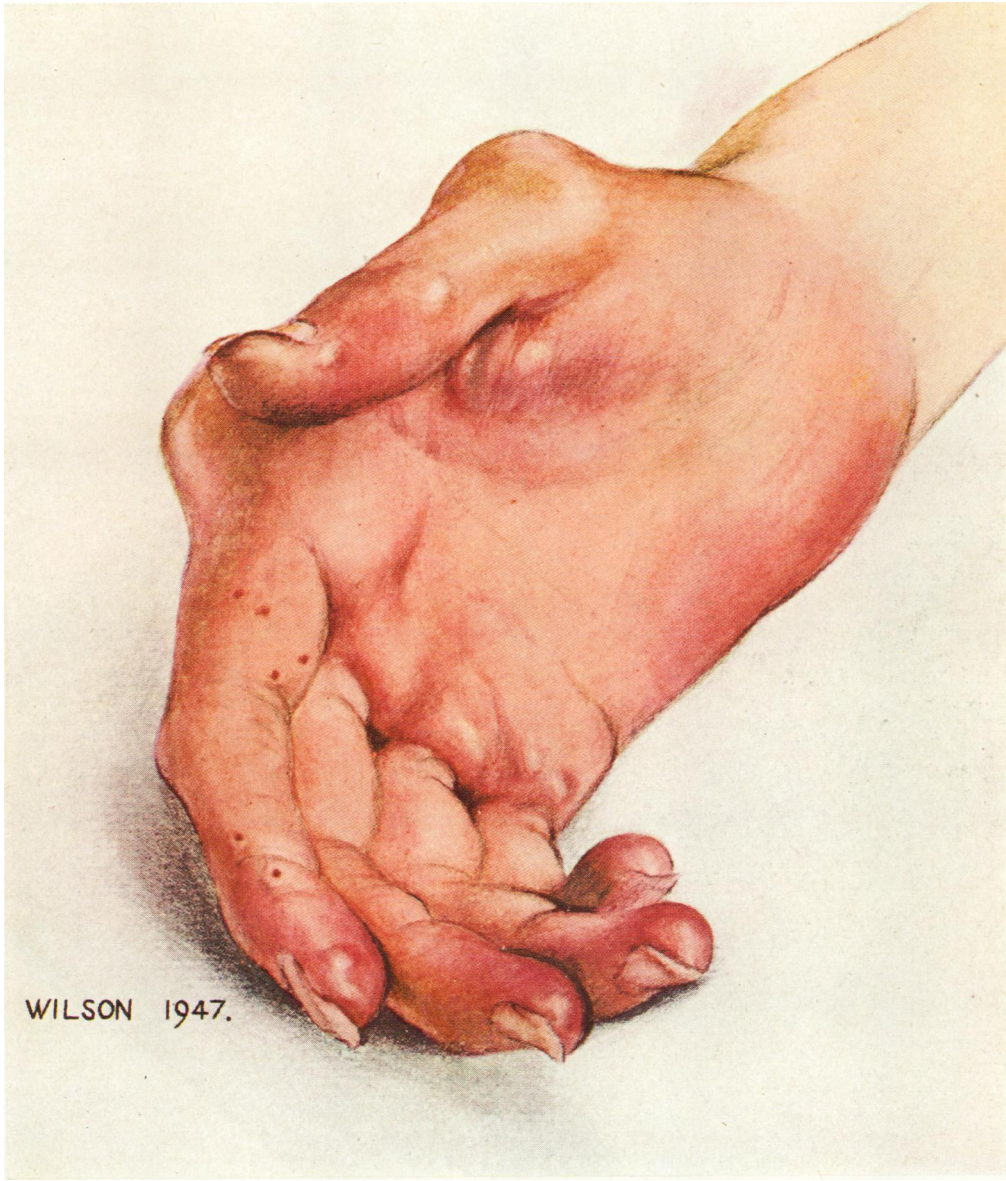


FIG. 12.—Case 2. Painting of right hand to show cutaneous nodules in various stages of development.

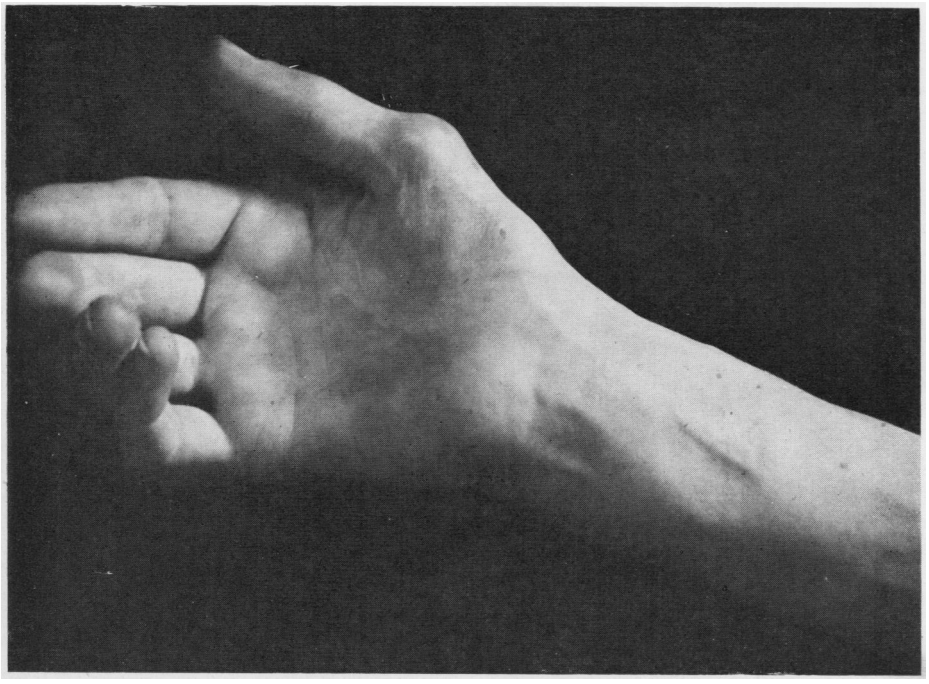


FIG. 15.—Case 2. Para-articular swelling over flexor muscle tendons with pitting oedema.

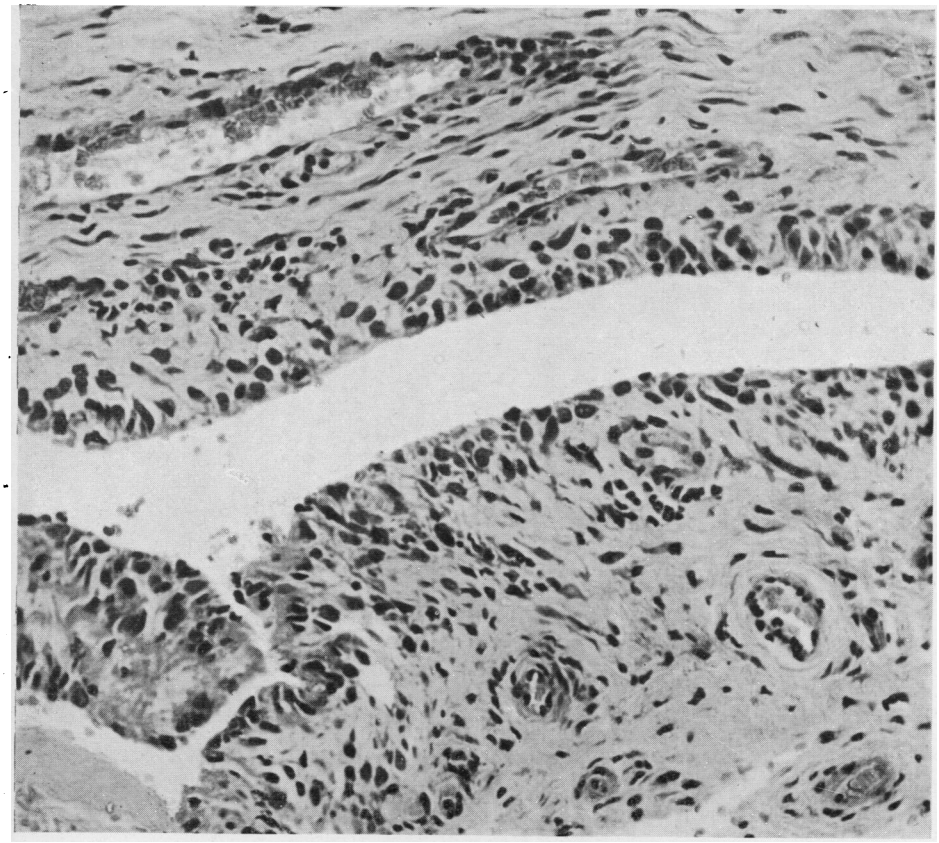


FIG. 16.—Case 2. Synovial membrane (stained haematoxylin and eosin, × 280) showing perivascular polymorph infiltration beneath hypertrophied lining membrane.

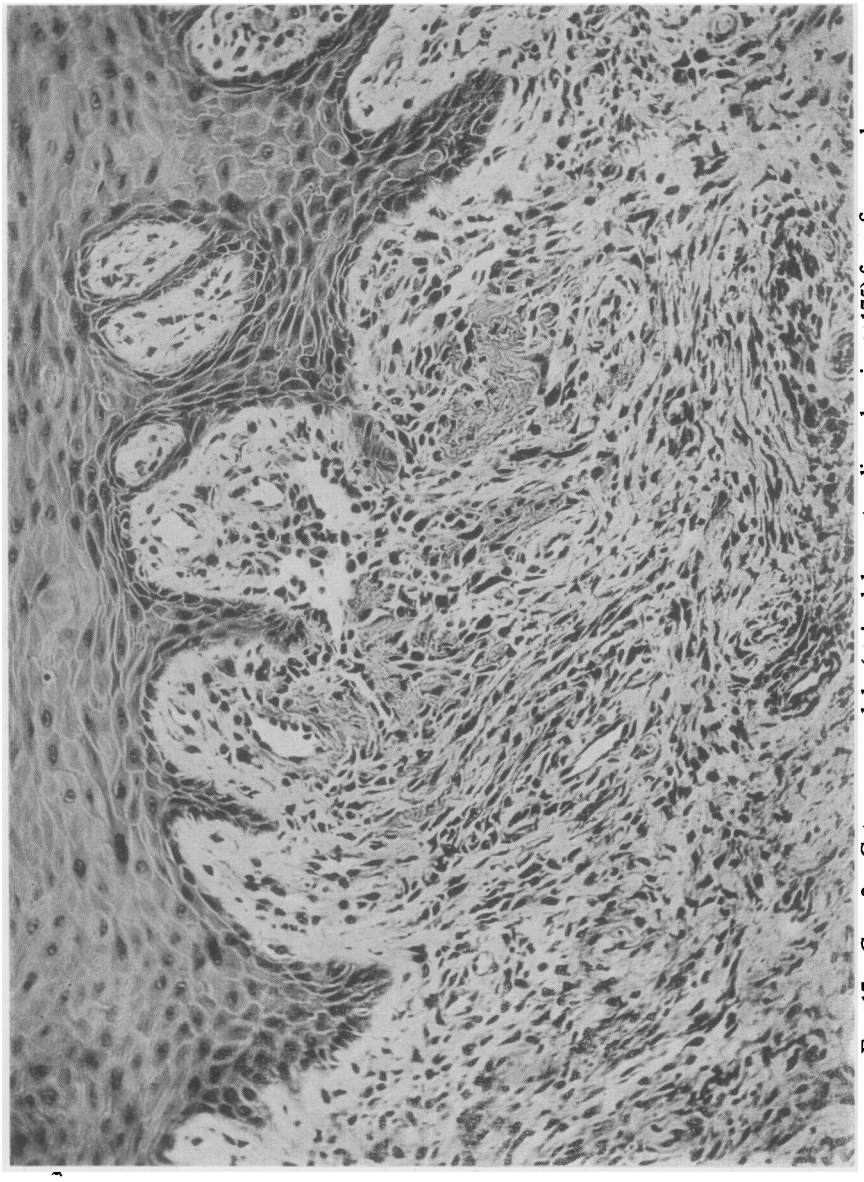


FIG. 17.—Case 2. Cutaneous nodule (stained haematoxylin and eosin, ×175) from finger pad.

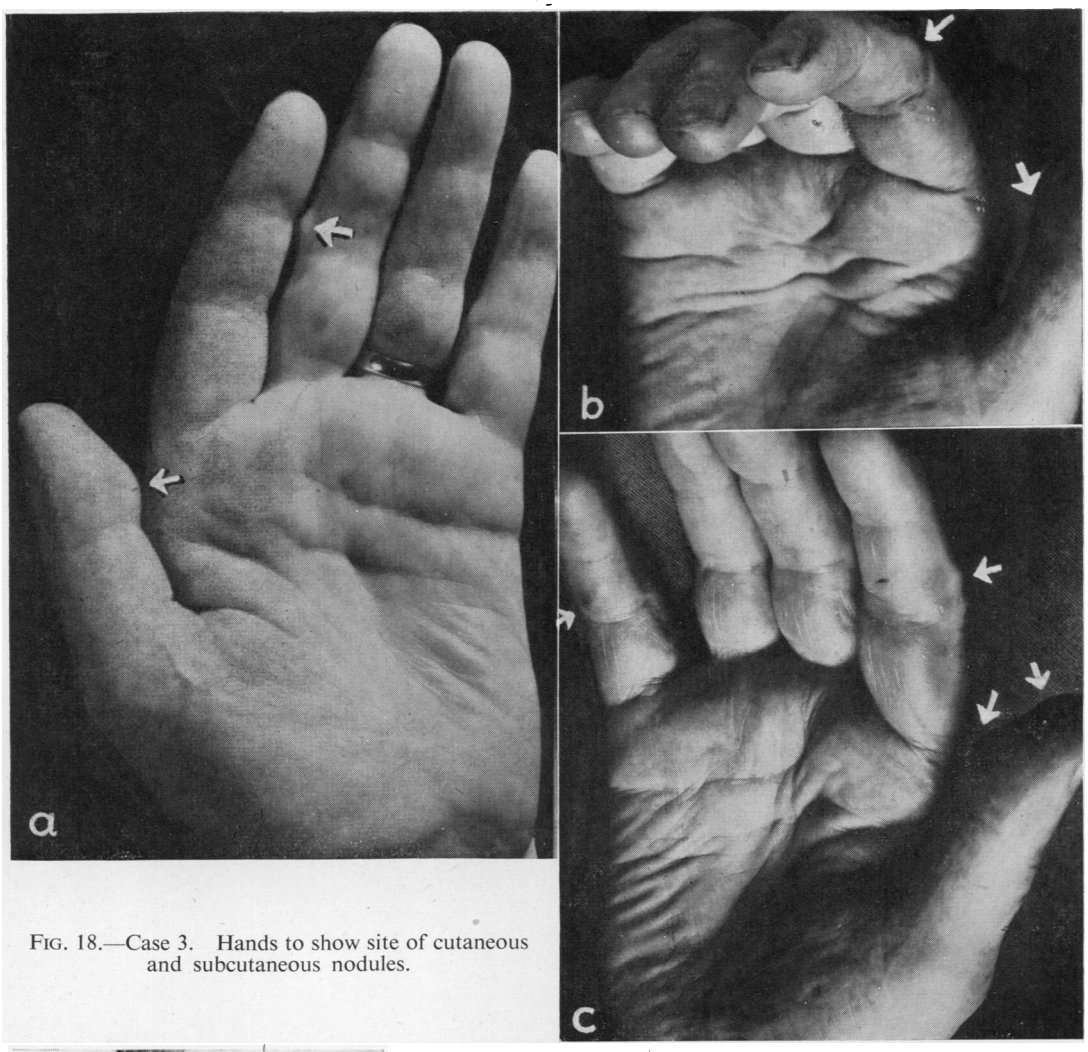


FIG. 18.—Case 3. Hands to show site of cutaneous and subcutaneous nodules.

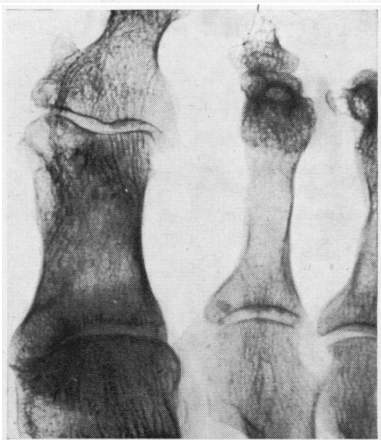


FIG. 19.—Case 3. Radiograph of big toe: note "cyst" formation and similarity to changes in Case 1.

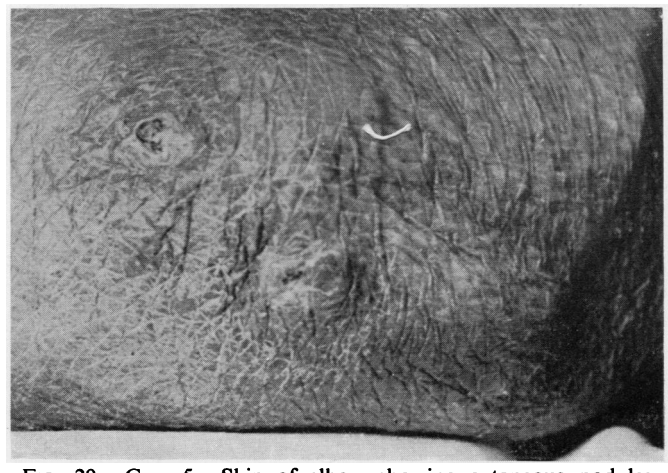


FIG. 20.—Case 5. Skin of elbow showing cutaneous nodules.

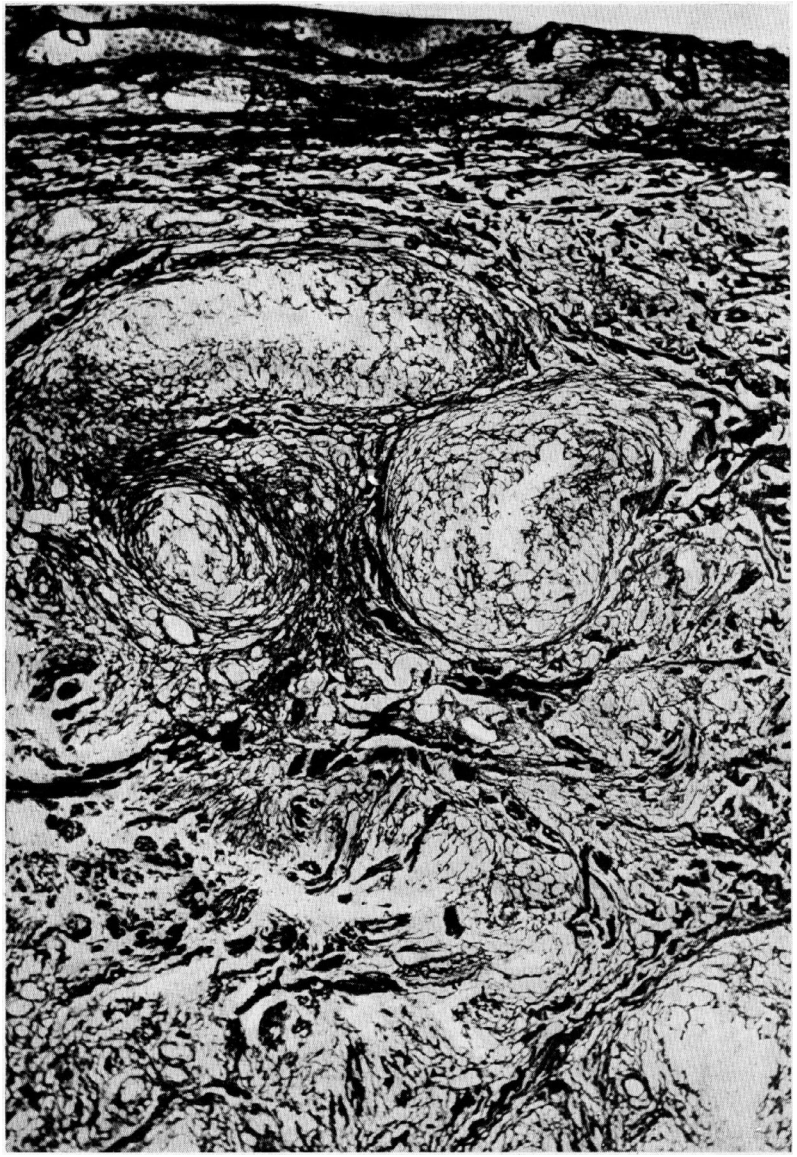


FIG. 21.—Case 5. Cutaneous nodule (stained haematoxylin and eosin, × 90) from elbow showing superficial collections of " gland-like " histiocytes and—deeper—the usual necrotic nodule.

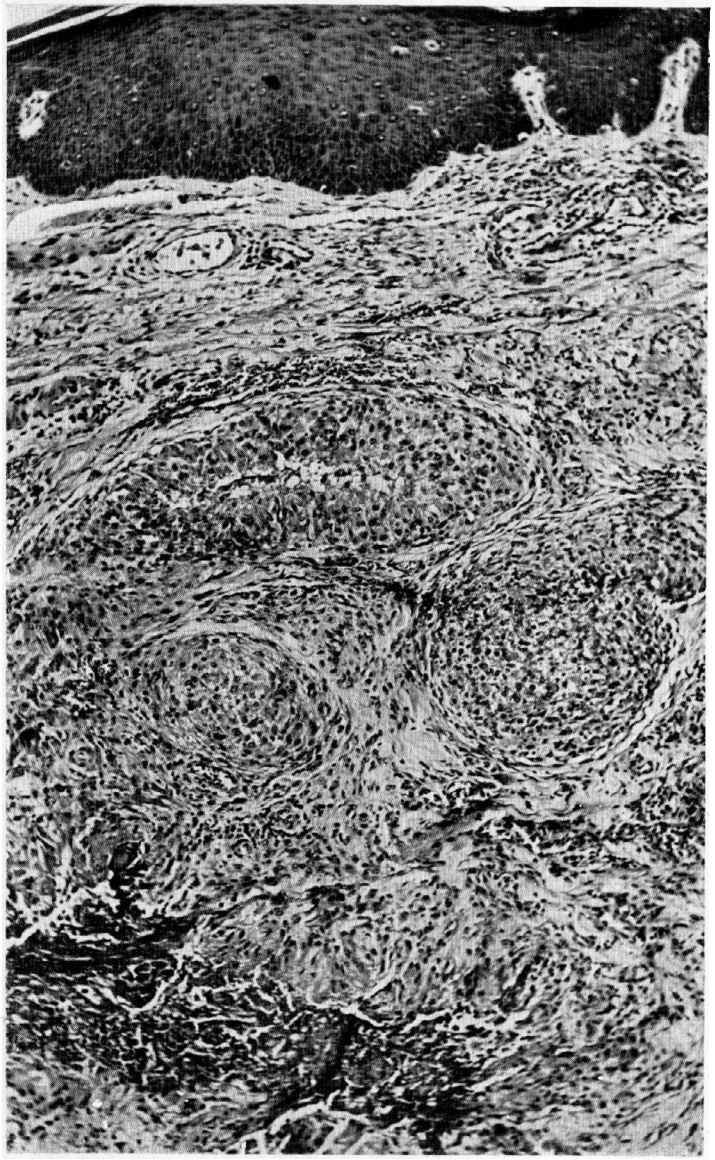


FIG. 22.—Case 5. The same, stained for reticulin (× 90).

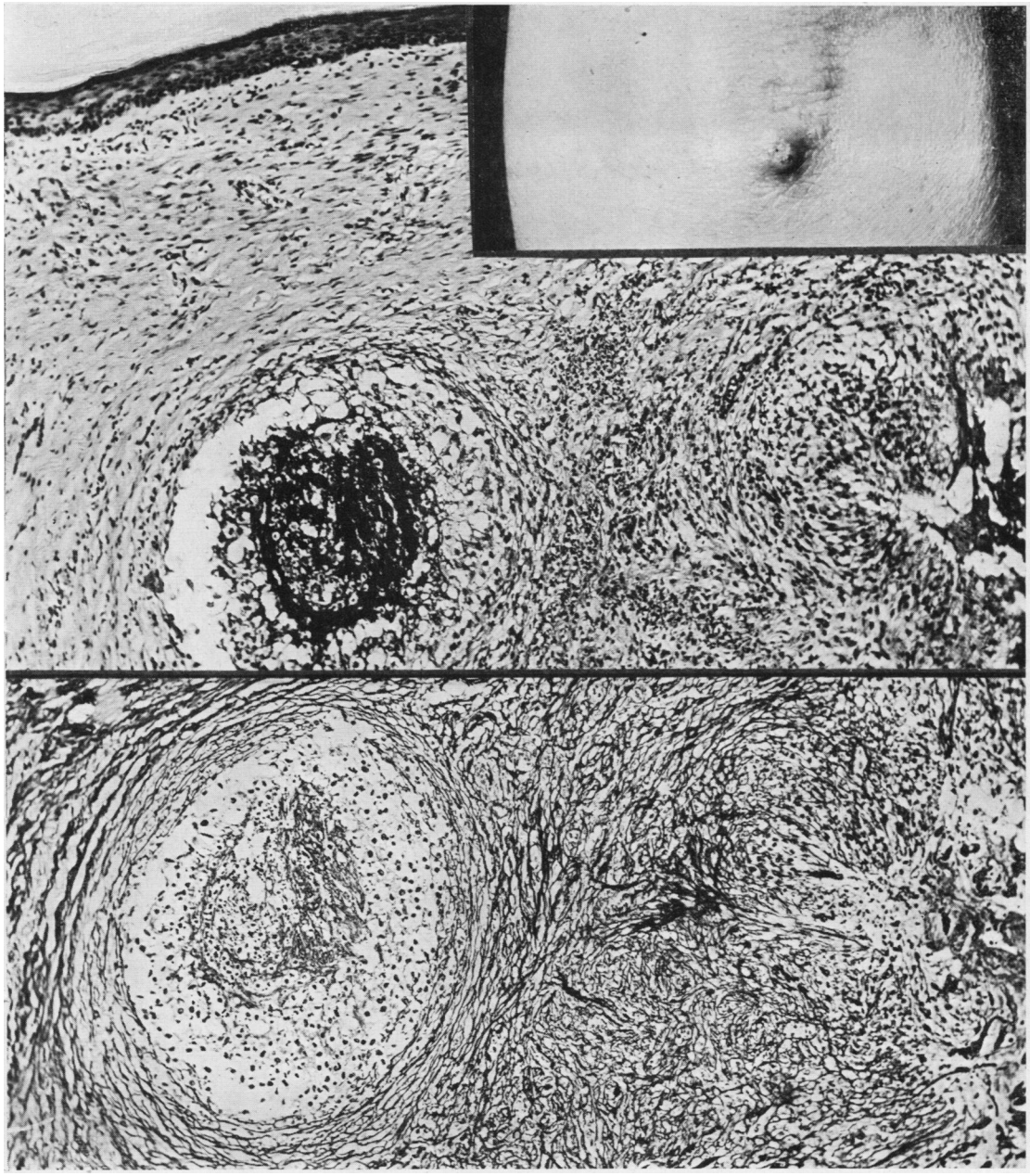


FIG. 23.—Case 6. Cutaneous nodule from elbow, with sections of same (stained haematoxylin and eosin (right), and reticulin (left)). Note, below, "necrobiosis": above, histiocyte nest with only slight reticulin development. × 90

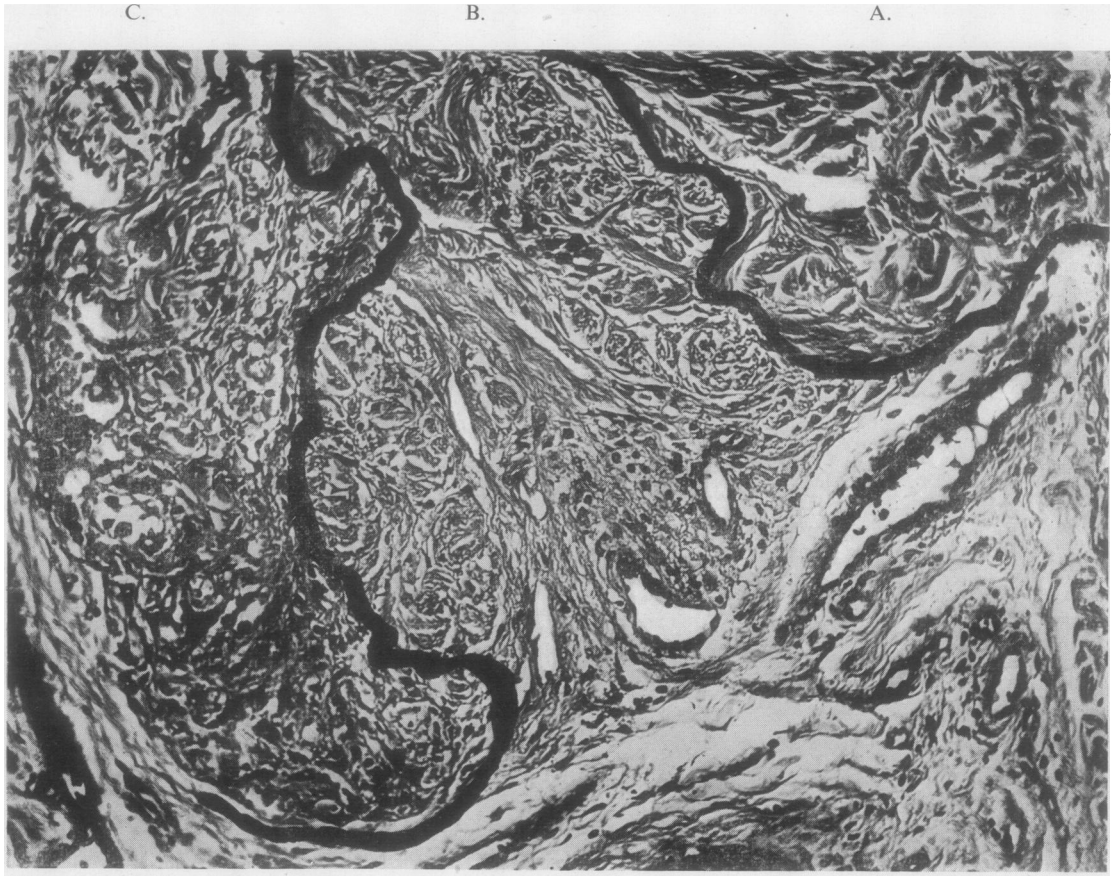


FIG. 24.—Case 1. Presumed early stage in nodule outskirts (stained azocarmine, × 280). Note three zones: A, normal collagen; B, collagen bundles separated into fibrillae; C, zone of cellular infiltration and degeneration of collagen. (Zone boundaries drawn in.)

of the nodule, the scab of which finally desquamated, leaving a small scarred area, slightly depressed and characteristically pigmented, the pigmented patch being about 1 mm. across. They were sore for the first day or two only, then the scab formed and desquamated in about four days or longer. A few appeared occasionally on the dorsum of the terminal phalanx of the index finger, but, as a rule they affected the pads of the thumb and index fingers, only rarely appearing on the third and fourth fingers. None was seen on the fifth finger. At the time of writing these skin nodules are still occurring on the digits, chiefly on the terminal pads but also on the more proximal flexor pressure pads. At one time (May 18, 1948) twenty-seven cutaneous lesions in various phases of development or involution were counted on the palmar aspect of the fingers and thumbs. Two of them were biopsied (see below).

More ordinary subcutaneous rheumatoid nodules of a larger size (10 to 30 mm. across) appeared gradually during this time on both elbows, over the sacrum, over the dorsum of the fourth and fifth right proximal interphalangeal joints, over the left ulnar-styloid process, over the third right metacarpo-phalangeal joint, over both Achilles tendons, and in the sheath of the left peronei (see Fig. 13). There were also similar nodules apparently in the sheath of the left long thumb extensor tendons and a nodular thickening in the main bulk of the extensor muscles below the left elbow. These nodules were permanent and both clinically and histologically differed in no way from the ordinary subcutaneous nodule of rheumatoid arthritis. Cystic change occurred in one of the olecranal nodules, later biopsied.

Towards the end of the first week in hospital an indurated swelling appeared in the palm of the right hand, affecting the aponeurosis of the second, fourth, and fifth fingers, which were contracted as in Dupuytren's contracture and could be neither passively or actively extended (Fig. 14). This lasted two days only and then completely disappeared to be followed by a similar condition in the palm of the left hand affecting the third finger. Recurrences were noted a week later affecting the right third and fourth fingers for a few days, and several times

since then. They came on very suddenly, in eight hours, and were thought to be due to involvement of the palmar fasciae, since the contraction involved the proximal interphalangeal joint mostly. According to the patient, these were also brought on by local trauma, such as, on one occasion, that involved in peeling apples.

Tenosynovitis with effusion was noticed on many occasions, both with and without crepitus, involving the right or left flexor longus pollicis, the carpi radialis, and the long thumb extensor sheaths, and lasting for about two or three days only. The swelling was tender for the first day and usually involved one forearm only at a time, recurring every few weeks. Other transient periarticular swellings were noticed from time to time over the dorsal aspect of the carpus and over the ventral aspect of the forearm proximal to the wrist (Fig. 15) lasting a few days and occasionally pitting on pressure. The left upper forearm was the seat of a recurrent hot red brawny swelling without nodularity involving the whole flexor surface, unassociated with effusion of the elbow joint and lasting about a week at a time, possibly due to inflammation of the fasciae between the flexor muscles.

The joints themselves showed the same recurrent pattern, shoulders and knees being affected most, wrists, finger joints, ankles, elbows, and metatarso-phalangeal joints next. While the knees showed effusions at all times, this was variable in content, but the finger joints became gradually more swollen; effusions were palpable in right second, third, fourth and fifth, and left second, third and fifth metacarpo-phalangeal joints, in right second and third and the left second, third and fifth PIP joints, and in both first carpo-metacarpal joints. These stayed swollen, and the hand grip was decreased to about one fifth of normal, more so in the right than in the left hand, probably due to the greater involvement and limitation of the right wrist (for example, 17 cm. Hg. left, 1 cm., Hg. right, compared with 50 or 60 cm. for an average normal female). Raynaud-like phenomena were marked in cold weather. Biopsy of one affected metacarpo-phalangeal joint and of the olecranal nodule showed changes consistent with a diagnosis of rheumatoid arthritis (Fig. 16). A digital pad nodule was also biopsied (Fig. 17).

From August 1946, following a sore throat, she lost her voice and could talk only in a husky whisper: this lasted with occasional intermissions for over a year.

Treatment during this time, consisting of heat, active and passive movements, exercises, splints, and salicylates, gave no more than symptomatic relief. The sedimentation rate, 43 mm. per hour (Westergren) on admission, fell gradually to 20 and stayed between 20 and 35 mm. during the next two years. The antistreptolysin titre was 160 units per ml.; colloidal gold 5 units. On several occasions the white count was low, reaching 3,000 per c.mm. with 33 per cent. polymorphs on one occasion, and, together with the serositis, joint effusions, albuminuria, and facial rash suggesting lupus erythematosus of the subacute disseminated or visceral type. No really characteristic rash or subsequent atrophy was, however, seen.

Summary.—The patient showed changes distinctly resembling rheumatoid arthritis but of an acute and recurrent type, associated with pericarditis, tenosynovitis, fasciitis, and nodules, both in and beneath the skin. There was also a facial rash, leukopenia, fever, and transient albuminuria.

Comment.—This case showed well the nature of the stimuli producing nodules in the finger pads. They were produced by pressure due to household duties and experimentally by pencil-point pressure. Other points of interest were the hoarseness, the marked flushing of the butterfly area of the face (recalling the rash of lupus erythematosus), and the flushing of the palms seen so frequently in rheumatoid arthritis and also in pregnancy, diseases of the liver, etc. The pericarditis again points to the acuteness of the condition. While a few cases of rheumatoid arthritis and particularly of Still's disease, can be shown at necropsy to have had pericarditis, this is not a frequent finding and, in fact, was picked up here first from the electrocardiogram. It seems possible that more frequent electrocardiogram records might display this picture in other cases.

Three other cases will be recorded more briefly.

CASE 3

R.H., a woman aged 57, at the time of her first admission to hospital (Feb. 6, 1943) had previously been in good health (except for typhoid fever at the age of 16) until five years after the menopause which occurred at the age of 50. Her feet then became painful and swollen, after which the hands and knees became involved. She had been in bed for four months prior to admission.

One of her brothers had a similar illness, and another was said to have died of it.

Examination.—The hands showed involvement of the left and right second metacarpal, the right fourth and left second PIP joints of both wrists: there was interosseous wasting and ulnar deviation. Both knees and ankles were swollen and showed slight limitation. General physical examination showed no noteworthy abnormality. She was afebrile; the sedimentation rate was 70 mm. in one hour (Westergren). The haemoglobin was 10·6 g. per cent. *X*-ray examination showed rarefaction and loss of cartilage in the right knee and left wrist and carpus. She was transferred to another hospital where a course of gold therapy was given. Nodules appeared on the left elbow a year later and on the right elbow three years later, just prior to her second admission (June 10, 1946).

From about February 1946 she had a continuous series of small nodules on the fingers of both hands, generally following use of the household broom. They lasted for a few days up to two weeks or longer and then if the patient abstained from work tended to disappear. They

were very painful "as if festering" during the early stages of development and made it difficult for her to pick things up.

Examination showed the characteristic changes of rheumatoid arthritis in the various joints affected. Classical nodules were present over both ulnar crests and over the long extensor tendons of the toes above the ankle. Small cutaneous nodules about 5 mm. in diameter, cystic on palpation, were present in the digital pads of both thumbs and of the second and third fingers of the right hand, and along the grip contact areas of both thumbs, of the right index finger and the right fifth finger (Fig. 18). Her grip was weak (4 cm., right, and 2 cm. Hg, left), compared with a normal female grip of 50 to 60). There was also a transient contraction of the palmar fascia of both hands, involving the skin and limiting full extension of the second and third right fingers, which disappeared a week later. Later the usual fixed palmar contracture occurred, complicated occasionally by sticking of the fourth finger in flexion for a few minutes such as might be produced by a swollen tendon or a shrunken sheath.

Investigations.—Haemoglobin was 15·1 g. per cent. M.C.H. 31; white blood cells numbered 3,400 per c.mm. of blood, 63 per cent. polymorphs. The Wassermann reaction was negative, the electrocardiogram normal; there was no urine abnormality. The sedimentation rate was 46 mm. in one hour, rising later to 70 and 92. Biopsy of the elbow nodule and of one of the dorsolateral digital nodes of the grip contact area showed, in the former, the characteristic histological picture of rheumatoid arthritis with central necrosis and a well-marked palisade layer. The latter nodule was more richly cellular and showed a fibrinoid latticework with necrosis and infiltration with polymorphs. A radiograph now showed complete loss of cartilage in both knees, both wrists, and the carpal joints with erosions in the first, second, third, fourth and fifth left, and the first, second, and third right metacarpo-phalangeal joints. The terminal big toe joints showed changes similar to but at an earlier stage than in Case 1 (Fig. 19).

Summary.—This patient had classical rheumatoid arthritis, and in addition digital pad nodules related to pressure and transient palmar contractures.

Case 4

I.M. A woman aged 28 developed alopecia totalis at the age of 15, associated with a marked depressional neurosis. At the age of 24 subtotal thyroidectomy was performed, but it is improbable that she had Graves's disease: there are now no residual signs.

Rheumatoid arthritis started at the age of 22 in the fourth month of her first pregnancy, and involved hands, knees, and feet. She now shows rheumatoid involvement of hands, feet, and knees with ulnar deviation and effusions. There is radiological bony involvement of carpus, metacarpals, and metatarsals. Urine, electrocardiogram, and blood count are normal. The erythrocyte sedimentation rate is 6 and 7 mm. in one hour (Westergren). Cholesterol is 210 mg. per cent., and the basal metabolic rate +5 to 10 per cent. She has developed a number of cutaneous nodules, usually following the use of the household broom, on the dorsal and contiguous surfaces of the thumb, index, and fifth finger joints, but has had no palmar contractures and no finger pad nodules. Biopsy shows characteristic rheumatoid granulomata.

Case 5

S.C., a woman aged 75, had had rheumatoid arthritis for twenty-nine years: it seemed now quiescent but had left her completely crippled, bedridden, and dependent on others for all the offices of life. Radiologically the hands showed typical carpal and metacarpal changes. She died of uraemia due to hydronephrosis. At necropsy both elbow regions showed many small cutaneous and subcutaneous nodules (Fig. 20); histologically they resembled closely the atypical digital pad nodule of Case 1 (Figs. 21 and 22).

Case 6

F.G., a woman aged 47, has been followed for over ten years in this clinic. She had had typical deforming rheumatoid arthritis showing radiological changes and a raised blood sedimentation rate. She developed subcutaneous nodules (typical microscopically) and after fourteen years of arthritis one *cutaneous* nodule on the elbow. This showed on section the same picture as in Cases 1 and 5 (Fig. 23).

Histological Changes

In Synovial Membrane.—Synovial membrane in Case 2 (Fig. 16) differed little from that seen in ordinary acute cases of rheumatoid arthritis: note that polymorphs rather than lymphocytes predominate. Case 1, however, showed more marked differences, resembling in several particulars those changes described by Hench and others as characteristic of palindromic rheumatism. The synovial lining cells were hypertrophic and arranged in a palisade layer. The surface was often covered with fibrin, which might be incorporated in the lining layer: these changes are common to a number of chronic synovial conditions, including tuberculosis and rheumatoid arthritis, and are seen in Hench's illustrations. The underlying connective tissue, however, contained many inflammatory cells, often surrounding dilated superficial capillaries, and consisting largely of polymorphonuclears (Fig. 9). In the chronic stage of rheumatoid arthritis, even in the not infrequent absence of lymph follicles, the cellular infiltrate consists predominantly of lymphocytes and plasma cells: polymorphonuclears are relatively less frequent, despite their marked preponderance in the synovial fluid, a fact which has never been adequately accounted for. In Hench's biopsies from cases of palindromic rheumatism the predominant cell was the polymorphonuclear leucocyte.

Other changes noted in Case 1 are the presence of fragmented granules (? collagen), (Fig. 6) and of cartilage detritus undergoing absorption, as is seen in rheumatoid arthritis. Thus, by histological criteria also, this case presents articular features resembling both rheumatoid arthritis and palindromic rheumatism.

Nodules.—Subcutaneous nodules removed from these patients were not markedly different from those encountered in classical rheumatoid arthritis (Fig. 4). In Case 1 they were perhaps rather acute in that no large amount of necrosis had occurred: in Case 2 rapid progression led to the incorporation of recognizable adipose tissue within the central necrotic area, and some increased oedema in the outer zones. Case 3 showed a well-marked ancient lesion with large necrotic zone and well-organized palisade layer.

The cutaneous nodules from the lateral aspects of the fingers of Cases 3 and 4 differed scarcely at all from the above description. Cases 1, 5, and 6 showed a different and almost identical histological picture (Figs 5, 21, and 23), although the Case 1 biopsy was of a digital pad nodule and the biopsies of Cases 5 and 6 from the elbows of old rheumatoid patients. Beneath the epidermis, nests of proliferating cells were seen, some in mitosis, sometimes becoming vacuolated towards their centre, some containing a few multinucleated giant cells. These were grouped around the periphery of deeper seated but still cutaneous nodules. The latter showed fibrinoid centres containing necrotic collagen fibres and pyknotic cells, mainly polymorphonuclear, although these cells were only rarely seen in the palisade and outer zones. The palisade layer was very thick and consisted of many layers of cells becoming vacuolated towards the necrotic zone and containing fat droplets: giant cells of foreign-body type were seen occasionally in it: it was bounded on the outer side by a peripheral skin of fibrous tissue. This palisade layer seemed to be a later and larger development of the nests, in which the centre portion had undergone necrosis. On the outskirts of the nodule, lobulated areas were seen where slightly oedematous and frayed bundles of altered collagen fibres were being invaded by dark staining macrophages (Fig. 24). This was apparently the first stage of nodule formation, since all stages therefrom towards the fully developed lesion were seen. A similar early stage is seen also in granuloma annulare, mostly in the cutaneous collagen bundles—and is a common finding in the acute rheumatic fever nodule. Reticulin stains showed the presence of altered (black-staining rather than brown-staining) argyrophil fibres in the middle of the necrotic areas, indicating the incorporation of larger collagen fibres in the undigested state: the nests of proliferating histiocytes seen in the cutis showed a few very fine new fibres, indicating that these areas form by cell proliferation (Fig. 23); if transformation of existing collagen occurs it is a very complete digestion. Thus the sequence we posit is (a) collagen alteration, (b) cellular infiltration, (c) nest formation, (d) central necrosis. Whether the initial change is in collagen or in the ground substance with secondary collagen changes we cannot say. This slightly different picture in the skin nodules compared with the subcutaneous ones is thought to be dependent on their superficial localization and hence earlier biopsy, as well as on the different pattern of collagen and ground substance therein: again it is to be emphasized that the digital pad nodules of our palindromic-like case (Case 1) were identical with cutaneous nodules from the elbows of old and deformed rheumatoid cases.

A unique picture was seen in the two digital pad nodules removed from Case 2 (Fig. 17). Immediately beneath the basal cell layer a collection of histiocytes, plasma cells, and lymphocytes was seen surrounding small amorphous hyaline masses staining lightly with eosin. The keratin layer was thickened and showed blister formation over the central infiltrated area: vessels in the neighbourhood showed a few histiocytes and lymphocytes around them. These were ancient resolving lesions, having been present for several weeks. They could be described as miliary rheumatoid nodules.

Discussion

Cutaneous Nodules.—Only rarely is it difficult to distinguish histologically between the subcutaneous nodules of rheumatic fever and those of rheumatoid arthritis (Bennett and others, 1940). All our cases showed true rheumatoid nodules; they could be distinguished (but with some difficulty) from the rare subcutaneous nodule (see Gray, 1914; Goldschmidt, 1925; Grauer, 1934), of granuloma annulare, as seen in the four cases of that condition that we have biopsied. The nodules of necrobiosis lipoidica diabeticorum also resemble closely the lesions of granuloma annulare, as Ellis and Kirby Smith have shown: since 10 per cent. (Goldberg, 1943) to 30 per cent. (Ellis and Kirby Smith, 1942) of patients with this lesion are not diabetic, the distinction, both clinical and pathological, if it is a real one, may be difficult.

The fibrous nodules on extensor surfaces recorded in primary diffuse atrophy or acrodermatitis chronica atrophicans (Herxheimer and Hartmann, 1902) are said to resemble the rheumatoid nodule,

but as Sweitzer and Laymon, 1935, Jessner and Lowenstamm, 1924, and Hövelborn, 1931, include typical cases of rheumatoid arthritis with skin atrophy in this category, some such fibrous nodules (situated as a rule over the subcutaneous ulna bone—" ulnar bands ") may indeed be merely rheumatoid. Others may be of the type associated with scleroderma (Gray, 1923; Fletcher, 1921), since many of the acrodermatitis chronica atrophicans cases are recorded as showing sclerodermatous change (compare Jessner and Lowenstamm, 1924, and Sweitzer and Laymon, 1935).

We have had no experience of the juxta-articular nodes of syphilis and allied infections (Hopkins, 1931), but from the excellent pathological description of Tuta and Coombs (1942), differentiation should be very easy.

If we eliminate the occasionally seen ulceration of subcutaneous nodules through the true skin, the existence of *cutaneous* rheumatoid nodules seems to be largely unrecognized (see Keil's (1938) complete and careful monograph on rheumatic subcutaneous nodules). There are two doubtful descriptions from the last century (Middleton, 1887; Bury, 1889), but it is difficult to classify what is described. The former concerned flattened elevations on the skin (pea to hazel-nut in size) of the pads of the fingers (illustrated), adherent to the skin but not to deeper structures and accompanied by other subcutaneous nodules on knuckles and tendons in a woman of 39 years who had had acute rheumatism aged 13 and 36 years with, between, frequent pain and swelling in various joints. Biopsy showed inflammatory cells and blood vessels but the histology is not described sufficiently to be helpful.

The latter case is even less clearly defined and may well have been one of erythema elevatum diutinum. Much confusion seems to have arisen as a result of the inclusion in the original account of erythema elevatum diutinum by Crocker and Williams (1894) of Bury's case which most dermatologists believe to have been one of granuloma annulare (cutaneous type). While Graham Little originally held (1908) that erythema elevatum diutinum was a variety of granuloma annulare, a view still held by many, he and Goldsmith later thought (in a discussion of Gray's case, 1932) that erythema elevatum diutinum differed from granuloma annulare in the absence of discrete nodules: this is a view which has been championed by Combes and Bluefarb (1940), who point out that erythema elevatum diutinum is bilaterally symmetrical, whereas granuloma annulare is seldom so: it affects middle-aged and old men, as against the children and young females with granuloma annulare. It is a flat raised red plaque with no central clearing, as compared with the depressed centre and nodular periphery of granuloma annulare, and histologically it is characterized by polymorph infiltration rather than by necrosis.

It is interesting to note, however, that in the clinically typical cases of erythema elevatum diutinum described by Trimble in 1926 acute attacks of recurrent polyarthritis occurred and polymorphs were not seen in the biopsied tissue: fibrosis, round-cell infiltration, and foam cells (such as are seen in rheumatoid nodules) were noted. Similarly in both the two cases described by Weidman and Besançon (1929), acute infections and recurrent polyarthritis occurred with nodules and plaques over knuckles, elbows, etc. Biopsy showed necrosis with polymorphs in the necrotic area, and the photograph shows a cutaneous nodule closely resembling what is usually seen in granuloma annulare and not distinguishable from those described in this paper as part of the rheumatoid arthritis syndrome. The clinical description of the skin lesion is, however, very different since the plaque-like aspect was quite absent in our cases. We may conclude that the description and labelling of skin manifestations has outrun correlation with other aspects of these diseases and that the nosological status of these above-mentioned eruptions must remain for the moment undetermined.

The only paper on cutaneous nodules in rheumatism of recent years is by Rosenberg (1934), describing two cases. The first was a woman of 46 years who had had pain in her hands, wrists, and knees for seven months, and who showed on examination swelling and extreme tenderness of the interphalangeal, metacarpo-phalangeal, and carpal joints (being unable to close her fists completely) as well as in her knees and elbows. The sedimentation rate (32 mm. in one hour, Westergren), haemoglobin (77 per cent.), erythrocytes (3·8 million per c.mm. of blood), leucocytes (7,000 per c.mm.), and *x*-ray appearances (decalcification only), were all compatible with but not diagnostic of rheumatoid arthritis. She developed in the six weeks prior to admission nodules on the volar and dorsal aspects of fingers and palms, red, varying in size from a pinhead to a hazel-nut, and not painful except on firm pressure. A new crop developed prior to admission lasting one month and a third crop three months later, affecting this time the neck, forehead, and cheeks, and disappearing in one month. Biopsy showed only a few lymphocytes and plasma cells, aggregated round the cutaneous vessels. The photographs of finger, face, and biopsied nodule are unhelpful, and it is indeed difficult to

imagine what such facial nodules might be, perhaps sarcoid or erythema nodosum, which sometimes occurs on the face (Bluefarb and Morris, 1941). The second case suggests subacute bacterial endocarditis with Osler's nodes although repeated blood cultures were negative (migratory joint pain, blowing apical systolic murmurs, anaemia, slight polymorpho-leucocytosis, and septic fever for five weeks with crops of red pimples on extremities and chest, biopsy of which showed polymorphs and round cells in the walls of the cutaneous blood vessels).

In our Cases 1, 2, and 3, these digital nodules at one stage resembled clinically Osler's nodes. Often painful or, at least, tender when they first appeared, they follow closely Osler's account of Mullen's description. " Small swollen areas, some the size of a pea . . . raised red . . . near the tip of the finger which may be slightly swollen . . ." In those first seven cases the nodes were " not beneath but in the skin ", " affecting the digital pads, thenar and hypothenar eminences of the sides of the fingers " with a slightly opaque centre " in all probability caused by minute emboli " (Osler, 1908-9). Blumer (1926) remarks that such nodes " have a small brownish stain behind them and occasionally leave a small scab which may be picked off ", a description closely corresponding to the digital nodules of Case 2 in this paper. However, although Keil amongst forty-two cases of subacute bacterial endocarditis has observed a haemorrhagic element with tiny discoloured spots in the depth of the skin, those nodes never suppurated or desquamated. The nodules described in this paper contain a necrotic centre and have shown a tendency to fibrosis with sometimes slight scaling over the opaque spot, resembling more the condition we have seen clinically in acute lupus erythematosus than the Osler node. These lesions are seen both in the disseminated discoid and in the acute visceral variants. Such tender, red nodules, often with slight induration, occurred in ten out of forty-two fatal cases of generalized lupus erythematosus and in four out of seventeen patients who subsequently recovered and who probably represent dissemination of a chronic discoid lesion (Bywaters and others, 1939). The finger and toe pads in that series were tender, swollen, sometimes with haemorrhagic areas, sometimes papular or blistered, and often ending in local desquamation, just as in Case 2 above. In six out of seven cases where blood cultures were made, findings were negative, and in only one of ten cases was verrucous endocarditis (Libman-Sacks) found at necropsy. Libman and Sacks (1924), Keil (1938), Coburn and Moore (1943), Ginzler and Fox (1940), and others have also seen such digital lesions in cases of verrucous endocarditis and lupus erythematosus. No biopsy examinations on these finger lesions of lupus erythematosus are available, and the histology of the Osler node rests upon two reports only (Merklen and Wolf, 1928; Lian and others, 1929), and our own observations (Glynn and Bywaters, unpublished data). It is enough to say that these lesions are not in the least like those figured in this paper, being merely what one might expect from a mildly septic embolus. In cases of primary or para-amyloidosis simulating scleroderma (Gottron, 1932), dermatomyositis (*Acta path. mic. scand.*, 1944), lupus erythematosus (Brunsting and Macdonald, 1947), and rheumatoid arthritis (Magnus-Levy, 1938), small digital nodules are sometimes seen, occasionally with painful finger tips (Michelson and Lynch, 1934). These turn out histologically, however, to be amyloid infiltrations of vessel walls (Weber and others, 1937). Finally, it is necessary to distinguish between nodules arising in the true skin and those arising in subcutaneous tissues which ulcerate through the skin to the surface, a phenomenon we have studied histologically in two cases.

Palmar and Digital Contractures.—These lesions, seen in Cases 1, 2, and 3, seemed to resemble Dupuytren's contracture, with flexion at the proximal interphalangeal and metacarpo-phalangeal joints: they involved the palmar fascia, which was adherent to the skin, producing dimpling on extension of the fingers. In Case 2 this was associated with a palpable swelling in the palm. A striking factor was the involvement first of one hand and then, a day or so later, of the symmetrical fingers of the other hand while the first had become free again. The probable mechanism is a rapidly evolving granuloma of the palmar aponeurosis. While we have seen, not infrequently, in rheumatoid and gouty cases, nodules in the tendons and in the tendon sheaths, these have produced, not acute transient finger contractures, but finger fixation or pseudo-ankylosis. Only very briefly in the development stage of such chronic granulomata does the patient complain of the finger momentarily sticking. Similar contractures have been seen by Scheele (1885) in a boy of 13 years with chorea and nodules involving the third, fourth, and fifth fingers of both hands lasting less than one month. Keil (1938) records a case of rheumatic fever in a girl with profuse nodule formation who developed bilateral third and fourth finger contractures of Dupuytren type with nodules in the palmaris longus fascia. Berkowitz (1912) records three cases of rheumatic fever in children, with many nodules showing similar transient finger contractures lasting

between one week (Case 1) and one month (Case 2), and we have recently seen a similar transient contracture due to palmar nodule formation in three children with rheumatic fever. Flexion contractures of the fingers have also been seen in a case thought clinically to be lupus erythematosus, but found at necropsy to have periarteritis (Bywaters and others, 1939). We have found no reference to such transient contractures in rheumatoid arthritis.

Relation to Lupus Erythematosus.—Synovitis is one of the characteristic manifestations of lupus erythematosus. It is usually mild: the biochemical and cytological changes in the synovial fluid differentiate it from rheumatoid arthritis, and the synovial membrane histologically appears different (Bywaters, Doniach, and Nellen, 1947). But occasionally lupus erythematosus patients are seen with joint deformities clinically and radiologically indistinguishable from rheumatoid arthritis: in eight of forty-two patients, deformity or spindling was present (Bywaters and others, 1939), and in one recent patient excised subcutaneous nodules closely resembled the rheumatoid granuloma. The clinical resemblance of the finger-tip lesions of the cases described in this paper to those of acute lupus erythematosus, the presence of pericarditis in Case 2, and finger contracture in lupus erythematosus has already been noticed.

It will have been remarked also that Case 2 showed a butterfly erythema of the face with slight residual squaming and widening of the pores, clearing up rapidly but leaving telangiectasia over the nose. Thus in her case there were grounds for supposing that she had acute lupus erythematosus. Arthritis, serositis, albuminuria, fever, facial rash, finger-tip lesions, and leukopenia, which are the most important features of acute lupus erythematosus, were all seen in this patient. Despite this, there are two points against that hypothesis. Thus in acute lupus erythematosus with albuminuria, recovery is very rare and it is unusual for a remission to last as long as this has done. Secondly, I have neither seen a case nor found records of cases with multiple large nodules, although, as mentioned above, a recent and unique case of typical discoid lupus erythematosus, with dissemination and visceral involvement ultimately recovering, has shown two nodules closely resembling those of rheumatoid arthritis. While Case 2 could be made to fit either pigeon-hole, she fits better into this series of rheumatoid arthritis (variant form with cutaneous nodules). The other patients showed no multiplicity of signs relating them to lupus erythematosus.

Relation to Lipoidosis.—While Layani (1939) and Weber (1944) have each published a case of joint disease apparently resembling rheumatoid arthritis with xanthomatous nodules associated with raised cholesterol figures (maxima 1,344 and 350 mg. per cent. respectively), only one case has been described (by Graham and Stansfield, 1946), where a rheumatoid-like type of joint deformity due to xanthomatosis has been associated with a normal blood cholesterol. Histologically there was no evidence at all of any rheumatoid-like process. Radiographs of the hands (which Dr. George Graham kindly allowed me to see) showed erosions of subchondral bone closely resembling that seen in rheumatoid arthritis but with several abnormal features such as para-articular erosions and rarefactions which are not seen in rheumatoid arthritis, substantiating the view that this was primarily a granulomatous infiltration of tendon and capsular insertions by xanthoma cells. The character of the joint lesions and nodules left no doubt that this was a primary xanthomatosis mimicking rheumatoid arthritis in the same way that amyloid infiltration of the joints sometimes does in multiple myelomatosis (Stewart and Weber, 1938). In Layani's case (detailed fully by Vishnevsky, 1939) the radiographs of the hands are (contrary to her statement, "ce ne sont pas les mains de rheumatisante") typical of an advanced stage of rheumatoid arthritis, and we have seen several such "mains-en-lorgnette" with quite normal cholesterol levels. It seems probable that that case was one of hypercholesterolaemia complicating an established rheumatoid arthritis with quite typical radiographs at four years from onset and three years before the first blood analysis.

A remarkable clinical story resembling in several respects that of Case 1 is recounted by Reed and Sosman (1942).

A Jewish woman, aged 21, complained of recurring migratory attacks, over a year or so, of pain, swelling, heat, and limitation, lasting in each joint for one or two days and affecting hands, wrists, elbows, hips, knees, and feet. The adjacent soft tissues would also on occasion become swollen. In between attacks these joints were quite normal. Active use of the joints and cold both tended to produce symptoms, the picture of which was not unlike rheumatic fever. Small subcutaneous nodules on the posterior aspect of both arms appeared, lasting several days and leaving ecchymotic spots. She suffered from sore throats, epistaxis, and loss of weight. Moderate enlargement of the metacarpo-phalangeal joints of both hands was seen, with soft-tissue swelling over the dorsum and spindling of the digits: however, there was neither heat, pain, nor limitation of movement. There was a rough systolic murmur in the basal area; A-V conduction was prolonged. The erythrocyte sedimentation rate was 15 to 18 mm. in one hour, the cholesterol 149 mg. per cent., leucocytes

5-6,000 per c.mm. of blood. Thus so far the story is very similar: but the patient had typical attacks of "osteomyelitis" with drainage in both femora at the age of 10 and 13, and biopsy of the bones showed typical Gaucher cells. Radiographs showed enlargement of spleen and liver, many irregular cystic defects in the long bones, and flask-shaped femora. The hands showed narrowing of interphalangeal joints without erosion. In our own patient Gaucher's disease is ruled out on histological, clinical, and radiological grounds, and indeed the above history is unique and not at all characteristic of the usual case of Gaucher's disease.

In Case 1 some of the radiological changes, especially those developing in the terminal phalanx of the left big toe, resembled lipoid infiltration as seen for instance in the Hand-Schüller-Christian syndrome. Bone biopsy (of the finger) showed, however, neither the characteristic picture of this nor of Gaucher's disease. The marrow spaces were filled by small, regular, somewhat finely vacuolated cells which might have been filled with lipoid (no fat stain was done) as is sometimes seen in other granulomata, for example, in rheumatoid nodules and in the pigmented villous xanthogranuloma with giant cells and iron filled macrophages occurring in the joint cavities or tendon spaces (Jaffe and others, 1941) and thought now to be a sclerosing haemangioma with retention of macrophagic properties for iron granules or fat. Indeed, a modern view of Hand-Schüller-Christian's syndrome is that this condition is not a primary disturbance of lipoid metabolism but a chronic granuloma, with secondary lipoid characters closely related to Letterer-Sive disease, eosinophilic granuloma of bone, and osteitis fibrosa disseminata (Albright), and possibly related to the reticuloses (see Mallory, 1942). Certainly the presence of cholesterol is very common in rheumatoid nodules, both as crystals in the central necrotic area and in the cells forming the palisade layer, presenting in haemotoxylin-and-eosin-stained sections as foam cells. I have also seen large crystals of cholesterol floating free in synovial fluid from such cases. There seems to be no reason for separating such cases from the ordinary type of rheumatoid arthritis with nodules showing only a small amount of cholesterol, as Fletcher (1946) has done. This has already been recognized by Kersley and others (1946), who stress also the presence of cholesterol in gouty nodules (see also Chauffard and Troisier, 1921).

Thus, despite the atypical radiological appearances, we do not believe that this case falls into the category of lipoidosis, either primary, secondary, or granulomatous. Biopsies from other places showed no evidence in favour of this hypothesis, and indeed even the radiological appearances differ very considerably from that of the hands in the only published case of xanthomatosis with joint involvement and normal cholesterol (Graham, personal communication).

Relation to Palindromic Rheumatism.—"Palindromic" (recurrent) rheumatism was described as a new syndrome by Hench in 1940. The full description by Hench and Rosenberg (1944) of thirty-four cases has been largely confirmed by subsequent case reports. It seems to be comparatively rare, since Hench's estimate of five or six cases per year is from a total annual turnover of 4,000-4,500 new cases which are already highly selected. It is characterized by recurrent transient attacks of joint pains and swelling which last a few hours or days and then subside completely, but, unlike intermittent hydrarthrosis, very many joints are affected in turn. Attacks may occur daily, usually towards evening, or more often, or several times a year only, lasting over a period of many years, for example, up to twenty-five years, without leaving any clinical, histological, or radiological residua. In an attack the synovial membrane is inflamed and the joint contains a fibrinous polymorphonuclear exudate. Para-articular soft-tissue swellings also occur, affecting the dorsum of the hand or the upper forearm or elsewhere. Intracutaneous and subcutaneous nodules were found in three cases, in the digital pads or over the fingers, occurring at sites of pressure: one such nodule was biopsied but no central necrosis or palisade was seen. Tenosynovitis with effusion and hoarseness of the voice was also noticed. The sedimentation rate was raised (average 32 mm. in one hour in sixteen cases during or just after an attack); blood uric acid was normal; cholesterol was slightly raised (between 225 and 315 mg. per cent. in nine of eleven patients), and slight leucocytosis was present in some cases but in no case was this higher than 16,800 per c.mm. of blood. In two patients slightly subnormal figures were found.

This general picture is confirmed on the clinical side by ten out of thirteen subsequent publications under this title reporting twelve cases (Cain, 1944; Thompson, 1942; Mazer, 1942; Ferry, 1943; Paul and Logan, 1944; Grego and Harkins, 1944; Paul and Carr, 1945; Wingfield, 1945; Neligan, 1946; Hopkins and Richmond, 1947). Five cases recorded under this title by Saloman, 1946, and Perl, 1947, have not been included as confirmatory since the data given are insufficient to make a diagnosis. Of the two cases briefly recorded by Weber (1946), the first suffered from recurrent pain in the hip joints, migraine, and iritis but showed no real

similarity to palindromic rheumatism as defined by the originator of the term. (The second case cited by Weber is Case 1 of this paper, and was thought to be "half way between palindromic rheumatism and angioneurotic oedema"). It will be seen, therefore, that the diagnosis of palindromic rheumatism fitted Case 1 very well until it was discovered firstly that radiological changes were present, secondly, that the nodules were of rheumatoid type with central necrosis, and thirdly that cartilage destruction was occurring, as evinced by the finding of cartilage detritus embedded in and undergoing absorption by synovial membrane.

Case 2 also showed many of these features; articular swellings related to housework, cutaneous nodules related to pressure, hoarseness, teno-synovitis, and para-articular swellings in the palm, on the dorsum of the hand, and in the forearm, closely corresponding to Hench's description. But she had well-marked radiological changes of rheumatoid arthritis, and like Case 1 the nodules, cutaneous and subcutaneous, were those of rheumatoid arthritis.

Case 3 was even more clearly one of rheumatoid arthritis, but again she presented the digital pad lesions and the palmar contractures shown by the other two cases. Hench and Rosenberg (1944) have concluded on the basis of their experience that this picture is *not* merely a palindromic variant of rheumatoid arthritis. On the basis of our much smaller experience we would conclude that the cases we have described form a "palindromic" variant of rheumatoid arthritis: this is based on the presence of rheumatoid nodules and radiological bone changes. While it is possible that the one nodule that Hench biopsied was atypical, or that the section failed to include the central necrotic area, it is more likely that his description is correct and that these nodules of palindromic rheumatism are entirely different from those of rheumatoid arthritis. It is even more difficult, if we are describing the same syndrome, to account for the complete absence of significant radiological bone change in Hench's thirty-four cases and the ten cases described by other authors, and its presence in our case. The possibility exists, of course, that radiological change will occur given a long enough follow-up, as indeed happened in Case 1. When seen by Dr. Parkes Weber in 1942 (Weber, 1946) no radiological changes were visible, but five months later such changes were quite obvious in both hands and feet. It is difficult to think, however, that this possibility applies to most of the recorded cases whose disease had lasted, before radiographic examination, for many years (average of seven years for Hench's thirty-four cases). We must conclude, therefore, that the syndrome we are describing is not palindromic rheumatism, but a rheumatoid variant which may approach it very closely, all degrees of which, from the fairly straightforward rheumatoid of Case 4 to the highly "palindromic" degree of Case 1, may be manifest. It would be interesting to know whether such cases as ours occur in the vast material presenting annually at the Mayo Clinic. This conclusion of ours is in agreement with the views of Walter Bauer and his group at the Massachusetts General Hospital. Thus, Ropes (1944) states that "of the relatively few typical cases of this (i.e. palindromic) syndrome seen in our clinic, the majority have occurred in patients with definite evidence of rheumatoid arthritis . . . *x*-ray changes or progressive symmetrical joint disease". She points out further that intermittent hydrarthrosis also, in the majority of their cases, is a phase in the development of rheumatoid arthritis, a view supported by the observations of Ghormley and Cameron, 1941, and Cecil, 1940. Kuhns (1945) also remarks that he has seen three cases diagnosed as palindromic rheumatism who later developed damage to the articular surfaces and pronounced deformities. Given a long enough follow up, will all cases show this?

It should be added finally that there is nothing to suggest that these cases fall into the rather obscure and doubtfully distinct categories of angio-neural arthrosis (Solis-Cohen) or allergic arthritis (Kahlmeter).

Relation to Gout.—There is no evidence that any of these cases suffered from gout. At the same time, the recurrent attacks of arthritis in gout, with complete restitution in the early phases and gradually progressive permanent involvement in the later stages, and the appearance of nodules or tophi which histologically closely resemble rheumatoid nodules except for the uric acid crystals and their accompanying giant cells, all point to a somewhat similar pathological process in that disease. This has been previously pointed out by Verhoeff and King (1938) in their discussion of rheumatoid scleromalacia perforans. That joint involvement can occur as the result of a metabolic disease is seen not only in gout, and in Graham's case of "lipoid gout" cited above, but in para-amyloidosis with or without multiple myelomatosis, where subcutaneous ulnar nodules may also be found (Tarr and Ferris, 1939). Case 1 was, in fact, thought for a long time to be and was treated as, one of gout. The value of "Atophan" was perhaps doubtful, as it is in gout, but it was the only drug that the patient continued to use fairly

consistently. The case illustrates even better than classical rheumatoid cases these clinical and pathological similarities with gouty arthritis. While, viewed from the standpoint of a biochemist, every disease may be considered as a metabolic disease, we submit that there is a very special case for considering rheumatoid arthritis (and specially such a variant as we have described) from this point of view. The metabolic view of gout has led us only a little nearer to an understanding of its genesis, but recent studies on biochemical changes in unaffected relations of gouty patients (Talbott, 1940) and on the heredity factor in rheumatic fever (Wilson, 1940) point to relatively unexplored avenues of approach in the rheumatic diseases.

Relation to Rheumatoid Arthritis.—This series of cases shows a graded passage from Cases 4, 5, and 6, a not very unusual type of rheumatoid arthritis, to Case 3 (with the characteristic transient palmar contractures and digital pad nodules), to Case 2 (still showing characteristic rheumatoid radiological findings), to Case 1 (in whom the differences from accepted ideas of rheumatoid arthritis were so great that nine eminent specialists were unable to make that diagnosis). Yet these four cases obviously resemble each other far more than, for instance, Case 1 resembles palindromic rheumatism or Case 2 lupus erythematosus. Histological criteria establish them all as rheumatoid arthritis, and, in the absence of direct aetiological identification (as by the finding of a specific organism), the only definitive criteria of a disease entity are such anatomical specificities and such a common (although uncommon) clinical picture.

We believe that this is a variant of a pathological process which, under other slightly different circumstances, produces classical rheumatoid arthritis, and which is related again but more distantly to others of the unexplained mesenchymal disease, such as palindromic rheumatism, lupus erythematosus, scleroderma, dermatomyositis, peri-arteritis nodosa, and possibly even gout. While for the purposes of diagnosis and hence for prognosis and treatment differences between syndromes are to be emphasized, for non-utilitarian or research purposes it is the similarities in each different syndrome which should be explored. Pigeon-holing of sick men and women is a necessity to the clinician in his daily craft but a hindrance in his pursuit of truth. Emphasis of that point is the purpose of this presentation.

Summary

Three cases are described in detail of a variant type of rheumatoid arthritis with transient digital pad nodules, transient palmar contractures, and transient para-articular swellings. Biopsy material showed the nodules to be of rheumatoid type. Radiologically, changes in the juxta-articular bone were seen, atypical in Case 1 and identical with those of rheumatoid arthritis in the others. Case 2 showed pericarditis, leukopenia, fever, albuminuria, a butterfly rash, and other features often seen in acute disseminated lupus erythematosus with visceral manifestations. The relation of these cases to palindromic rheumatism and to other mesenchymal diseases is discussed.

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Une forme d'Arthrite Rhumatismale Caractérisée par la Récurrence de Nodules de la Pulpe Digitale et de l'Atteinte de l'Aponévrose Palmaire, Analogue au Rhumatisme Palindromique

RÉSUMÉ

L'auteur décrit en détails trois cas d'une variété d'arthrite rhumatismale avec apparition transitoire de nodules de la pulpe digitale, de contractures palmaires, et de gonflement para-articulaire. La biopsie a montré que ces nodules étaient du type rhumatoïde. A l'examen radiologique on a constaté des modifications des os voisins de l'articulation, modifications atypiques chez le sujet 1 et identiques à celles de l'arthrite rhumatismale chez les autres. Le sujet 2 présentait de la péricardite, de la leucopénie, de la fièvre, de l'albuminurie, une éruption en papillon, et d'autres manifestations fréquemment présentes dans le lupus érythémateux disséminé aigu avec des manifestations viscérales. L'auteur discute la relation entre ces observations et le rhumatisme palindromique et d'autres affections du tissu conjonctif.