FROM THE RACKHAM ARTHRITIS RESEARCH UNIT AND THE DEPARTMENT OF PATHOLOGY, UNIVERSITY OF MICHIGAN, ANN ARBOR

Synovial Specimens Obtained by Knee Joint Biopsy

By

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It has been my privilege to spend the past two months with our Swedish friends at the Karolinska Sjukhuset in the Department of Internal Medicine. This experience has been very rewarding, exceeding all my expectations. I wish to express my warm appreciation to Professor Nanna Svartz who made this possible and to thank her for the kind invitation to participate in these meetings. I am honored to do so and hope that our report will be of interest. The material to be presented represents the work of several individuals in our Investigative Unit in which respect I would like to particularly mention the names of Dr. Mikkelsen and Dr. Castor. These studies have been carried out in collaboration with our colleague Dr. A. James French, Professor of Pathology. Our preliminary observations have been reported in an earlier publication [1].

Our findings confirm the experience first reported by Drs. Polley and Bickel [2, 3] of the Mayo Clinic in 1951. Since Dr. Hench has been closely concerned with Dr. Polley in the development of this technique we will be especially interested in his comments. It gives me further pleasure to recall the part played in the historical development of this subject by another of our very distinguished colleagues here today, Dr. Forestier. In 1932 he described [4] a method of obtaining synovial tissue by use of a dental nerve extractor introduced into the joint space through a large caliber, hollow needle and by which he obtained a number of biopsy specimens.

Description of the Instrument and Procedure

The Polley-Bickel biopsy instrument is simply constructed. The main part is a hollow, round stainless steel tube with a trocar point and a hooked lip. A hollow tubular knife with a sharp cutting rim fits inside the outer tube. An extractor with a corkscrew-like tip fits within the inner cutting tube enabling

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one to remove biopsy specimens without withdrawing the instrument from the joint space.

Punch biopsy has been carried out in a standard treatment room in our Research Unit, not uncommonly on out-patients. Standard surgical practice and rigid aseptic technique must be followed since the danger of introducing infection exists whenever a needle is inserted into a joint. The knee joint is approached laterally or medially through the suprapatellar pouch (Fig. 1). The skin, subcutaneous tissues and joint capsule in the path of the instrument are carefully infiltrated with procaine. Synovial fluid is aspirated through the hollow needle and examined for cytological and physical chemical characteristics [5, 6]. If there is no appreciable effusion, distention of the synovial space with 30 to 50 ml. of physiological saline solution may facilitate introduction of the instrument. About four specimens of the synovium are then obtained from the perimeters of the joint space and fixed immediately in 10 per cent formalin. Specimens are prepared in the routine manner and stained with hematoxylin and eosin. Except for the moment when the synovium is cut the procedure is relatively painless. Patients are permitted to walk immediately after the procedure but are requested to avoid any unnecessary activity for 24 hours.

Merits of Synovial Biopsy as a Teaching Aid and Research Potentialities

Previously we have had but little opportunity to acquire first hand knowledge of the morphological characteristics of normal synovium or the alterations which may occur in disease. In the United States medicolegal obstacles are largely responsible for the fact that joints are rarely examined after death. Even if permitted such an examination is difficult and time consuming, especially in inexperienced hands.

The Polley-Bickel biopsy instrument has provided a simple and safe method of obtaining synovial specimens with a frequency previously not feasible. Bimonthly conferences are held in our Research Unit at which biopsy material is reviewed by us. This has proved to be a very rewarding exercise and has become a valuable part of our teaching program. We have come to appreciate that changes in synovial morphology must be interpreted in the light of all available clinical, laboratory and x-ray information.

It has also been evident that in interpreting synovial morphology one must be aware of the normal variation that occurs in different areas of the knee joint [7]. Synovium can be classified into three major types depending on the nature of the underlying tissue [8]. These three types occur in reasonably consistent intra-articular locations. Specimens from the distal suprapatellar pouch, overlying the quadriceps tendon, show only few synovial cells, few folds and few blood vessels above the collagenous bundles of the tendon; this is the fibrous type of synovium. Specimens from the proximal portion of the suprapatellar bursa show one to several layers of synovial cells, more numerous

Table 1. Diagnostic Value of Punch Biopsy of the Knee Synovium
142 Patients

Technical failures	6	4 %
Of diagnostic aid	50	35 %
Not helpful	83	59 %
Misleading	3	2 %

folds and villi and a subintimal layer of loosely arranged collagen fibers, varying amounts of fat and thin walled blood vessels; this is the mixed type of synovium. Specimens from the patellar synovial fold, the marginal synovium and the posterior popliteal pouch are distinguished by the predominance of areolar or adipose tissue in the subintimal region.

In addition to advancing our knowledge of synovial morphology, punch biopsy provides a source of material for histochemical and tissue culture techniques. In Professor Svartz's laboratory we have used this method to obtain tissue for electron microscopy, a purpose for which it is especially convenient because tissue fixation in osmium solution is essential within a minute or so following disruption of the blood supply.

Diagnostic Value of Punch Synovial Biopsy

This report is based on evaluation of knee synovial tissue obtained on 160 occasions from 142 patients. Incidence of failure to obtain synovial tissue has been about five per cent. Ability to obtain satisfactory material has been decidedly improved by experience. Complications have been few, consisting of mild transient hemarthrosis and superficial thrombophlebitis in two instances each. In no case could intra-articular infection be attributed to punch biopsy.

The diagnostic value of the procedure has been carefully studied (Table I) and correlated with pertinent clinical and laboratory information. Punch biopsy was considered of definite diagnostic aid in 50 cases (35 per cent of the group of 142 patients). In 83 cases (59 per cent) synovial changes were either absent or too slight to suggest a definite diagnosis. In only three instances was an incorrect diagnosis suggested by this procedure.

Rheumatoid Arthritis

There were 51 individuals in whom the diagnosis of definite rheumatoid arthritis was warranted on the basis of the criteria of the American Rheumatism Association [9]. In 26 (or 51 per cent) of this group, synovial characteristics were compatible with this diagnosis. The frequently encountered pathologic alterations observed in rheumatoid arthritis included (1) hyperplasia of the intimal lining cells of the synovium and oftentimes fibroblastic proliferation throughout the synovial tissue, (2) varying degrees of loss of the normally

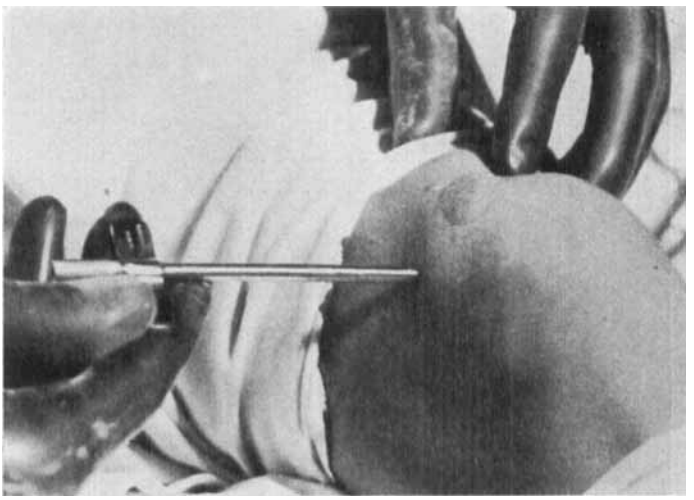

Fig. 1. The Polley-Bickel biopsy needle in place. Reprinted by permission from Zevely, H.: Am. J. Med. 20: 510, 1956.

distinct fibrillar appearance and bundle arrangement of the collagen, (3) subintimal edema, (4) inflammatory cell infiltration, including lymphocytes and plasma cells, which in some instances form follicle-like collections, and (5) vascular changes including congestion, increased numbers of vessels, thickening of vessels walls and perivascular cuffing with inflammatory cells.

Case 1 (Fig. 2) M.M. 702810. This material was obtained from a 27 year old woman with rheumatoid arthritis of 7 years duration involving only the knees; after a remission of one year, exacerbation occurred three weeks before this biopsy. Osteoporosis was the only radiological finding. The synovial fluid nucleated cell count was 40 000 per cu ml. of which 97 % were polymorphonuclear cells; mucin clot was fair and viscosity was inferior. There was reversal of the albumin/globulin ratio; the sedimentation rate was elevated. You see an increased number of small blood vessels beneath the synovium, with hypertrophy of the cells in the walls of the vessels; there is thickening of the synovial cell layer and increased stroma. This, then, is hypertrophic villous synovitis. One does not see in the subsynovial tissue the infiltration of leukocytes which the joint fluid differential count might lead one to expect.

Case 2 (Fig. 3) K.N. 871206. This material is from a 51 year old man seen in the Rheumatologic Department, Medical Clinic, at the Karolinska Sjukhuset.[1] In an eight year period rheumatoid arthritis had involved multiple joints with cartilaginous and bony destruction. The hemagglutination test (Svartz and Schlossmann) was positive (1/4,096); the sedimentation rate was 81 mm/hr. (Westergren); there was a persistent anemia. The joint fluid contained much fibrin debris; the nucleated cell count was 8 200 per cu ml. of which 85 % were polymorphonuclear leukocytes. This biopsy shows hypertrophic villous synovitis; there is reduplication of the synovial lining cells which in some areas are in palisade arrangement; there is infiltration in the subsynovium by lymphocytes and plasma cells which in some places appear in aggregates. There has been, in addition, profound alteration in the collagen.

[1] Through the courtesy of Dr. Börje Olhagen and Dr. Kåre Berglund.

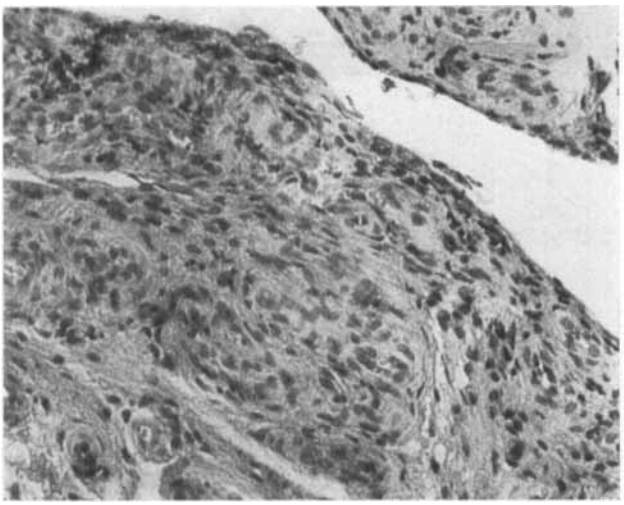

Fig. 2 (Case 1) M.M. Rheumatoid arthritis, A.R.A. Stage I.* Hypertrophic villous synovitis. Magnification × 500. Reprinted by permission from Zevely, H.: Am. J. Med. 20: 510, 1956.

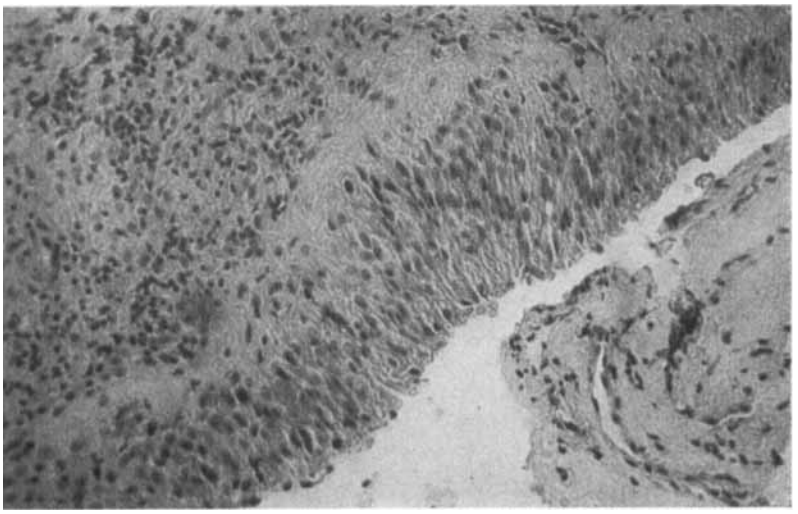

Fig. 3. (Case 2) K.N. Rheumatoid arthritis, A.R.A. Stage III. Hypertrophic villous synovitis. Magnification × 280.

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* Classification of Steinbrocker et al. (10) adopted by the American Rheumatism Association. Stage I denotes early rheumatoid arthritis with osteoporosis the only radiographic abnormality. Stage IV denotes bony or fibrous ankylosis; stage II and III are intermediate and include cartilaginous and bony destruction.

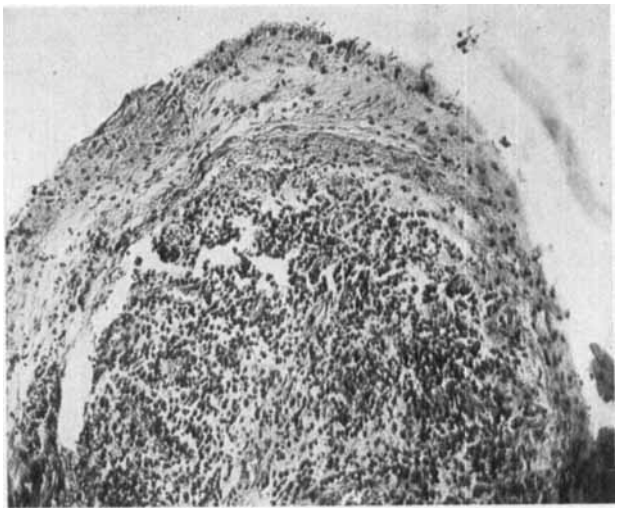

Fig. 4. (Case 3) L.W. Rheumatoid arthritis, A.R.A. Stage IV. Clinically inactive with normal sedimentation rate. Chronic hypertrophic synovitis, heavy inflammatory cellular infiltrations including lymphocytes and plasma cells beneath synovium. Magnification × 210. Reprinted by permission from Zevely, H.: Am. J. Med. 20: 510, 1956.

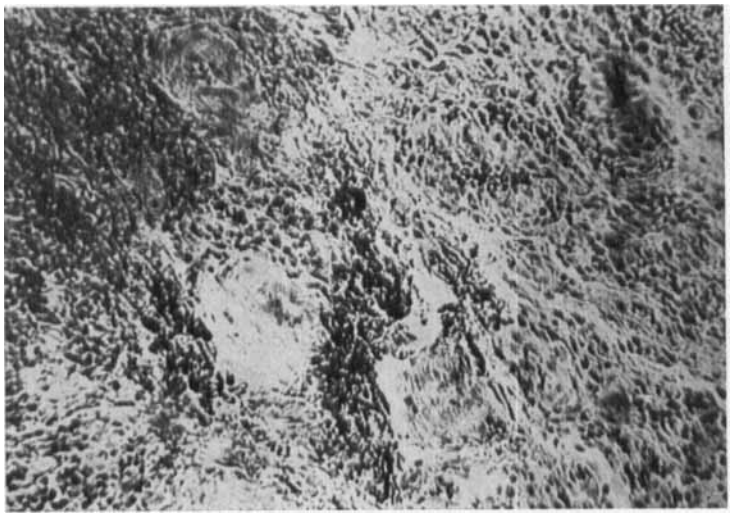

Fig. 5. (Case 4) E.K. Swelling and pain of six month's duration of sternoclavicular joint. Conventional biopsy showing chronic active hypertrophic synovitis. Magnification × 280.

Case 3 (Fig. 4) L.W. 793474. This 57 year old man had had rheumatoid arthritis for 7 years, there was ankylosis and subluxation of several joints; rheumatoid nodules were present. Clinically, however, the disease was inactive with a normal sedimentation rate. The synovial fluid nucleated cell count was 9 700 per ω ml. of which 79 % were polymorphonuclear leukocytes; mucin clot and viscosity were abnormal. This biopsy specimen shows a heavy inflammatory cellular infiltration of lymphocytes and plasma cells beneath the synovium. There is increased vascularity; perivascular collections of cells are seen.

In each of the preceding cases, in which the disease varies from early active to late inactive stages, the material obtained by synovial biopsy is compatible with the clinical diagnosis of rheumatoid arthritis. One observes, however, that it is not possible to correlate synovial morphology with the duration, stage of progression or activity of the rheumatoid process. There was, furthermore, often poor correlation between synovial fluid characteristics and histologic changes in the synovial membrane. The situation, in one respect, is similar to that which may be found in experimentally produced polyarthritis, as Professor Svartz [11] pointed out sometime ago, where an elevated synovial fluid total cell count due to polymorphonuclear leukocytes may be observed without, at the same time, predominance of this cell in the subsynovial tissue where, indeed, the predominate cells are often mononuclear.

Case 4 (Fig. 5) E.K. 715698. This 43 year old man had six months before experienced swelling and pain of the right sternoclavicular joint. The sedimentation rate was elevated. This conventional biopsy of the sternoclavicular joint shows a chronic active hypertrophic synovitis with heavy lymphocytic and plasma cell infiltration with occasional follicles; vascular changes are prominent. Cultures were negative for tuberculosis and fungi.

It was then learned that four years before multiple peripheral joints had been involved by a rheumatic process which had subsided within one year without gross residual changes. This biopsy specimen (Fig. 6) was taken from a clinically normal knee. The small amount of joint fluid obtained had a nucleated cell count of 100 per ml. of which 80 % were mononuclear cells; mucin clot formation and viscosity were excellent. In spite of the normal joint fluid, this biopsy specimen shows changes consistent with mild rheumatoid synovitis; there is fibrin within the joint space and thickening of vessel walls in the subintimal tissue.

Case 5 (Fig. 7) D.S. 620015. This 27 year old woman had a 7 year history of monarticular arthritis of a knee with a persistent effusion, low grade inflammation and pain; one remission had occurred during a pregnancy. A small nodule was observed in a flexor tendon sheath. The total nucleated cell count of the synovial fluid was 6 300 per cu ml. of which 73 % were polymorphonuclear cells; the physical chemical features were inferior. This biopsy specimen shows increased numbers of blood vessels and inflammatory cellular infiltration with lymphocytes and plasma cells. There is some proliferation of synovial cells, loss of definition of collagen fibers and subsynovial edema. Cultures and animal studies were negative for tuberculosis. This is monarticular, early rheumatoid arthritis on the basis of the clinical findings, the joint fluid characteristics, the presence of what was probably a rheumatoid nodule and the morphological features of this biopsy specimen.

Synovial biopsy may be particularly helpful in establishing the nature of monarticular cases of arthritis and particularly to differentiate between rheumatoid arthritis, tuberculosis and gout. These studies suggest that the morphologic features of rheumatoid arthritis may persist even though the joint fluid has become essentially normal. This, of course, is in keeping with a distinguishing

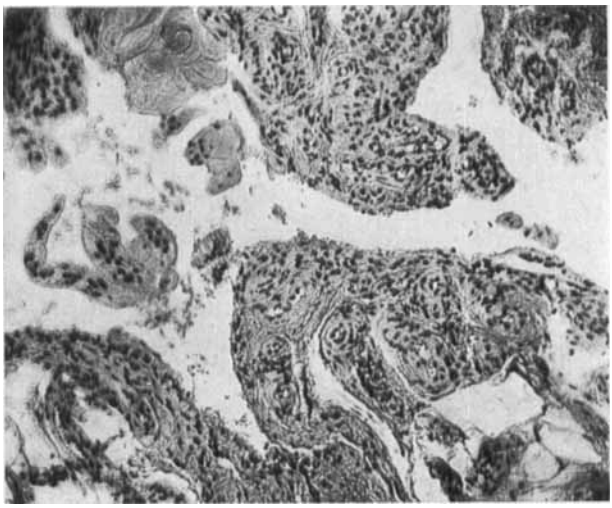

Fig. 6. (Case 4) E.K. Needle biopsy specimen obtained from a clinically normal knee (but involved by a rheumatic process four years previously). The changes seen resemble those observed in a sternoclavicular biopsy (Fig. 5); chronic active hypertrophic synovitis, rheumatoid arthritis, A.R.A. Stage I. Magnification × 210. Reprinted by permission from Zevely, H.: Am. J. Med. 20: 510, 1956.

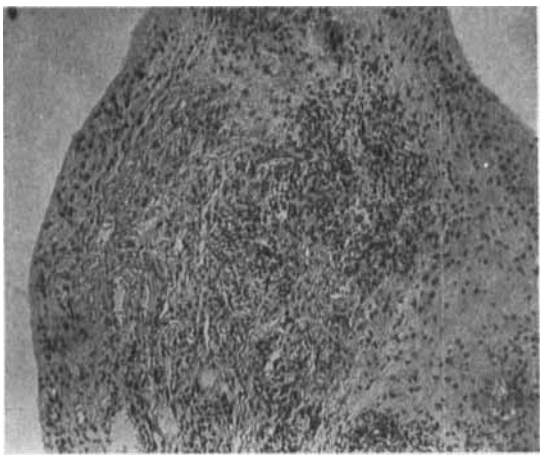

Fig. 7. (Case 5) D.S. Monarticular rheumatoid arthritis, A.R.A. Stage I. Chronic active hypertrophic synovitis. Magnification × 210. Reprinted by permission from Zevely, H.: Am. J. Med. 20: 510, 1956.

feature of the disease, e.g., the tendency to "remissions" and exacerbations. Case 4 is of particular interest in demonstrating the similarity in synovial characteristics in a clinically active and a clinically inactive joint. This recalls the statement of Bick [12] that: "synovial tissue from any one joint bears so close a resemblance to that from other joints when examined microscopically that it cannot be differentiated. This applies to both normal and diseased tissue." In short, even though the clinical features of a remission from rheumatoid arthritis may be well established, one might wonder if the morphological alterations in the synovia ever disappear.

Other Connective Tissue Diseases

To our disappointment, no essential difference in synovial appearance was observed between rheumatoid arthritis and rheumatoid arthritis with the "L.E.cell" phenomenon; Juvenile rheumatoid arthritis; Sjögren's syndrome with rheumatoid arthritis; intermittent hydrarthrosis; "rheumatoid arthritis" with psoriasis and peripheral joint involvement in ankylosing spondylitis. Synovitis, with morphologic features resembling those of rheumatoid arthritis, exists in these conditions. Unfortunately, to our knowledge, there are no additional histologic features which distinguish these conditions with certainty.

Case 6 (Fig. 8) V.K. 758983. This 30 year old woman had a fascinating 18 year history of intermittent effusion of the right knee recurring every twelve to fourteen days and lasting approximately one week. The joint was moderately warm and a definite effusion was present. The sedimentation rate, serum proteins and x-rays were normal; the hemagglutination test was repeatedly negative. On repeated synovial fluid examinations the nucleated cell count ranged from 2 200 to 14 500 per cu ml. of which invariably from 90 to 100 % were mononuclear cells; the physical chemical qualities were essentially normal. In this section through a villus we see low grade cellular infiltration; there is definite hypertrophy of the synovial cell layer, edema is present; perivascular cuffing is especially apparent. The differential diagnosis rests between atypical rheumatoid arthritis and intermittent hydrarthrosis; we personally favor the latter possibility. In this and in subsequent biopsies, however, the morphological features are indistinguishable from those of rheumatoid arthritis.

Synovitis may also occur in rheumatic fever, serum sickness, lupus erythematosus, dermatomyositis and in scleroderma. Certain morphological differences were sometimes apparent in these conditions; often the changes were minimal and limited to very mild cellular infiltration. Generally, however, these were quantitative differences; qualitatively, the alterations in synovia were so similar that synovial biopsy was not conclusive in differentiating these diseases.

Case 7 (Fig. 9) N.N. 859370. Recurrent and cyclic migratory polyarthritis had been present in this 22 year old man for 5 months. Upon admission both knees and ankles were swollen, warm and tender. He was moderately febrile; there was slight tachycardia and right bundle-branch block; the sedimentation rate was 34 mm/hr; there was a moderate blood leukocytosis. The antistreptolysin titer was normal; the C-reactive protein was 6 plus and became normal by the time of discharge. The hemagglutination test was negative; there was reversal of the albumin/globulin ratio; "L. E. cell" were not found; the serum urate was normal. The

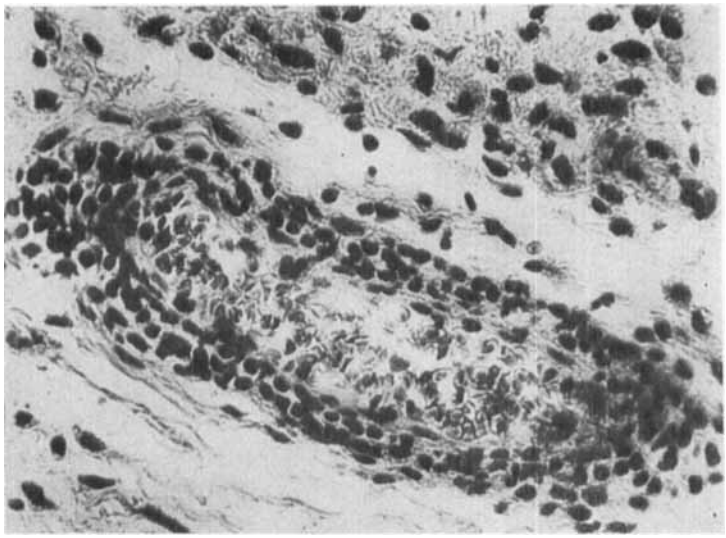

Fig. 8. (Case 6) V.K. Intermittent effusion of a knee of 18 year's duration. Chronic villous synovitis. Intermittent hydrarthrosis or possibly atypical rheumatoid arthritis, A.R.A. Stage I. Magnification × 1 000.

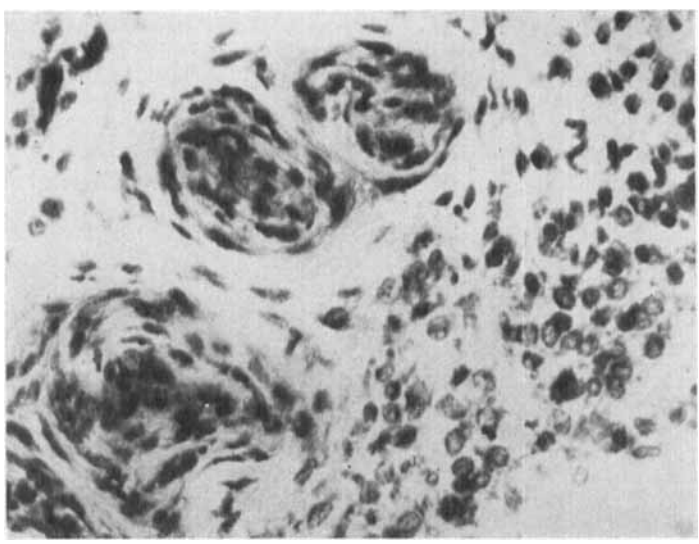

Fig. 9. (Case 7) N.N. Cyclic migratory polyarthritis of 5 month's duration. Proliferation of synovial cells; subsynovial infiltration and increased vascularity. Pathologic changes insufficient to permit histopathological classification. Probably acute rheumatic fever. Magnification × 1 000.

synovial fluid nucleated cell count was 13 300 per cu ml. with 85 % polymorphonuclear leukocytes; mucin clot was good; viscosity was poor. This biopsy material shows proliferation of the synovial cells; subsynovial infiltration and increased vascularity with thickening of the blood vessel walls. It is not normal synovia; it shows some of the features of a mild inflammatory process but pathologic changes are insufficient to permit histopathological classification. This patient responded very satisfactorily to salicylates. The discharge diagnoses was migratory polyarthritis, probably rheumatic fever; palindromic rheumatism, however, still remained a possibility as did rheumatoid arthritis.

Reiter's Syndrome and Infectious Arthritis

Synovial biopsy has been carried out on seven patients with the clinical features of Reiter's syndrome. It was sometimes observed that in this condition the clinical picture, the joint fluid characteristics and synovial morphology appeared to complement one another. In some individuals the synovial fluid and synovial changes were quite similar to those observed in rheumatoid arthritis or, on the other hand, strongly suggested an infectious process because of marked inflammatory infiltrations. In other instances, despite clinical manifestations of a severe inflammatory process in multiple joints, accompanied by striking joint fluid leukocytosis, the synovial morphology was surprisingly inconspicuous, with edema and slight cellular infiltration in the subsynovium.

Acute purulent synovitis, due to pyogenic infections, in the few examples examined by us, is often accompanied by a very high synovial fluid nucleated cell count, sometimes in the range of 200 to 300 thousand cells per cu ml., with a striking polymorphonuclear leukocytosis; the fluid is often quite turbid, containing much cellular debris. The synovial changes are those of intense inflammation with increased vascularity and polymorphonuclear cellular infiltration; necrosis leads to changes in the architecture of the synovia. A purulent exudate is commonly seen in the joint space.

Early diagnosis of tuberculous synovitis is essential to institute appropriate curative chemotherapy. Synovial needle biopsy, productive of material with the characteristic histologic pictures, is a useful adjunct to diagnosis, allowing one to proceed without delay to proper treatment. However, in a patient in whom tuberculous synovitis is suspected and in whom the punch biopsy is negative, one may well be left with no alternative but to proceed to conventional arthrotomy.

Case 8 (Fig. 10) H.T. 806834. This 18 year old boy recovered from pulmonary tuberculosis at the age of 10. Since the age of 4 the right knee had been intermittently painful and swollen. The capsule was thickened; an effusion was present. X-rays showed marked cartilage destruction and subchondral bone changes. The sedimentation rate was normal. Clinically the monarticular arthritis was considered traumatic or infectious in origin. The synovial fluid nucleated cell count was 11 400 per cu ml. of which 48 % were mononuclear cells; the physical chemical qualities were very poor. This synovial biopsy, which is highly magnified, revealed considerable proliferative changes with fibrotic reaction and several lesions highly suggestive of epitheloid tubercles (atypical Langhan's type cells) without caseation necrosis. The patient was placed on antituberculosis therapy; at a later date, by which time the synovial fluid culture had been reported positive for tuberculosis, the joint was fused.

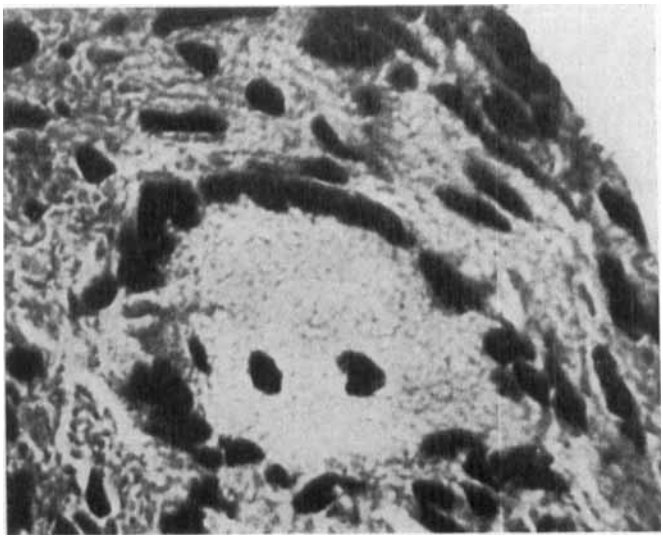

Fig. 10. (Case 8) H.T. Monarticular arthritis (knee) of 14 year's duration. Tuberculous synovitis with atypical Langhan's giant cell; no caseation necrosis. Magnification × 2 000.

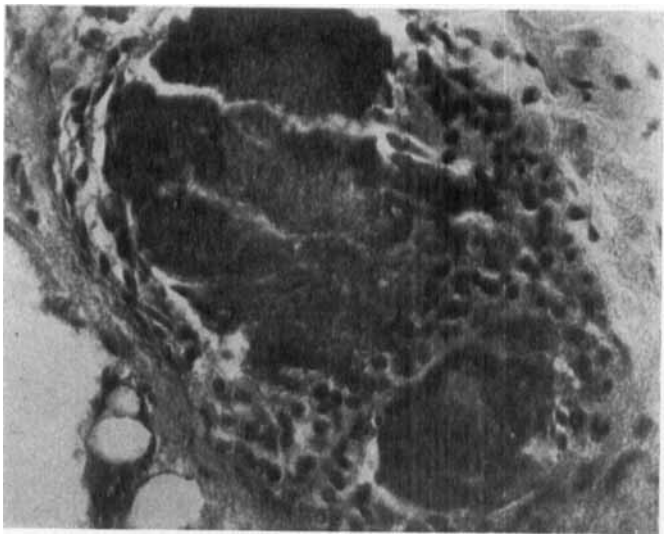

Fig. 11 (Case 9) P.H. Gout without obvious tophi elsewhere; multiple collections of urates in synovium in concentric aggregates surrounded by zone of lymphocytes and plasma cells. Magnification × 1 000.

Gout

In our opinion the only pathogonomonic change encountered in this material was the presence of urate deposists in the synovium from six of the 15 cases of gout. This was a finding we had not anticipated; otherwise, the synovial changes were often indistinguishable from rheumatoid arthritis. Eight of these individuals were experiencing acute gouty arthritis in the biopsied knee joint. The trauma of the biopsy appeared to be well tolerated; instillation of intra-articular hydrocortisone was occasionally helpful at the conclusion of the procedure. In patients with acutely inflamed and sensitive joints premedication with demerol may be advisable. Only three of these patients had visible tophi elsewhere. The serum urate [13] was elevated (6.1 to 14 mgm. per cent) in ten; it was normal (below 6 mgm. per cent) in three. To the best of our knowledge the normal serum urate values did not represent the effect of recently administered uricosuric agents. Urate deposits were observed in material fixed in either formalin (10 %) or absolute alcohol. Since urates may dissolved in formalin, absolute alcohol should be routinely employed as the fixative when the diagnosis of gout is suspected.

Case 9 (Fig. 11) P.H. 785836. Fourteen days before admission this 80 year old man had experienced his initial attack of polyarthritis which began in an elbow, migrating then to a knee and wrist. The knee was warm, tender and contained a moderate effusion. No tophi were visible. The serum urate was repeatedly normal. Th synovial nucleated cell count was 6 450 per cu ml. of which 65 % were polymorphonuclear leukocytes; the physical chemical qualities were very poor. In this synovial specimen there are multiple collections of urates surrounded by a narrow zone of lymphocytes and plasma cells. This specimen was fixed in formalin.

These findings were regarded with great interest for we had not appreciated that urate deposits may appear in the synovium in the initial attack of acute gout. In this individual urates could not be found in the material obtained at a repeat biopsy six days later. In other individuals, with nontophaceous gout of several years duration, urates have been observed in synovium obtained, in asymptomatic periods, from clinically normal knees.

Neuropathic Joint Disease

Biopsy material has been obtained from the knees of 6 patients with neuropathic joint disease; 5 of these individuals had neurosyphilis; the Charcot joint in the other patient was related to spina bifida. The distinguishing feature, in each instance, was the widespread deposition of limesalts in the subsynovium. This finding is not, however, pathogonomic since it may be observed in other conditions, especially where repeated trauma has occurred. Evidence of inflammation was minimal in both the joint fluid and synovial tissue.

Comments

The material described in this study would not have been obtained had the Polley-Bickel synovial biopsy needle not been available. Conventional arthro-

tomy would have been refused by most of these patients because of the period of incapacity and the expense associated with the operation. In contrast, punch biopsy is rapid, it is relatively inexpensive and painless and it is a safe procedure. With experience the incidence of failure to obtain adequate tissue (Table 1) specimens has been under four per cent. It has, we think, been a reasonably successful diagnostic aid. Expert advice is required in interpretation of synovial morphology by whatever means it is obtained. Under the conditions of the study synovium obtained by needle biopsy suggested an incorrect diagnosis or was misleading in only three instances. These statements are not meant to imply that biopsy by this means can ever take the place of arthrotomy when this operation is indicated. The principle limitation associated with the punch biopsy is the fact that it is a blind procedure. The knowledge [7] that synovium may vary widely in appearance from one location in the joint to another is important in this respect and is true for normal as well as diseased tissue. When the procedure yields negative information, or inadequate specimens of tissue, it may be repeated or supplemented with arthrotomy.

Summary

Major complications have not occurred on the 160 occasions that synovial needle biopsy (Polley-Bickel) has been performed in 142 selected patients. This convenient technique may be developed into an invaluable teaching aid in rheumatic diseases and a ready source of material for histochemical study and tissue culture. Incidence of failure to obtain adequate specimens have been about five per cent. Synovial morphological characteristics must always be correlated with pertinent clinical and laboratory information. Histological abnormalities proved to be of definite diagnostic aid in 50 cases; in the remainder, changes were non-specific or too slight to suggest a definite diagnosis. Urate deposists in 6 of 15 cases of gout constituted the only observed pathognomonic change; otherwise, biopsy was most often fruitful in rheumatoid arthritis, neuropathic arthropathy and specific infectious arthritis. No essential difference in synovial appearance was observed between rheumatoid arthritis and juvenile rheumatoid arthritis, peripheral joint involvement in ankylosing spondylitis, "rheumatoid" arthritis with psoriasis and Sjögren's syndrome with rheumatoid arthritis. Within and despite these limitations the procedure may prove a most useful diagnostic tool in selected patients with rheumatic diseases.

ACKNOWLEDGEMENT

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