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Fine-Structural Changes of the Synovial Membrane in Arthrosis Deformans*

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Summary. The known light microscopic findings in the inner part of joint capsules in arthrosis have largely been verified and in part supplemented by scanning and transmission electron microscopic examinations. Whereas in arthrosis of the hip joint sclerosis of the synovial membrane predominates with atrophy of the layer of lining cells, in arthrosis of the knee joint more polymorphic structures of the surface occur with variable but moderate hyperplasia and hypertrophy of the synovial cells. Inflammatory cell proliferations and infiltrates of the same degree as in non-specific arthritis and rheumatoid arthritis were not observed. Thus, the absence both of characteristic changes of the individual synovial cells and of more extensive inflammatory infiltrates in association with atrophy and sclerosis of the synovial folds may be regarded as an indirect indication of the synovial reaction in arthrosis deformans.

Zusammenfassung. Durch raster- und transmissionselektronenmikroskopische Untersuchungen ausgedehnten Synovektomie-Materials wurden die bekannten lichtmikroskopischen Befunde an der inneren Gelenkkapsel weitgehend bestätigt und teilweise ergänzt. Während bei chronischer Coxarthrose die Sklerose der Synovialmembran mit Atrophie der inneren gelenkauskleidenden Zellschicht im Vordergrund steht, kommen bei Gonarthrose polymorphere Oberflächenstrukturen mit wechselnder, im ganzen aber mäßiger Hyperplasie und Hypertrophie der Synovialzellschicht vor. Entzündlich-hyperplastische überschießende Zellproliferationen und Infiltrate wie bei unspezifischer Arthritis und rheumatoider Arthritis werden bei Arthrosis deformans nicht beobachtet. Das Fehlen charakteristischer Veränderungen der einzelnen Synovialzellen und das Fehlen eindeutiger entzündlicher Infiltrate werden zusammen mit der Sklerose und Atrophie der Synovialfalten als indirekter Hinweis auf eine synoviale Reaktion auf arthrotische Gelenkveränderungen gewertet.

The changes of the articular surfaces in arthrosis deformans have been elucidated as to their pathogenetic course; they are predominantly manifested in the joints of the lower extremities due to greater stresses of pressure acting upon them. Subsequently alterations of the synovial membrane appear, when the arthrotic changes of the articular surfaces are advanced. The findings in the synovial membrane are characterized, according to *light microscopic examinations*, by enlargement and numerical increase of the villi (Freund, 1927; Pommer, 1927; Keefer *et al.*, 1934; Parker *et al.*, 1934). Following the studies by Laewen and Biebl (1934), Soeur (1949), and Lang (1958) of the senescent changes of the synovial membrane, Ruckes and Schuckmann (1962) pointed out that fibrosis and hyalinosis of the synovial membrane lead with advancing age and also in

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arthrosis to an increase in distance between the surface and the capillary layer of the synovial membrane. Lloyd-Roberts (1953) additionally observed hyperplasia of the synovial cells. Jaffe (1972) noted, besides hypertrophy and hyperplasia of the lining cell layer adipose, fibrous, and necrotic synovial villi.

Electron microscopic examinations in a few cases of arthrosis deformans were first reported by Roy (1967), and Ghadially and Roy (1969). They observed focal proliferations of B-cells and cells of the intermediate type; the ergastoplasm of the synovial cells was irregular and more tortous, the Golgi apparatus was smaller than in normal synovial cells; fat droplets, rod shaped inclusions, and varying large lysosomes occured. Diagnostic difficulties in delimiting chronic non-specific inflammations from those of rheumatoid arthritis in our sections of synovial tissue led us carry out, in addition to light microscopic studies, scanning and transmission electron microscopic examinations on this material, including all cases of arthrosis deformans.

Clinical Observations

The synovial specimens were obtained from 26 patients with the clinical diagnosis of arthrosis deformans (or osteoarthritis, the designation used in the anglo-american literature); the tissue submitted was in 13 patients from the hip joint, in 12 patients from the knee joint, and in 1 patient from the ankle joint. One of the patients was 40 years old, and the others ranged between 60 and 78 years of age with the symptoms starting shortly before the age of 60 in the latter group. Physical examinations of the involved knee and ankle joints disclosed thickening of the joint capsule, deformity of the articular ends, limited motion, and enlargement of the entire joint. In 6 patients, the affected knee joints contained an effusion of 20 to 60 ml of fluid without increase of the regional temperature. Examinations of the joint fluid disclosed in average 4000 to 6500 cells per ml, with predominance of lymphocytes, and no bacteria; the total protein ranged from 1.8 to 4.0 g/l, the albumen from 1.4 to 2.7 g/l. The sedimentation rate of the blood ranged from 19 to 44 mm per hour; the test for C-reactive protein was positive in 6 cases, but the tests for rheumatoid factor were negative in all cases. The roentgenograms invariably revealed narrowing of the articular space, uneveness of the articular surfaces with subchondral cysts, and protrusion of marginal otheophytes.

The procedures performed were arthrotomies for removal of free bodies or reconstruction of the articular ends, subtotal synovectomies, partial or total arthroplastic replacements of articular ends, and in one case arthrodesis.

Material and Methods

The specimens of synovial tissue obtained at surgery were immediately thereafter separated from their adipose and connective tissue of the outer capsule under buffered glutaraldehyde. For the light microscopic examinations, several strips of synovial membrane were fixed in 10% neutral formaldehyde. The paraffin sections were stained with hematoxylin-esosin, iron-hematoxylin-picrofuchsin (van Gieson) combined with resorcin-fuchsin, Goldners modification of Massons trichrome stain, and the PAS reaction.

For the scanning electron microscopic examinations, the specimens were fixed in buffered glutaraldehyde, postfixed in 2% osmium tetroxyde, washed for two hours, dehydrated in

Fig. 1. Top view of synovial membrane with plump atrophic folds in arthrosis of hip joint. ×60

alcohol of ascending concentrations and dried according to a modification by Rosenbauer and Schlösser (1972) of the Semper method of Schmelzer (1933). After 3 changes in absolute alcohol, the specimens were placed in carbol-xylol, xylol-turpentine oil, and purified turpentine oil. The subsequent drying process was achieved in a thermostat undre revolving air, whereby the specimens shrink less and maintain their property to be cut. One part of the dried specimens was obliquely coated in a Jeol vacuum vaporizer JEE 43 with gold, and the other part with carbon and gold. The specimens were examined with a scanning electron microscope JSM-U3 (JEOL) which was fited out with a SMU 3-Aid additional imaging device for gamma and S control, a four step image enhancer (LWU-Kontron), and an electronic un-distorting device. The photos were taken at an accelerating voltage of 15 and 25 kV.

For the transmission electron microscopic examination 1–2 mm cubic portions of synovial membrane were fixed in buffered glutaraldehyde, postfixed in osmium tetroxyde, dehydrated in alcohols, and embedded in Durcupan or in Araldite. Proper sections of synovial membrane, selected from semithin sections, were contrasted with uranyl acetate and with lead citrate.

Light Microscopic Findings

The synovial membrane of the knee joints showed mostly a cover of one to four rows of synovial cells contigous with each other in varying density. In some instances with more pronounced round cell infiltration of the capillary and subsynovial layers, the lining of synovial cells was broader. Within one knee joint, moderately hyperplastic synovial cells occasionally alternated with less hyperplastic synovial cells. The subsynovial infiltrates occured only perivascularly and focally, and comprised mostly lymphocytes. The synovial villi showed similar and sometimes advanced changes, mainly marked sclerosis of the stroma, like occasionally the flat synovial membrane; their blood vessels were constricted by fibrosis.

The synovial membrane of the hip joints was characterized by more pronounced sclerosis. The inner part of the capsule was sometimes so hyalinized that a continous row of lining cells was no longer recognizable. Also blood vessels of the capillary and subsynovial layer participated in that sclerosis, and underwent fibrous obliteration. Perivascular lymphocyte infiltrates were occasionally observed.

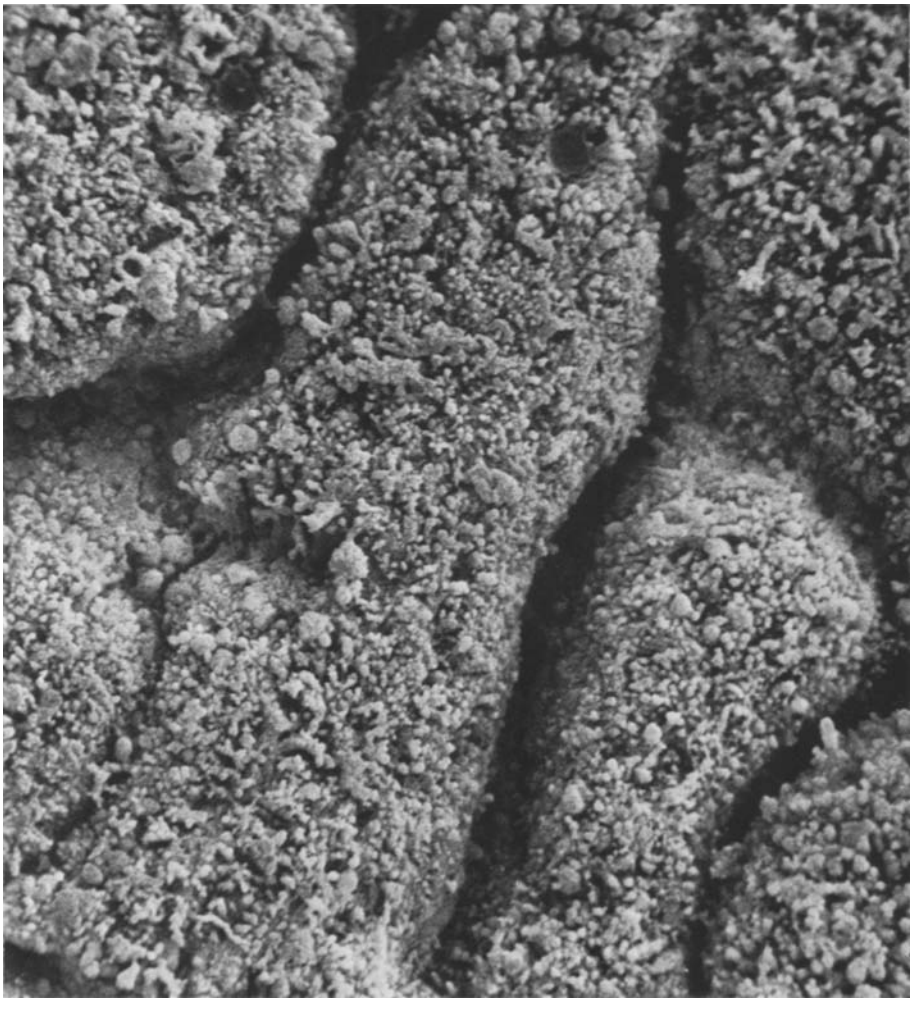

Fig. 2. Varying thick synovial folds with polymorphic surface in arthrosis of knee joint with effusion. ×350

Scanning Electron Microscopic Findings

The folds of the knee joints were relatively coarse, and their surface (Fig. 2) was essentially very cellular and polymorphic. The synovial membranes of the hip joints had a less coarse sometimes almost smooth surface (Fig. 1) which was essentially less cellular and polymorphic than that of the knee joints. Only occasionally inflammatory cells appeared on the surface. In some areas, rounded plump cells predominated, which were covered by a varying dense net of fibrin and strips of hyaline material (Fig. 3). Where synovial cells by themselves without precipitates constituted the surface, two types of cells could be differentiated; one of them was characterized by varying broad, sometimes polygonal

Fig. 3. Partly smoothened deposits of fibrin shreds on the synovial membrane in arthrosis of knee joint with effusion. ×860

processes (Fig. 4), and the other by rather uniform villous protrusions. The intercellular spaces between the lining cells were as polymorphic as the cells themselves, and varied in depth.

Transmission Electron Microscopic Findings

The synovial lining was formed of rows in varying thickness of mostly monomorphic elements. Only rarely accumulations of synovial cells were observed in which the A-cells with numerous lysosomes were of similar proportion as the B-cells with more pronounced ergastoplasm (Fig. 5). In such sections, the lining

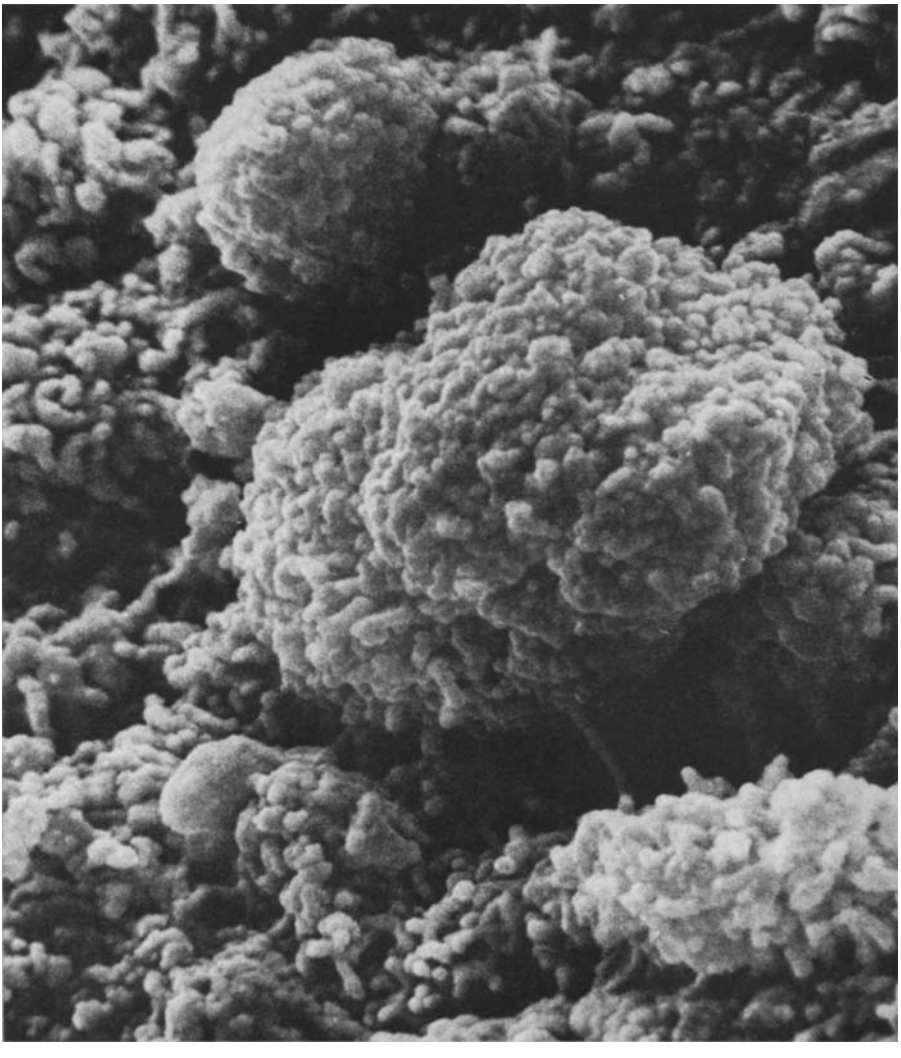

Fig. 4. Synovial cells with irregular villous surface. ×7800

cells had numerous filopodia. However, more frequently (especially in the sections from the hip joint) the synovial cells were cuboidal or rounded, and did not expand conspicious filopodia or villi on to the surface (Fig. 6). In such instances, the B-cells with widened ergastoplasmic tubes predominated. Usually, the cells of loose synovial arrangement had a cytoplasm with only few special organelles. In most sections of synovial membrane the lining cells bordered wide intercellular spaces without discernible intercellular material. Where the superficial cells lay rather close to each other, the intercellular substance was formed of a homogeneous relatively transparent or a fine fibrillar material. No in-

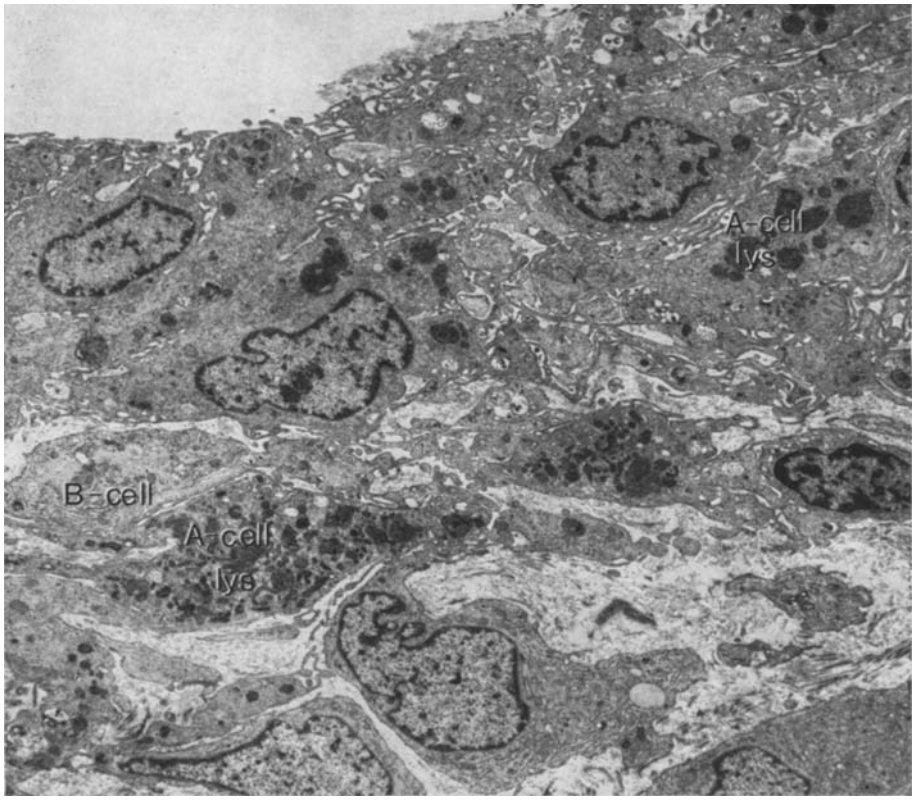

Fig. 5. Cross section of a slighthly hyperplastic synovial membrane with villous surface, numerous A- and B-cells, and with lysosomal activity (*lys.*). ×5300

flammatory cells occured between the lining cells. In a fair number of instances, the superficial layer consisted only of plump cell processes with signs of advanced cytolysis. Sometimes desquamating synovial cells were mixed with cellular detritus and fibrin. Solely in sections of arthrosis of the hip with markedly atrophic and sometimes unicellular synovial layer, mature collagen fibrils lay close to the surface (Fig. 7).

The subsynovial connective tissue showed in some cases focal infiltrates of lymphocytes and a few plasmacytes. In their vicinity occurred fine granular precipitates of calcium salts. The changes of the blood vessels in the capillary layer varied. The endothelial cells of the capillaries were conspiciously large, and were positioned on a delicate basement membrane. The smooth muscle cells in the walls of arterioles and small arteries were often separated by interposed collagen, yet the lumina of these blood vessels were relatively wide.

Discussion

The findings in the synovial membrane varied widely within the totality of the sections. In some instances, infiltrates of chronic inflammatory cells pre-

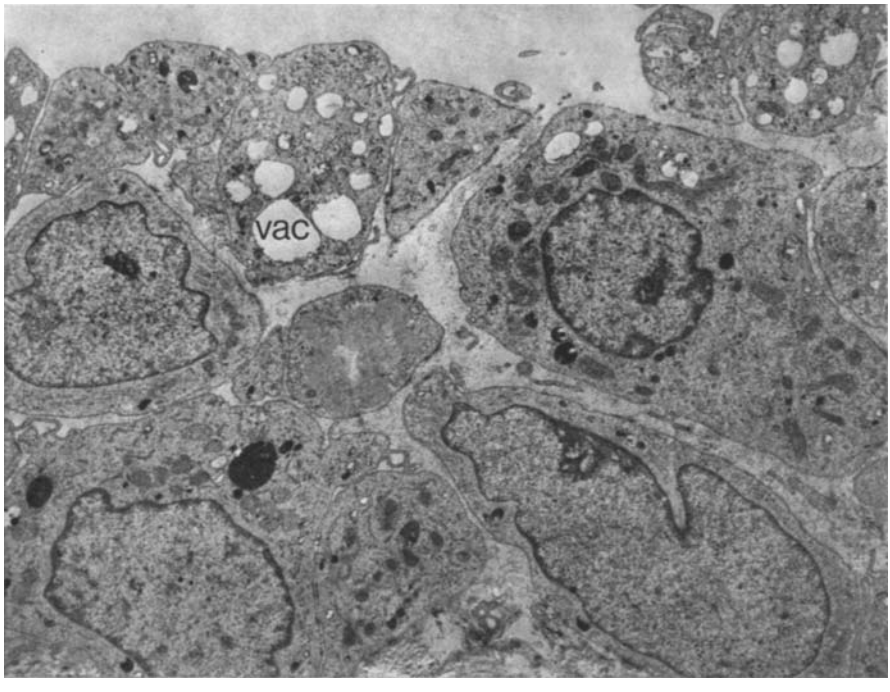

Fig. 6. Rounded atrophic synovial cells in arthrosis of hip joint. Vacuolization (*vac.*) of superficial cells. ×5300

dominated along with moderate hyperplasia and hypertrophy of the synovial membrane; these changes were probably elicited by chronic irritation from the ulcerated articular surface or from separated fragments of cartilage and bones which sometimes also caused hemorrhages. In these cases, the synovial cells had many tentacular processes, and their participitation in the increased formation of joint fluid was suggested by their rich lysosomal content.

Synovial membranes with cuboidal or rounded contour of the cells and monomorphic nuclei probably represented an intermediate stage between the inflammatory reaction and the sclerosis of the synovial membrane.

The full picture of synovial atrophy and sclerosis with development of collagen fibrils up to the single-rowed layer of synovial cells was chiefly pronounced in the sections with arthrosis of the hip joint. In these, the plump surface of the synovial folds and villi as compared with the polymorphic synovial surface in arthrosis of the knee joint became very distinct by the scanning electron microscopy.

Comparison of the outlined types of manifestation of synovial changes in arthrosis indicates that two pathogenetic factors, inflammatory reaction and atrophy or sclerosis, overlap each other in the development of the changes in arthrosis. Differentiation of these changes from those in rheumatoid arthritis is made possible by the more pronounced hyperplasia and hypertrophy of the

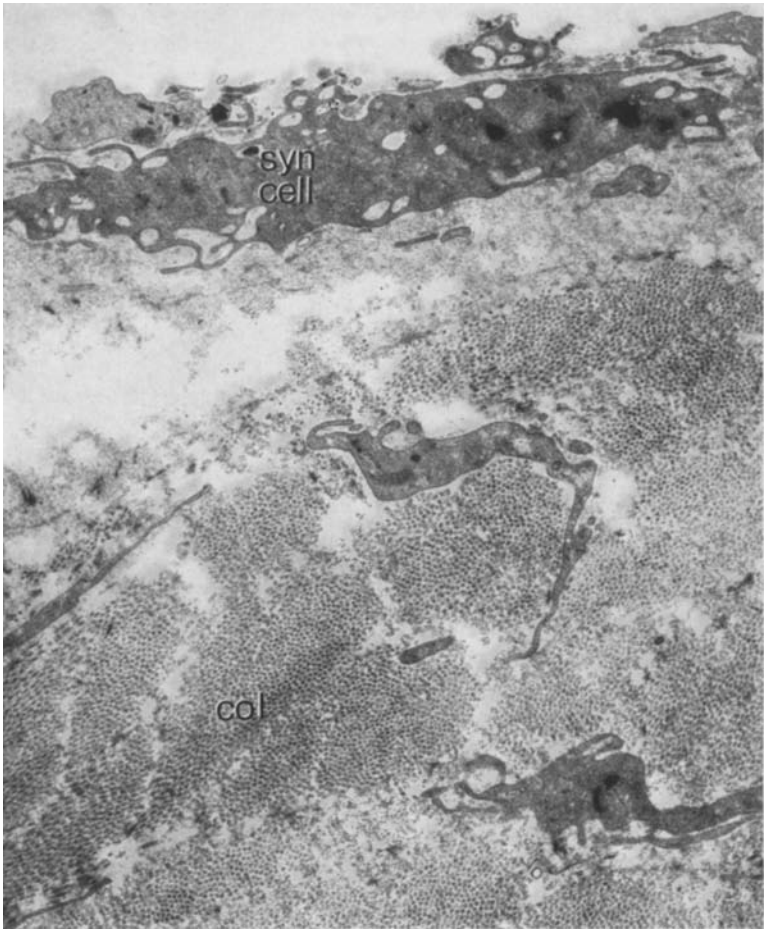

Fig. 7. Sclerosed synovial membrane with single rowed surface layer in arthrosis of hip joint (*col.* mature collagen; *syn. cell* superficial synovial cell). ×13500

synovial membrane in the latter. Also focal necroses and substitution of the synovial cells by fibrinoid, which often occur in rheumatoid arthritis, were only occasionally observed and then scantily in arthrosis (Wyllie *et al.*, 1966; Ghadially and Roy, 1967; Fassbender, 1970; Huth *et al.*, 1972). The monomorphy of the round synovial cells in long standing arthrosis of the hip joint, and in some instances of arthrosis of the knee joint in contrast to rheumatoid arthritis became evident again by scanning electron microscopic examination (Gryfe *et al.*, 1969; Goldie, 1969; Wysocki *et al.*, 1972; Klein *et al.*, 1972).

Inflammatory infiltrates such as narrow lymphocytic and plasmocytic perivascular cuffs were observed in the sections of this study much less frequently and also more scantily than in those of rheumatoid arthritis. The sclerotic changes of the vascular walls in the fibrosed synovial membrane determine the increased

distance between the lumina of the capillaries and the synovial surface as was pointed out by Ruckes and coworkers (1962). By interference in the diffusion and resorption processes of the synovial membrane, sclerosis with obliteration of vascular lumina probably aggravates the arthrotic joint affection. On the other hand, intraarticular effusions seemed to occur in arthrosis, as was observed in the knee joint, when the sclerosing synovial changes were associated with inflammatory infiltrates. The question remains, wether such inflammatory infiltrates promoted the formation of an intraarticular effusion or wether they were merely the expression of a scavenger reaction.

Although the changes of the joint lining cells in arthrosis have been regarded by Lang (1934), Laewen and Biebl (1934), and Ruckes and Schuckmann (1962) as noncharacteristic, a comparison of the findings with those in other joint diseases suggests that the small range of reaction by the synovial membrane and the absence of characteristic cytological changes have to be regarded as an indication of an unspecific synovitis in arthrosis. Even in the presence of inflammatory reactions examination of the synovial membrane permits differential diagnostic evaluation on the fact that the inflammatory reactions involve only focally some areas. In contrast to posttraumatic synovitis, the reactive inflammatory cellular infiltrates are more sparse and less polymorphic.

Scanning electron microscopic and transmission electron microscopic examinations confirmed essentially the changes revealed by light microscopy in the synovial membrane of arthrosis. Beyond this, the comparative examinations disclosed that an exhaustive study of a larger material of specimens permits in some way to infer the nature of the joint affections from the changes of the lining cell layer. In the histopathologic evaluation of synovial membranes from arthrotic joints, the joint from which the tissue was removed has to be taken in consideration. It appears that the type of involved joint, the coadaptation of articular surfaces, and the extent of the articular cavity, the modality of incoming stresses, and the incidence of exposures to traumata may have an essential influence on the reaction of the synovial membrane.

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