Acta orthop. scand. *48*, 129–137, 1977

POSTOPERATIVE SYNOVIAL FLUID

Metabolic Response to Meniscectomy or Synovectomy

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The metabolic response of synovial tissue to surgery was investigated by synovial fluid analysis after two types of operations, medial meniscectomy and synovectomy. Analyses of intra-articular fluid were also performed in non-operated patients with traumatic effusion or chronic synovitis in the knee. It was found that the knee joint metabolism in chronic synovitis is shifted towards anaerobic glycolysis in both operated and non-operated patients whereas meniscectomized and traumatized knees are more capable of maintaining oxidative metabolism. The data also demonstrate that one of the main reasons for decreased oxygen supply on the articular surface after meniscectomies or synovectomies is excessive intra-articular effusion which, according to earlier investigations, produces pressure in the joint cavity and inhibits local capillary circulation.

Key words: synovial fluid analysis; synovial tissue metabolism; synovial gas tensions; meniscectomy; synovectomy; joint trauma; chronic synovitis; tissue repair

Accepted 21.i.77

The useful information obtained from analysis of the synovial fluid has rendered this procedure an important factor in the diagnosis of joint disease. Under normal conditions the synovial tissue is highly vascular, and it serves as a dialyzing membrane between the joint cavity and the circulation. Plasma dialysate flows into the joint cavity and serves to lubricate as well as to supply oxygen and other nutrients to the joint cartilage (cf. Yehia & Duncan 1975).

Recent investigations have demonstrated that synovial fluid oxygen tension decreases to low levels in the knees of arthritis patients (Falchuk et al. 1970, Lund-Olesen 1970, Treuhaft & McCarty 1971, Goetzl et al. 1974 a, b). In general, the lowest oxygen tensions have been found in inflammatory joint disease, followed in turn by degenerative and traumatic joint disease. These observations suggest the possibility that prolonged synovial fluid hypoxia might cause chondrocyte damage and death at the articular surface.

The low synovial fluid PO_2 in arthritic joints signifies a changeover of local tissue from predominantly aerobic to a largely anaerobic, glycolytic metabolism (McCarty 1974). Ropes & Bauer (1953) observed an inverse relationship between synovial fluid glucose and lactate levels. Glucose diffuses into cells and is phos-

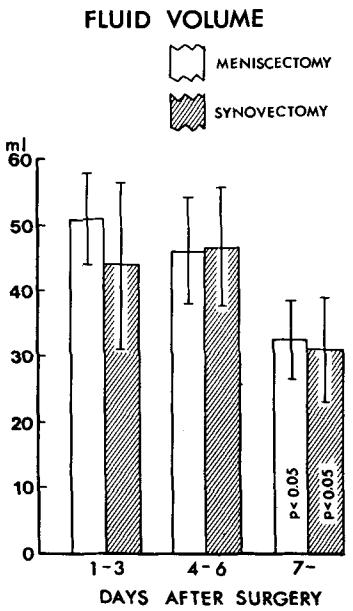


Figure 1. Volumes of postoperative synovial fluids from knees of patients after medial meniscectomy or synovectomy. Each column indicates the mean ± the standard error of the mean. The decreases in fluid volumes between the first and the third time groups were statistically significant ($P < 0.05$ both for meniscectomies and synovectomies; t-test).

phorylated which prevents it from diffusing out again until it is metabolized to pyruvate which in turn is converted to lactate.

Little is known about the metabolic response of synovial tissue to surgical trauma. In the present work this topic was investigated by means of postoperative synovial fluid analysis after two different types of operations, medial meniscectomy and synovectomy. For comparison, synovial fluid analyses were also performed in non-operated hospitalized orthopedic patients with traumatic effusion or chronic synovitis in the knee joint.

PATIENTS AND METHODS

Postoperative synovial fluid analyses were carried out consecutively after 27 medial meniscectomies and 10 synovectomies.

The mean age of the meniscectomy patients was 39 years. Eighteen cases were caused by traumatic distorsion and the preoperative period from the time of injury to the operation varied from 3 to 8 months. In nine patients the rupture was due to degeneration of the semilunar cartilage. The meniscectomies were carried out through a medial curvilinear or transverse incision and no postoperative tube drainage was employed. Mobilization of the knee was started on the first postoperative day, and weightbearing was initiated 10 to 14 days after surgery.

Indications for total synovectomy were rheumatoid arthritis (four patients), degenerative joint disease (three patients), and postoperative arthritis (three patients). The mean age of this group was 36 years. The synovectomies were performed through two separate parapatellar incisions, medial and lateral, followed by 2 days postoperative tube drainage. Mobilization of the knees was started on the first postoperative day and weightbearing was initiated 10 to 14 days after surgery.

Additionally, synovial fluid analyses were performed in five patients with traumatic effusion in the knee joint after a fresh injury (three intra-articular fractures and two distorsions) and in nine non-operated patients with chronic synovitis (six patients with rheumatoid arthritis, two patients with a degenerative joint disease, and one postoperative arthritis).

The knees of the operated patients were inspected daily and if marked fluctuation was noted, all accumulated fluid was aspirated with a sterile hypodermic needle into a heparinized glass syringe. The dead space of the syringe was filled with anoxic saline solution to prevent air bubbles from entering the sample. The volumes of the aspirated fluids were measured and the samples were placed on crushed ice and carried to the laboratory for the assay of PO_2, PCO_2, and pH determination. Samples were injected into a thermostated cuvette containing either a Clark-type oxygen electrode or a Severinghaus carbon dioxide electrode. The electrodes were connected with a gas monitor type PHM 71 (Radiometer, Copenhagen, Denmark). Zero adjustment of the O_2 electrode was obtained with gaseous nitrogen and calibration was performed at 37° C using aerated saline solution with a PO_2 of 150 mmHg. The PCO_2 electrode was calibrated against two moistened gas mixtures with CO_2 tensions of 20 and 60 mmHg, respectively. The pH of the fluid specimens was measured by means of a Radiometer pH meter attached to a Radiometer blood micro system type BMS 2 and the gas monitor.

Glucose in the synovial fluid was measured enzymatically with glucose oxidase (C.P. Boehringer et Soehne GmbH, Germany; Biochemical

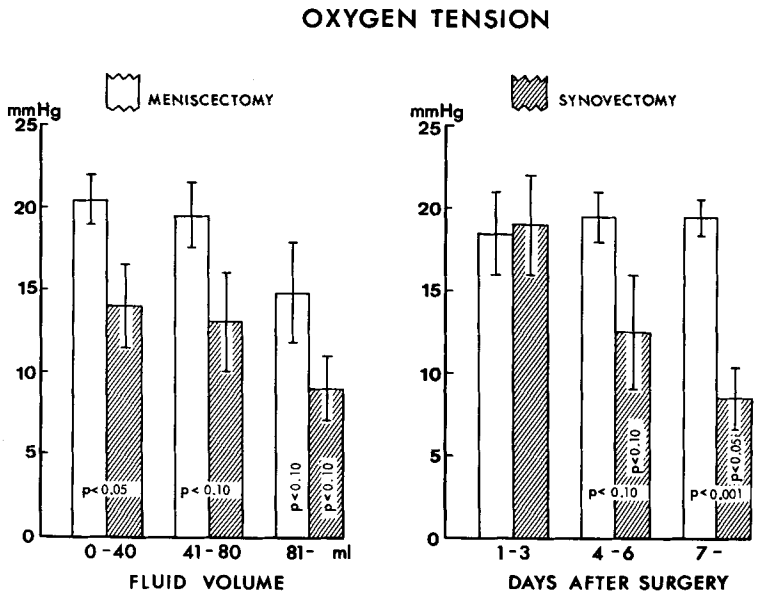


Figure 2. Oxygen tensions of postoperative synovial fluids from knees of patients after medial meniscectomy or synovectomy. In the first volume group the difference in PO_2 levels between meniscectomies and synovectomies was statistically significant ($P < 0.05$). In synovectomized patients, $P < 0.05$ for the decline of PO_2 between the first and the third time group. In the third time group, $P < 0.001$ for the difference of PO_2 between meniscectomies and synovectomies; $P < 0.10$ denotes almost significant.

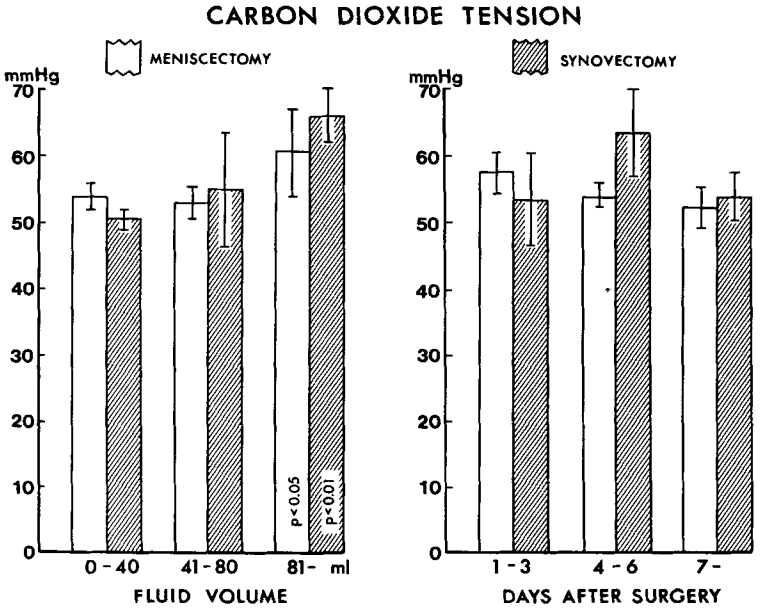


Figure 3. Carbon dioxide tensions of postoperative synovial fluids from knees of patients after medial meniscectomy or synovectomy. The statistically significant results are indicated as P-values (t-test) in the corresponding columns.

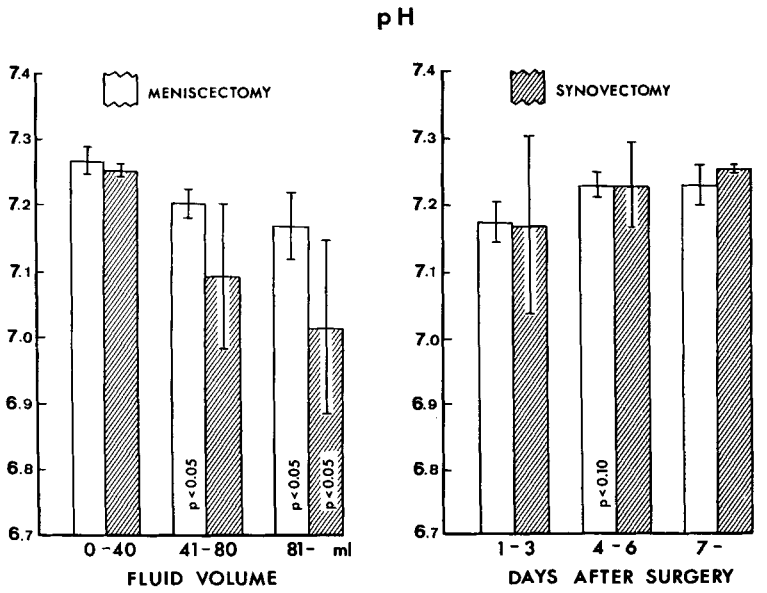


Figure 4. The pH of postoperative synovial fluids from knees of patients after medial meniscectomy or synovectomy.

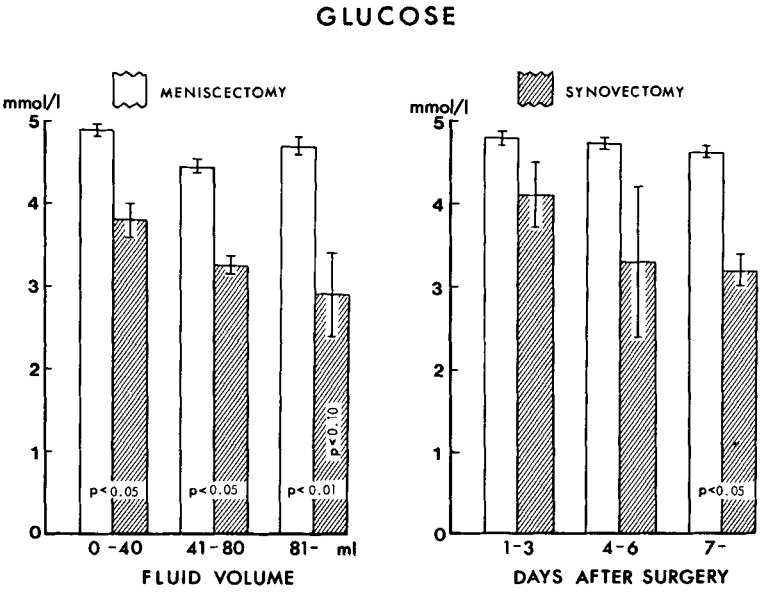


Figure 5. Glucose concentrations of postoperative synovial fluids from knees of patients after medial meniscectomy or synovectomy.

Test Combination). For determinations of synovial fluid pyruvate and lactate, a 1.0-ml aliquot of fluid was deproteinized by adding an equal volume of ice-cold 1.0 M perchloric acid. Pyruvate and lactate were determined by the standard ultraviolet methods (C. P. Boehringer et Soehne GmbH; Biochemical Test Combination) using a Beckman DU spectrophotometer. Hemoglobin was determined as cyanmethemoglobin as recommended by the European Society of Haematology

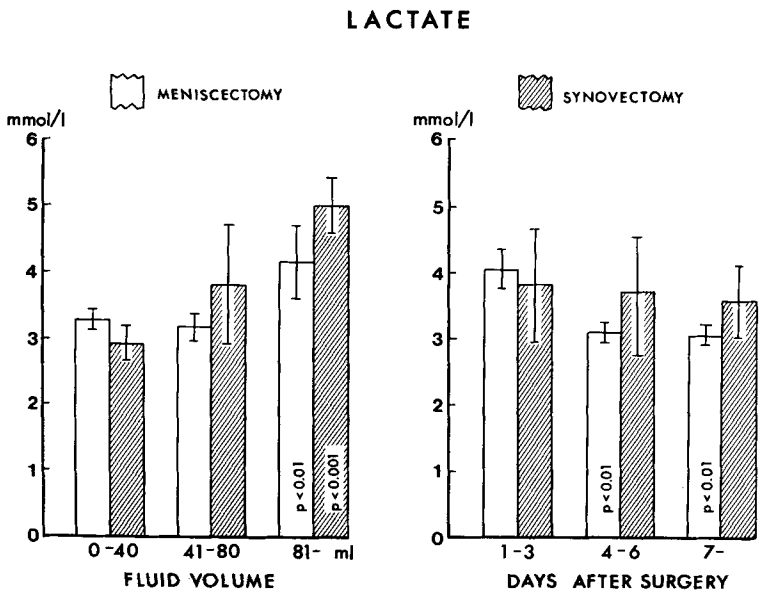


Figure 6. Lactate concentrations of postoperative synovial fluids from knees of patients after medial meniscectomy or synovectomy.

(1965). Protein was assayed with the Folin phenol agent as described by Lowry et al. (1951). Bacteriological examination of synovial fluid samples showed that all joints remained uninfected throughout the study.

The statistical significance of the results was calculated by means of Student's *t*-test and linear regression analysis.

RESULTS

During the postoperative period intra-articular accumulation of fluid declined gradually in both groups (Figure 1). Generally, the PO_2 levels after synovectomies were clearly lower than after meniscectomies (Figure 2). As healing progressed the PO_2 underwent a steep decline in the synovectomy group but remained unchanged after meniscectomies. The PCO_2 values were relatively stable throughout the observation period (Figure 3). Both operated groups showed elevated carbon dioxide tensions in the largest fluid samples. Overall, the mean pH increased slightly during the postoperative period and the lowest values were observed in the largest postsynovectomy fluid samples (Figure 4). Glucose concentrations of the intra-articular fluid were significantly lower after synovectomies than after meniscectomies (Figure 5). The difference in glucose levels between the groups was maintained throughout the observation period. Increases in fluid volumes were generally associated with elevations of lactate and the lactate/pyruvate ratio in both operated groups (Figures 6 and 7). In meniscectomies these parameters declined markedly during the early postoperative period. In both operated groups accumulations of CO_2 and lactate were associated with a linear decrease of pH (for meniscectomies, see Figure 8). In meniscectomized joints the mean hemoglobin concentration decreased noticeably in large fluid volumes but showed no essential changes during the course of healing. After synovectomies intra-articular hemoglobin underwent a slow decrease as tissue repair progressed. Changes in hemoglobin concentration

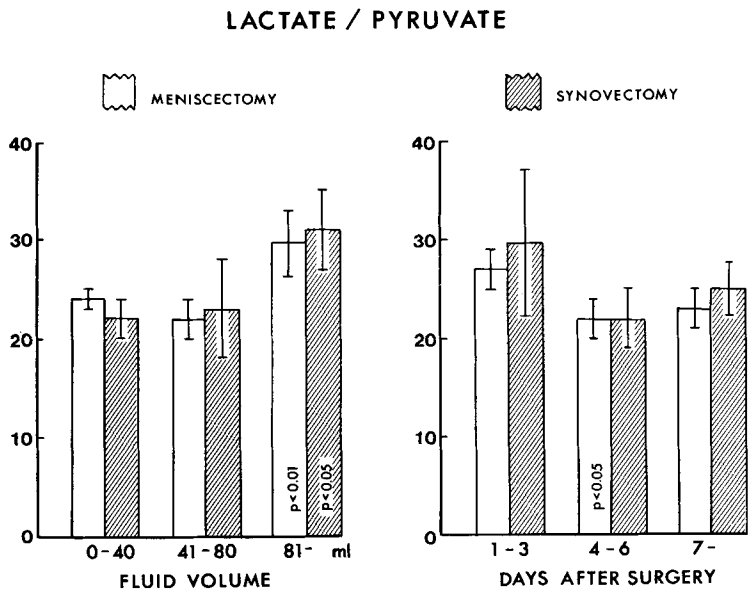


Figure 7. Lactate/pyruvate ratios of postoperative synovial fluids from knees of patients after medial meniscectomy or synovectomy.

were reflected in corresponding changes in total protein in both operated groups (Figure 9).

In meniscectomized joints a high PO_2 level was associated with elevated levels of pH ($r = + 0.65^{**}$) and hemoglobin ($r = + 0.36^{*}$) and with decreased values of PCO_2 ($r = + 0.74^{**}$) and lactate ($r = - 0.40^{*}$). Synovial fluid PCO_2 was directly related to the concentration of lactate ($r = + 0.50^{**}$) and the lactate/pyruvate ratio ($r = + 0.43^{**}$). Inverse relationships were demonstrated between levels of lactate and pH ($r = - 0.36^{*}$), and PCO_2 and pH ($r = - 0.75^{**}$). Intra-articular hemoglobin concentration demonstrated a direct correlation with total protein ($r = 0.94^{**}$).

In synovectomized joints a low PO_2 value was associated with a decreased glucose concentration ($r = + 0.69^{*}$) and lactate/pyruvate ratio ($r = - 0.65^{*}$). Both lactate concentration and lactate/pyruvate ratio were directly related to

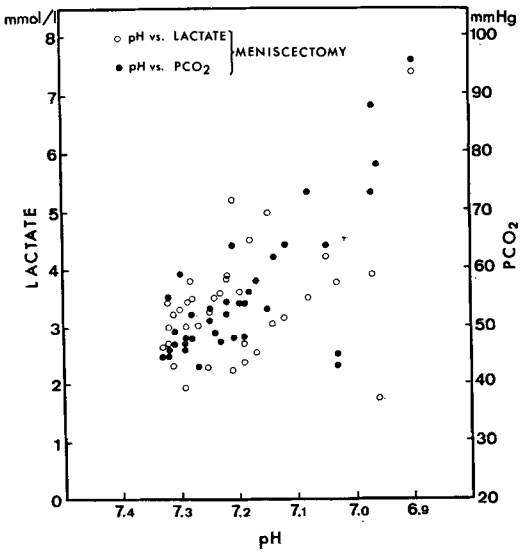


Figure 8. Relationship between postoperative synovial fluid PCO_2 or lactate and pH in knees of patients after medial meniscectomy.

* In linear regression analysis confidence limit for the correlation coefficient r was greater than 95 per cent.

** in linear regression analysis confidence limit for the correlation coefficient r was greater than 99 per cent.

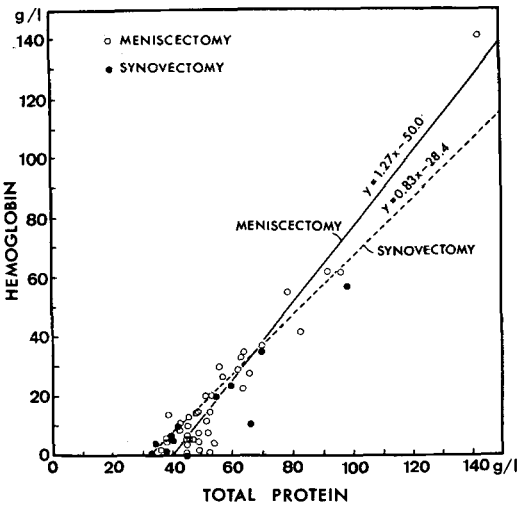


Figure 9. Relationship between hemoglobin and total protein concentrations in postoperative synovial fluids from knees of patients after medial meniscectomy or synovectomy. Linear regression equations are indicated.

carbon dioxide tension, with r= +0.84** and + 0.89**, respectively. Inverse relationships were found between lactate and pH (r = — 0.73*), and PCO_2 and pH (r = — 0.79*). Hemoglobin concentration correlated significantly with total protein concentration (r = + 0.93**).

In non-operated patients traumatic intra-articular effusions possessed markedly higher PO_2 levels, larger concentrations of hemoglobin as well as total protein, and lower lactate/pyruvate ratios compared with synovial fluids from joints with chronic synovitis (Table 1). In non-operated chronic synovitis joints, synovial fluid PCO_2 was inversely related to the levels of PO_2 (r = — 0.66*) and pH (r = — 0.91*).

DISCUSSION

This report suggests that large intra-articular accumulation of fluid reduces the availability of oxygen in the joint cavity (Figure 2). However, it is also possible that formation of fluid and tissue edema are enhanced by local hypoxia. To test the relative importance of these two effects, the following experiment was performed. All fluid accumulated in the joints of four meniscectomy patients and three synovectomy patients was aspirated, fluid volumes were measured, and the analyses mentioned earlier were made. After 24 hours, aspirations and measurements were repeated. The latter samples were 30 to 50 per cent of the original volumes, and the mean PO_2 levels were nearly twice the original values.

Correspondingly, decrease in intra-articular fluid volumes resulted in a decrease of both PCO_2 and the lactate/pyruvate ratio, whereas pH was elevated. These data demonstrate conclusively that one of the main reasons for decreased oxygen supply at the articular surface after meniscectomies or synovectomies is excessive intra-articular effusion. On the other hand, the rate of accumulation of fluid is likely to depend on the extent of trauma produced during surgery.

An additional factor decreasing the PO_2 levels, especially after synovectomy, could be increased oxygen utilization by the large surface of healing tissue. This is supported by the fact that the intra-articular PO_2 declined after synovectomies as healing progressed but remained nearly unchanged in meniscectomized patients. The overall high levels of intra-articular PO_2 in both operated groups in the early postoperative phase were probably caused by capillary bleeding after a fresh trauma and also by diffusion of oxygen from the air during operation.

Intra-articular accumulation of fluid probably produces excessive pressure in the joint cavity and this may inhibit capillary circulation and the supply of oxygen, as well as other nutrients, to the repair area. Jayson & St. John Dixon (1970) demonstrated that the intra-articular pressure in the normal knee at

Table 1. Analysis of synovial fluid in non-operated patients

	No. of patients	Age of patients	Fluid volume (ml)	PO_2 mmHg	PCO_2 mmHg
Trauma *	5	42 ± 11	38 ± 5	28 ± 3	52 ± 4
Synovitis	9	37 ± 6	71 ± 14	12 ± 3	54 ± 3
P (t-test)	–	NS	< 0.10	< 0.01	NS

* Duration from trauma to aspiration of fluid 1 to 3 days.
Figures indicate the mean ± S.E.M.

rest is approximately atmospheric, and with quadriceps contraction it becomes markedly negative. In the presence of effusion, this normal fall in intra-articular pressure is absent, or with larger volumes, reversed, so that a positive pressure results.

Postoperative PCO_2 values were elevated in samples with the largest fluid volumes (Figure 3), suggesting a decreased removal of CO_2 through the capillary bed. The major determinants of hydrogen ion concentration are PCO_2, the amount of lactate and buffering capacity. Therefore, as was expected, the accumulation of both CO_2 and lactate was associated with a decrease in pH (Figure 8). The lowest pH levels were observed in the largest fluid samples (Figure 4).

The low intra-articular glucose concentrations observed after synovectomies (Figure 5) could be due to impaired circulation at the surface of the joint cavity. Ropes & Bauer (1953) showed an inverse relationship between high intra-articular pressure and synovial fluid glucose concentration and suggested that glucose diffusion in the joint is impaired by blood vessel compression.

Results of studies of the concentrations of lactate (Figure 6) and the lactate/pyruvate ratios (Figure 7) showed that increase in the intra-articular fluid volume caused a shift of local metabolism towards anaerobic glycolysis. This change in cellular metabolism tends to increase the glucose consumption and may, therefore, contribute to the decrease of synovial fluid glucose levels. After meniscectomies the levels of the lactate/pyruvate ratio underwent a marked decline during healing, suggesting a change-over to more oxidative metabolism.

Obviously, some of the differences in various parameters between joints with small and large effusions could be due to qualitative alterations in the composition of intra-articular fluid causing variation in the osmotic pressure. Changes in the intra-articular hemoglobin concentration were reflected in corresponding changes in the total protein (Figure 9). Quite expectedly, the fluid hemoglobin levels underwent a gradual decline as post-operative bleeding ceased.

Synovial fluid analyses in non-operated patients indicated that in traumatic joints the intra-articular PO_2 was exceptionally high (28 mmHg), whereas the lactate/pyruvate ratio was lowest for the whole series (Table 1). On the other hand, in chronic synovitis joints the mean PO_2 was as low as 12 mmHg and the lactate/pyruvate ratio was elevated, reaching the levels recorded in post-operative fluid samples. The protein content in traumatic effusions was high due to intra-articular bleeding. Synovial fluid glucose concentrations showed no variation between the non-operated groups.

The present work supports and extends the earlier findings suggesting that the very low oxygen tensions found in synovial fluid from joints with chronic synovitis are pathologic (Lund-Olesen

with traumatic effusion or chronic synovitis in the knee joint.

pH	Glucose mmol/l	Lactate mmol/l	Lactate/ pyruvate	Total protein g/l	Hemoglobin g/l
7.19 ± 0.06	4.60 ± 0.41	3.09 ± 0.65	19.8 ± 1.5	67.0 ± 15.5	36.3 ± 22.3
7.28 ± 0.04	4.40 ± 0.29	3.44 ± 0.23	23.8 ± 1.0	45.3 ± 3.2	0.17 ± 0.12
< 0.10	NS	NS	< 0.05	< 0.05	< 0.05

1970, Treuhaft & McCarty 1971, Falchuk et al. 1971). Widespread obliterative endangitis and very high metabolism of synovial tissue observed in rheumatoid arthritis may affect the oxygen supply of the joint and oxygen consumption (Laws et al. 1963, Dingle & Page 1956). Direct measurements of *in vivo* oxygen consumption have shown that joints with rheumatoid arthritis utilize two to three times the oxygen of control joints (Goetzl et al. 1974 a). Obviously, the white cells present in the joints are not the major determinant of the steady state synovial fluid PO_2. This is supported by the study of Bodel & Hollingsworth (1966) who showed that the respiration of leukocytes in the synovial fluid of rheumatoid joints is less than 50 per cent of that of the leukocytes in peripheral blood.

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