Acta vet. scand. 1985, *26*, 340—351.

From the Institute of Surgery, Royal Veterinary and Agricultural University, Copenhagen, and Institute of Physiology, Odense University, Odense, Denmark.

# EXPERIMENTAL OSTEOARTHRITIS IN THE RABBIT

## III. ACUTE OSTEOARTHRITIS: SUBCHONDRAL $P_{02}$ AND OXYGEN CONSUMPTION AND DIFFUSION CAPACITY IN THE SYNOVIAL MEMBRANE

By

*Eiliv Svalastoga* and *Jørgen Grønlund*

SVALASTOGA, EILIV and JØRGEN GRØNLUND: *Experimental osteoarthritis in the rabbit. III. Acute osteoarthritis: Subchondral $P_{02}$ and oxygen consumption and diffusion capacity in the synovial membrane.* Acta vet. scand 1985, *26*, 340—351. — The earliest sign of osteoarthritis is acute synovitis with joint effusion and elevated intraarticular pressure, which causes compression of the intracapsular vein segments draining the epiphyseal bone compartment. The increased outflow resistance may cause a fall in the regional blood flow and thereby lead to a state of tissue hypoxia. The acute osteoarthritis may also affect the transfer of oxygen to the cartilage across synovial membrane because of the extensive inflammation with hypercellularity and edema.

In the present study we have investigated the subchondral $P_{02}$ and $P_{c02}$ in acute osteoarthritis. There was no significant difference between these gas tensions in the normal and osteoarthritic bone. We have also investigated the oxygen consumption and diffusion capacity in the synovial membrane. The latter was decreased by a factor of 4 in the osteoarthritic joints whilst the oxygen consumption was increased by a factor of 3.

mass spectrometry; membrane-covered catheters; outflow and inflow resistances.

The pathogenesis of primary osteoarthritis is unknown. However, morphological and physiological observations in the joint and epiphyses have led to the suggestion of tissue hypoxia as a pathophysiological mechanism for the degenerative changes in the subchondral bone and cartilage (*Brookes & Helal* 1968, *Arnoldi & Reimann* 1979). The earliest indication of osteoarthritis

is probably acute synovitis with joint effusion and elevated intra-articular pressure, which may cause a decrease in the subchondral blood flow due to the compression of the intracapsular segments of the vein systems draining the epiphyseal bone compartment. Experimental verification of this hypothesis awaits the development of reliable methods to measure the regional blood flow in the bone, but the demonstration of elevated intraosseous pressure in osteoarthritis and in simulated joint effusion have been taken as an indirect support of the hypothesis (*Arnoldi et al.* 1971, 1972, 1979, *Bünger et al.* 1981, 1983, *Grønlund et al.* 1984). At a constant rate of oxygen consumption the decrease in the blood flow inevitably leads to tissue hyoxia, which has been shown to stimulate osteogenic processes in osteoblast cultures (*Brighton et al.* 1969) very similar to those occurring in the osteoarthritic bone. Acute arthritis may also affect the transfer of oxygen to the cartilage across synovial membrane because of extensive inflammation with hypercellularity and edema (*Svalastoga & Reimann* 1985). These changes may increase the length of the diffusion path from the capillaries to the joint cartilage and increase the fraction of oxygen being metabolized on the travel along this path.

Investigations of the pathophysiological mechanisms involved in clinical osteoarthritis are complicated by the many different stages of the disease, the traverse of which may take up to several years. One way of circumventing this problem is to rely upon an experimental model of osteoarthritis and thereby obtain a defined and uniform experimental material with respect to the stage of the disease. Experimental osteoarthritis, which goes from the acute to the chronic stage in less than six months, can be induced in the knee joint of the rabbit by a traumatic insult (*Hulth et al.* 1970).

The present work continues a line of studies (*Kofoed et al.* 1983, *Grønlund et al.* 1984, *Svalastoga et al.* 1984, *Svalastoga & Grønlund* 1985) with the common aim of investigating the role of tissue hypoxia in the pathogenesis of experimental osteoarthritis in the rabbit. In two previous studies (*Kofoed et al.* 1983, *Svalastoga & Grønlund* 1985) we have described methods to measure the subchondral oxygen partial pressure and the rate of oxygen consumption and diffusion capacity in the synovial membrane. Two other studies (*Svalastoga et al.* 1984, *Grønlund et al.* 1984) have shown normal subchondral oxygen and carbon di-

oxide tensions in the end stage of osteoarthritis, and a fall in the subchondral $P_{02}$ and regional blood flow in normal joints after an artificial increase in the joint pressure. A recent study (*Svalastoga & Reimann* 1985) of morphological aspects of the experimental osteoarthritis has shown pronounced edema and hypercellularity in the synovial membrane at the 2 to 4 weeks stage of the disease. In the present study we have investigated the subchondral oxygen partial pressure and the rate of oxygen consumption and diffusion capacity in the synovial membrane of rabbits in this stage.

## MATERIAL AND METHODS

Three weeks before the experiments, 27 rabbits were subjected to an instability operation a.m. Hulth (*Hulth et al.* 1970) to induce unilateral osteoarthritis of the knee joint. This operation includes resection of the medial collateral ligament, extirpation of the medical meniscus and transsection of both cruciate ligaments. The operation was performed under pentobarbitone anaesthesia. At the 3 week stage of the induced osteoarthritis, 13 rabbits were utilized in the study of the subchondral $P_{02}$ and $P_{c02}$ and the remaining 14 rabbits were used to measure the oxygen consumption and diffusion capacity of the synovial membrane.

### *Subchondral $P_{02}$ and $P_{c02}$*

The subchondral $P_{02}$ and $P_{c02}$ were measured by a mass spectrometer (VG Micromass, SX 200, Middlewhich, England) in connection with a membrane-covered catheter, which has been described in detail elsewhere (*Lundsgaard et al.* 1980). The membrane covering the catheter is a diffusion barrier between the surroundings and the high vacuum chamber of the mass spectrometer. Gases, such as oxygen and carbon dioxide, dissolved in the surrounding medium penetrate this barrier at rates proportional to their bulk partial pressures. Thus, when the catheter tip is inserted into the bone tissue, the mass spectrometer signals of oxygen and carbon dioxide are linearly dependent on the local tissue $P_{02}$ and $P_{c02}$ values. The concentration of the catheter used in the present study was slightly modified compared to the previous version with respect to the sintered structure supporting the membrane. The surface of this structure was ground by a new technique which gives a large number of very small diffusion

areas. The advantage of this construction is that the so-called stirring-effect (*Grønlund et al.* 1985) is negligible. In other catheter constructions the oxygen signal depends on the perfusion of the tissue because of a significant, flow-dependent oxygen diffusion gradient in front of the membrane (*Lundsgaard et al.* 1978). In systems without oxygen metabolism or reversible binding of oxygen to hemoglobin this problem can be solved by using an in situ calibration technique based on simultaneous measurement of a reference gas with known partial pressure, but the validity of this technique in the bone tissue is questioned by observations made in the present study (see below). The mass spectrometer was calibrated by recording the oxygen and carbon dioxide signals in a blood sample whose $P_{02}$ and $P_{c02}$ were measured by a conventional acid/base and blood gas analyzer (BMS mk II, Radiometer, Copenhagen, Denmark). The background signals of the mass spectrometer were measured by closing a magnetic valve which separates the high vacuum chamber from the catheter.

The lateral aspects of the femoral condyles were blocked with a local anaesthetic without adrenalin (0.5 ml lidocain, 20 mg/ml). Next, the lateral femoral condyle was penetrated by a bone cannula (inner and outer diameters 1.4 and 2.0 mm) and the tip of the membrane-covered catheter was inserted via the cannula into a position where the diffusion area was exposed to the bone tissue of the medial condyle. The catheter was fixed in this position by a plastic cap which fitted in the flange of the bone cannula and thus prevented blood from leaking out of the bone compartment. The carotid artery was catheterized by an open ended polyethylene tube to enable blood sampling during the experiments. After stabilisation of the mass spectrometer signals of oxygen and carbon dioxide (usually within about 10 min) a blood sample was taken from the catheter in the carotid artery and the membrane-covered catheter was moved to the contralateral condyle. The bone cannula was then connected to a pressure transducer (Siemens-Elema 746) to record the intraosseous pressure. Finally, after measurement of the subchondral $P_{02}$, $P_{c02}$ and pressure, the rabbit was sacrificed by an overdose of pentobarbitone.

*Oxygen consumption and diffusion capacity in the synovial membrane*

A detailed description of the method and the experimental procedure and setup is given elsewhere (*Svalastoga & Grønlund* 1985). In short, the principle is to perfuse the joint cavity by saline saturated with atmospheric air and to record the oxygen partial pressure at different perfusion rates in the perfusate flowing out of the joint cavity. The partial pressure is measured by a catheter similar to that utilized in the measurement of the subchondral $P_{o2}$ and $P_{co2}$. Oxygen is removed from the saline perfusing the joint cavity partly due to the metabolism of the synovial membrane and partly due to the oxygen diffusion across the membrane along the partial pressure gradient from the perfusate to the capillary blood. A mathematical model of the system is used to derive an analytical expression for the relationship between the perfusion rate and the oxygen partial pressure in the perfusate flowing out of the joint cavity. The rate of oxygen consumption and diffusion capacity of the synovial membrane are formal parameters of the derived expression, which therefore allows the determination of their numerical values by a least square fit of the expression to the experimental data. Experiments were rejected if blood was detected in the perfusate or the perfusate accumulated in the joint cavity. By following this procedure, we obtained 48 points on the perfusate $P_{o2}$ vs. perfusion rate curve in 11 of the 14 osteoarthritic joints and 63 points in the 14 normal joints (reported previously, *Svalastoga & Grønlund* 1985).

## RESULTS

Fig. 1 shows the effect of stirring on the mass spectrometer signals of oxygen, carbon dioxide and the inert gas argon measured by the original (1A) and the modified version (1B) of the catheter. The signals were measured in a thermostatted (37°C) blood sample, which was stirred by repeated manual movements of the catheter up and down in the sample. The figure shows a considerable stirring effect of the oxygen and argon signals measured by the unmodified catheter. The relative magnitude of the stirring effect, defined as the change in the signal caused by stirring relative to the total signal, is 2.5 times larger for argon than for oxygen. However, the oxygen signal

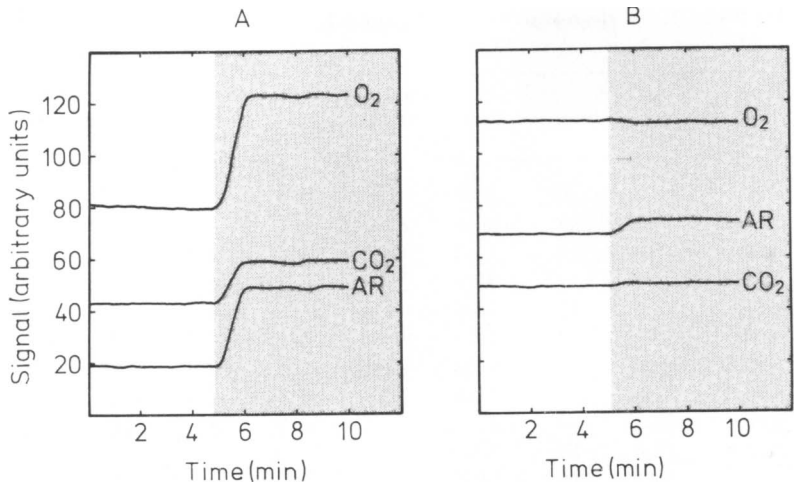


Figure 1. Effect of stirring on the mass spectrometer signals of $O_2$, $CO_2$ and Ar with the original (A and the modified (B) version of the membrane-covered catheter utilized in the study. Sheded areas show the signals obtained in the stirred blood sample.

obtained via the modified version of the catheter is practically unaffected by the stirring (Fig. 1B). The difference between the stirring effects of argon and oxygen casts doubt on the validity of a previously applied technique (*Kofoed et al.* 1983) to correct for the stirring effect of the oxygen signal by using argon as a reference gas.

Table 1 shows the subchondral $P_{02}$, $P_{c02}$ and pressure recorded in the normal and osteoarthritic bone together with the simultaneously measured arterial blood gases. Mean and standard error of mean (SEM) are given for each group of data. The data were analyzed by a computer with a multivariance program package (SAS, General Linear Models, *Helvig & Council* 1979). The difference between the subchondral pressures on the two sides is highly significant ($P < 0.01$), whilst the differences between the two sets of data of the subchondral $P_{02}$ and $P_{c02}$ are non-significant ($P > 0.05$, t-test). There is a significant positive correlation between the subchondral and arterial $P_{02}$ values ($P < 0.05$).

Fig. 2 shows the measured $P_{02}$ values in the perfusate flowing out of the osteoarthritic joint cavity as a function of the perfusion rate. The connected points were obtained in the same joints. A data reduction technique, which was described in a

Table 1. Subchondral $P_{02}$, $P_{c02}$ and pressure and arterial gas tensions obtained in 13 rabbits with unilateral osteoarthritis.

| Animal No. | Normal bone | | | Normal blood | | Synovitis bone | | | Synovitis blood | |
|---|---|---|---|---|---|---|---|---|---|---|
| | $P_{02}$ | $Pc_{02}$ (Torr) | Pressure | $P_{02}$ (Torr) | $Pc_{02}$ | $P_{02}$ | $Pc_{02}$ (Torr) | Pressure | $P_{02}$ (Torr) | $Pc_{02}$ |
| 1 | 32.7 | 59.8 | 6 | 78.7 | 41.5 | 35.4 | 40.7 | 18 | 62.1 | 43.0 |
| 2 | 25.8 | 50.6 | 27 | 66.0 | 38.1 | 20.1 | 51.0 | 36 | 58.2 | 39.4 |
| 3 | 34.9 | 37.8 | 14 | 45.3 | 41.6 | 24.3 | 64.7 | 32 | 43.1 | 39.3 |
| 4 | 68.3 | 30.4 | 7 | 88.9 | 34.5 | 54.2 | 43.5 | 28 | 100.4 | 34.8 |
| 5 | 17.7 | 55.7 | 17 | 50.4 | 40.1 | 19.2 | 54.7 | 23 | 42.4 | 36.9 |
| 6 | 40.7 | 35.0 | 9 | 54.4 | 44.0 | 35.5 | 36.2 | 7 | 44.7 | 42.4 |
| 7 | 25.8 | 48.6 | 18 | 91.2 | 28.9 | 15.5 | 57.9 | 38 | 56.7 | 33.3 |
| 8 | 38.9 | 42.8 | 8 | 54.9 | 34.5 | 35.9 | 56.6 | 22 | 54.6 | 34.5 |
| 9 | 40.4 | 64.3 | 4 | 77.0 | 43.4 | 54.9 | 53.9 | 12 | 85.5 | 38.0 |
| 10 | 28.1 | 75.8 | 10 | 37.0 | 50.2 | 45.0 | 73.6 | 22 | 48.9 | 51.8 |
| 11 | 74.8 | 40.7 | 15 | 92.5 | 31.0 | 30.7 | 56.9 | 27 | 84.2 | 36.9 |
| 12 | 19.3 | 49.6 | 30 | 76.5 | 30.5 | 31.8 | 57.0 | 36 | 95.4 | 32.4 |
| 13 | 28.8 | 46.3 | 32 | 65.2 | 41.2 | 4.2 | 91.6 | 37 | 66.6 | 43.4 |
| Mean | 36.6 | 49.0 | 15 | 67.5 | 38.4 | 31.3 | 56.8 | 26 | 64.8 | 38.9 |
| SEM | ± 4.8 | ± 3.5 | ± 3 | ± 5.1 | ± 1.7 | ± 4.1 | ± 4.0 | ± 3 | ± 5.6 | ± 1.5 |

previous study (*Svalastoga & Grønlund* 1985), was utilized to extract the numerical values of the rate of oxygen consumption and the diffusion capacity of the synovial membrane from the data in Fig. 2. The standard deviations of the two parameters were estimated by a previously described simulation technique. The results obtained in the normal (identical to those given by *Svalastoga & Grønlund* 1985) and the osteoarthritic joints are shown in Table 2. The diffusion capacity in the osteoarthritic joints is 4 times lower than in the normal joints and the rate of oxygen consumption is 3 times higher. The diffusion capacity in the osteoarthritic joints is significantly lower ($P < 0.05$) and the oxygen consumption is significantly higher ($P < 0.05$) than the corresponding normal values.

## DISCUSSION

The measurement of the oxygen partial pressure in tissue by membrane-covered sensors such as polarographic electrodes and mass spectrometer inlets is complicated by the existence of an oxygen diffusion gradient in front of the membrane (the so-called stirring effect). In previous studies we have attempted to solve this problem by simultaneous measurement of oxygen and

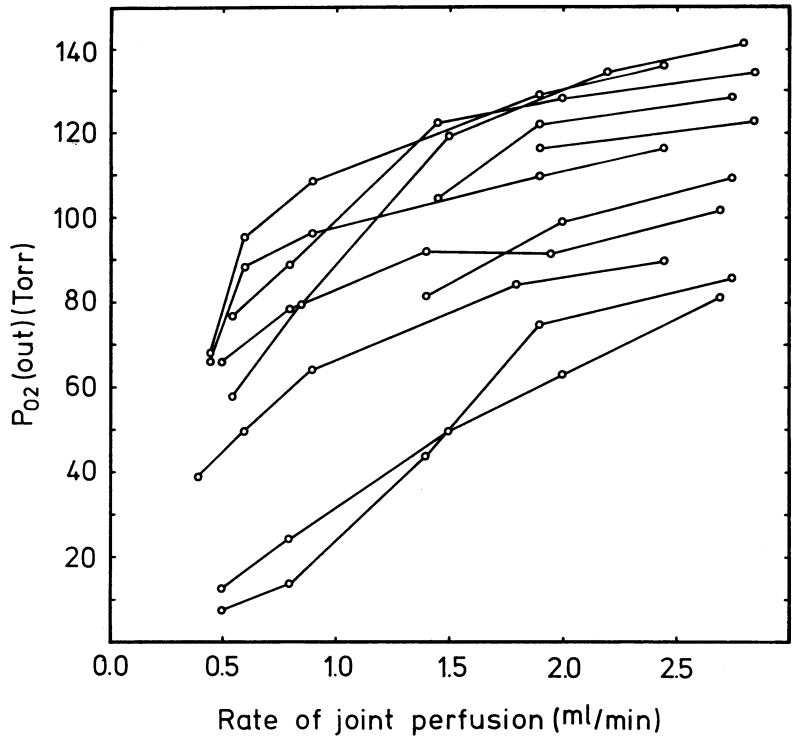


Figure 2. Relationship between $P_{02}$ in the perfusate flowing out of the joint cavity and the perfusion rate. Experimental points obtained in the same joints are connected.

Table 2. Rate of oxygen consumption and diffusion capacity in the synovial membrane of normal and osteoarthritic joints.

| | Diffusion capacity (± s) [µl $O_2$/min/Torr] | Oxygen consumption (± s) [µl $O_2$/min] |
|---|---|---|
| Normal | 0.039 ± 0.013 | 0.93 ± 0.90 |
| Synovitis | 0.010 ± 0.009 | 2.88 ± 0.47 |

a reference gas, argon, whose partial pressure has a fixed value of 0.93 % of the barometric pressure (= 7.1 Torr). The similarity between oxygen and argon with respect to the solubility and diffusion coefficients led to the assumption that the relative error caused by the stirring effect in the measured argon and oxygen partial pressures are equal. The observations in blood of a significant difference between the two stirring effects (above) gave

the impetus to the development of a new version of the membrane-covered catheter. The new catheter has a non-negligible stirring effect for argon in both blood (Fig. 1) and in the subchondral bone tissue. The subchondral argon partial pressure was measured together with the $P_{o2}$ and $P_{co2}$ values and found to be 22 % lower than the true $P_{Ar}$. We have chosen not to utilize the numerical value of this error to correct the measured oxygen partial pressure because the experiment in the blood sample (Fig. 1) provided a strong indication for the existence of an effectively negligible stirring effect of oxygen in the bone.

The combination of elevated intraosseous pressure and normal values of the subchondral $P_{o2}$ and $P_{co2}$ in osteoarthritis has several possible explanations. The elevated intraosseous pressure can be explained either by a decrease in the inflow resistance of the subchondral bone or an increase in the outflow resistance. The anatomical arrangement of the epiphyseal vein system (*Brookes et al.* 1961), the extensive histological changes in the synovial membrane (*Svalastoga & Reimann* 1985) and the increased joint pressure of osteoarthritis speak in favour of the latter explanation. The unchanged subchondral $P_{o2}$ and $P_{co2}$ in osteoarthritis can either be attributed to a fall in the rate of oxygen consumption in the bone compensatory decrease in the inflow resistance to maintain a constant regional blood flow. If it is assumed that the arterial pressure is 80 Torr and the venous pressure is 5 Torr the pressure drop across the inflow and outflow resistance in the normal joints are 65 Torr and 10 Torr (see Table 1). In the osteoarthritic joints the corresponding values are 54 and 21 Torr. These data show that despite an increase in the outflow resistance by 110 % the regional blood can be maintained at the normal level by a compensatory decrease in the inflow resistance of only 17 %. Thus, a possible mechanism to explain the unaltered gas tensions in osteoarthritis is that the initial increase in the outflow resistance causes a decrease in the regional blood flow and $P_{o2}$ and an increase in $P_{co2}$ and that these changes elicit a regulatory response in the inflow resistance to protect the tissue against the hypoxic insult. A previous study (*Grønlund et al.* 1984) have shown that this mechanism is unable to protect against hypoxia at very high joint pressures ($> 75$ Torr). Therefore the results reported here do not exclude hypoxia as a pathogenetic factor in osteoarthritis because active

movements in the joint may provoke intraarticular pressure spikes, which are absent in the immobilized animal.

The validity of the method used to measure the oxygen consumption and diffusion capacity has been discussed previously (*Svalastoga & Grønlund* 1985). The results support the hypothesis that tissue hypoxia plays an important role in the pathogenesis of the extensive degenerative changes in the joint cartilage of osteoarthritis. A dramatic fall in the transfer of oxygen across the synovial membrane is expected to occur when a reduction in the diffusion capacity by a factor of 4 is combined with an increase in the rate of oxygen consumption by 200 %. Previous calculations (*Svalastoga & Grønlund* 1985) have shown that this combination of changes in the oxygen transfer characteristics of the synovial membrane may lead to a change in the oxygen tension of the synovia from about 80 Torr to a value close to zero, and thereby cause a hypoxic insult to the chondrocytes. This conclusion is supported by previous observations in rheumatoid arthritis (*Lund-Olesen* 1970). *Lund-Olesen* managed to aspirate synovia from human joints with rheumatoid arthritis and found an average oxygen tension of 27 Torr as compared with the control value of 63 Torr.

*Goetzl et al.* (1971) used an experimental design, which allowed estimation of the in vivo oxygen consumption of the synovial membrane in human joints with rheumatoid arthritis. The rate of oxygen consumption was found to be 2—3 times higher than the value in the control group.

## ACKNOWLEDGEMENTS

The technical assistance of Birgit Jensen is warmly acknowledged. The work was supported by a grant from the Leo Research Foundation.

## REFERENCES

*Arnoldi, C. C., R. L. Lemberg & H. Linderholm:* Immediate effect of osteotomy on the intramedullary pressure of the femoral head and neck in patients with degenerative osteoarthritis. Acta orthop. scand. 1971, *42*, 357—365.

*Arnoldi, C. C., H. Linderholm & H. Müssbichler:* Venous engorgement and intraosseous hypertension in osteoarthritis of the hip. J. Bone Jt. Surg. 1972, *54B*, 409—421.

*Arnoldi, C. C. & I. Reimann:* The pathomechanism of human coxarthrosis. Acta orthop. scand. 1979, Suppl. 181.

*Arnoldi, C. C., I. Reimann, S. Bach Christensen & S. Mortensen:* The effect of increased intra-articular pressure on juxta-articular bone marrow pressure. IRCS Med. Sci. 1979, 7, 471.

*Brighton, C. T., R. D. Ray & L. W. Soble:* In vitro epiphyseal plate growth in various oxygen tensions. J. Bone Jt. Surg. 1969, *51A*, 1383—1396.

*Brookes, M., A. C. Elkin, R. G. Harrison & C. B. Heald:* A new concept of capillary circulation in bone cortex. Lancet 1961, *7186*, 1078—1081.

*Brookes, M. & B. Helal:* Primary Osteoarthritis, Venous Engorgement and Osteogenesis. J. Bone Jt. Surg. 1968, *50B*, 493—504.

*Bünger, C., S. Sørensen, J. C. Djurhuus & U. Lucht:* Intraosseous pressures in the knee in relation to simulated joint effusion, joint position, and venous obstruction. Scand. J. Rheum. 1981, *10*, 283—288.

*Bünger, C., S. Harving, J. Hjermind & H. Bünger:* Relationship between intraosseous pressures and intra-articular pressure in arthritis of the knee. Acta orthop. scand. 1983, *54*, 188—193.

*Goetzl, E. J., K. H. Falchuk, L. S. Zeiger, A. L. Sullivan, C. L. Hebert, J. P. Adams & J. L. Decker:* A physiological approach to the assessment of the disease activity in rheumatoid arthritis. J. clin. Invest. 1971, *50*, 1167—1180.

*Grønlund, J., H. Kofoed & E. Svalastoga:* Effect of increased knee joint pressure on oxygen tension and blood flow in subchondral bone. Acta physiol. scand. 1984, *121*, 127—131.

*Grønlund, J., O. Johansen & B. Jensen:* New transcutaneous $pO_2$ probe based on mass spectrometry with lov stirring effect. Med. & Biol. Eng. Comp. 1985, *23*, 254—257.

*Helvig, J. T. & K. A. Council:* SAS User's Guide. SAS Institute Raleigh, North Carolina, USA, 1979.

*Hulth, A., L. Lindbjerg & H. Telhag:* Experimental osteoarthritis in rabbits. Acta orthop. scand. 1970, *41*, 522—530.

*Kofoed, H., E. Svalastoga, J. Grønlund, B. Jensen, J. Kofoed & P. Svendsen:* Continuous measurement of subchondral $P_{02}$ and $P_{c02}$ by mass spectrometry. IRCS Med. Sci. 1983, *11*, 583—584.

*Lund-Olesen, K.:* Oxygen tension in synovial fluids. Arth. Rheum. 1970, *13*, 769—776.

*Lundsgaard, J. S., J. Grønlund & N. Einer-Jensen:* In vivo calibration of flow dependent blood gas catheters. J. appl. Physiol. 1978, *44*, 124—128.

*Lundsgaard, J. S., B. Jensen & J. Grønlund:* Fast responding flow independent blood gas catheters for oxygen measurement. J. appl. Physiol. 1980, *48*, 376—381.

*Svalastoga, E., J. Grønlund & H. Kofoed:* Subchondral $P_{02}$ and $P_{c02}$ are unaffected in experimental arthrosis. Acta orthop. scand. 1984, *55*, 514—516.

*Svalastoga, E. & J. Grønlund:* Experimental osteoarthritis in the rabbit. II. A new method to estimate the oxygen consumption and

diffusion capacity in the synovial membrane of the knee. Acta vet. scand. 1985, *26*, 326—339.

*Svalastoga, E. & I. Reimann:* Experimental osteoarthritis in the rabbit. I. Histological changes in the synovial membrane. Acta vet. scand. 1985, *26*, 313—325.

SAMMENDRAG

*Eksperimentel osteoartritis hos kaniner. III. Tidlig osteoartritis: Subchondral $P_{02}$ samt synovialmembranens diffusionskapacitet og metabolisme.*

I de tidlige stadier af osteoartritis er der som følge af ledeffusion og øget intraartikulært tryk en øget udløbsmodstand fra det subchondrale knoglekompartment. Dette kan medføre et fald i det regionale blood flow og dermed føre til subchondral hypoxi. Desuden er synovialmembranen inflammeret i de tidlige stadier med hypercellularitet og ødem, hvilket vil kunne nedsætte iltoverførslen fra kapillærerne til synovi.

I nærværende arbejde har vi ikke kunnet påvise ændringer i de subchondrale gastensioner i det akutte stadium men synovialmembranens metabolisme var øget med en faktor 3 og diffusionskapaciteten nedsat med en faktor 4.

*(Received April 30, 1985).*

Reprints may be requested from: Eiliv Svalastoga, the Institute of Surgery, Royal Veterinary and Agricultural University, Bülowsvej 13, DK-1870 Frederiksberg C, Denmark.