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Hemodynamics and metabolism in arthrosis

Studies in the rabbit knee

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Arthrosis was induced in the rabbit knee, making it unstable by ligament resection. Acidity and hypercapnia were found in the synovial fluid of the arthrotic knees, whereas oxygen partial pressure was normal. In arthrotic subchondral bone the intraosseous pressure and oxygen partial pressure were increased; intraosseous phlebography showed venous congestion. Histologic specimens showed increased subchondral bone formation, loss of cartilage and total depletion of glycosaminoglycans. The synovial membrane was hyperplastic and fibrosis was found in the underlying tissue. We suggest that changes in environmental haemodynamics and metabolism, although secondary in nature, may play an important role in the arthrotic process.

Venous congestion and increased intraosseous pressure (IOP) are known to be associated with arthrosis (Brookes & Helal 1968, Arnoldi et al. 1972, Arnoldi & Reimann 1979). *In vitro* studies of synovial fluid from degenerated joints have shown this to be relatively acidotic and sometimes hypoxic (Falchuck et al. 1970, Lund-Olesen 1970, Treuhaft & McCarty 1971).

The hemodynamic and metabolic environment of bone and joint structures in mature arthrosis has not been investigated previously. We have studied these parameters in an arthrosis model (Telhag & Lindberg 1972) and compared these findings with the results of measurement at the 3-week stage in the same model (Kofoed 1984).

Material and method

Seven adult female rabbits weighing 3.5 kg were used for the investigation. Eleven months prior to the measurements, the right knee joint was made by ligament resection to induce arthrosis (Telhag & Lindberg 1972). The left knee was used as control.

The animals were anaesthetized with pentobarbitone (25 mg/kg) i.v. and kept on spontaneous respiration. At locations where catheters and cannula were to be inserted, local anaesthesia was supplied (1 ml of 1 per cent Lidocain®. To avoid blood clotting 2500 IU heparin i.v. was used. The right carotid artery was cannulated to record mean arterial pressure and for acid-base and blood gas analysis (ABL-3, Radiometer, DK). Special bone cannulae (outer diameter 2.0 mm, inner diameter 1.4 mm) were introduced percutaneously into the subchondral bone of the medial femoral and tibial condyles, using image intensification to check the correct position. An identical cannula was introduced percutaneously into the knee joint through the patellar tendon, with the tip situated between the femoral condyles. Initially, the intraosseous pressure in both medial femoral condyles was measured by pressure transducers (Bentley Trantec 800®, UK) connected to a writer (Elema-Schönander, S). Following this, blood gas catheter (Lundsgaard et al. 1980) connected to the high vacuum chamber of a mass spectrometer (SX-200, VG Gas Analysis Ltd., UK), was introduced into the subchrondral bone of the femoral condyle. Oxygen and carbon dioxide tensions (pO_2 and pCO_2) were measured simultaneously and continuously *in vivo* until stable signals were obtained (within 5 min) and continued for 10 min, using the simultaneously measured argon signal for *in situ* calibration (Kofoed et al. 1983). After pO_2 and pCO_2 had been measured, pH was measured by a monocrystalline antimony pH-electrode (Kofoed & Lindenberg 1984), using the cannula in the tibial condyle for a calomel pH-reference electrode and the previously measured pO_2 for correction of the oxygen sensibility of the antimony electrode. pH was then measured in the synovial fluid by the same pH-electrode, and finally pO_2 and pCO_2 were measured *in vivo* in the synovial fluid by mass spectrometry. Arterial blood samples were drawn and analysed at the conclusion of every measuring procedure. The normal and the osteoarthrotic

side were alternated as the first side in the measuring procedure to avoid bias.

Following the measuring procedures, intraosseous phlebography was performed, using the cannula in the femoral condyles. 1 ml of 60 per cent Iodapaque® was injected simultaneously into the subchondral bone of the femoral condyles in 15 s. Radiographic exposures were taken 15, 45 and 180 s after the injection.

The animals were killed by an overdose of pentobarbitone, after which the knee joints were removed and fixed in formalin for 4 weeks and decalcified in formic acid for another 4 weeks. Specimens were taken from the weight-bearing parts of the femoral condyles, from the synovial membrane, and in addition to H & E staining, van Gieson staining was used for estimation of fibrosis in the synovial membrane and Saffranin O to detect depletion of glycoaminoglycans from the cartilage.

For statistical analysis the paired *t*-test and multiple regression analyses were used.

Results

The intraosseous pressure and oxygen partial pressure in the subchondral bone of the arthrotic side were increased ($p < 0.003$). Multiple regression analysis between the pressures and pH showed a correlation between intraosseous pressure and pCO_2 ($r = 0.8955$, $p < 0.002$) in arthrotic bone, but not in the normal control. A negative correlation was also demonstrated between log pCO_2 and pH ($r = -0.8234$, $p < 0.01$) in arthrotic bone, but not in normal bone or in synovial fluid. In arthrotic synovial fluid a significant hypercapnia and acidosis was found ($p < 0.028$ and 0.027, respectively) (Tables 1 and 2).

The phlebograms showed delayed emptying of the osteoarthrotic bone in all cases, as the contrast was present in detectable amount after 180 s, which was never the case on the normal side.

Table 2. Arterial values (SEM) during pressure measurements of subchondral bone (A) and synovial fluid (B)

	A (n 14)	B (n 10)
MAP	13.2 (0.36)	–
paO_2	11.2 (0.31)	12.5 (0.26)
$paCO_2$	3.85 (0.14)	3.45 (0.16)
apH	7.46 (0.01)	7.43 (0.01)

The results of the histological analyses always showed increased amounts of subchondral bone on the arthrotic side and the synovial membrane showed several layers of synoviocytes and fibrosis of the underlying tissue. The cartilage of the weight-bearing osteoarthrotic femoral condyles was totally depleted of glycosaminoglycans, as judged by Saffranin O staining.

Discussion

The present model of arthrosis is histologically (Telhag & Lindberg 1972), histochemically (Ehrlich et al. 1975, Reimann et al. 1982) and scintigraphically (Bohr 1976, Christensen et al. 1982) similar to human arthrosis. The histological specimens in the present series confirm this. The increased intraosseous pressure, in human arthrosis (Arnoldi et al. 1972, Tran et al. 1977) has been attributed to venous engorgement (Brookes & Helal 1968, Arnoldi et al. 1972, 1975), and experimental studies using

Table 1. Results of measurements in arthrotic and normal bone and synovial fluid Pressures are mean kPa (SEM)

	Subchondral bone (n 7)		Synovial fluid (n 6)	
	Arthrosis	Control	Arthrosis	Control
IOP	4.32 (0.83)	[a]1.96 (0.52)		
pO_2	7.44 (0.67)	[b]5.59 (0.47)	4.11 (0.97)	5.21 (1.01)
pCO_2	6.20 (0.32)	6.65 (0.35)	12.2 (2.1)	[c]7.19 (0.72)
pH	7.30 (0.04)	7.28 (0.04)	6.97 (0.08)	[d]7.32 (0.07)

Paired *t*-test, p-value; [a]0.002, [b]0.003, [c]0.03, [d]0.03

venous ligation to the leg have shown this to result in increased intraosseous pressure (Keck & Kelly 1965) and arthrosis of the knee (Brookes 1966, Abdalla & Harrison 1966). On this basis it has been suggested that venous engorgement might be an important and early factor in the arthrotic process (Arnoldi & Reimann 1979). Increased intraosseous pressure and venous congestion, as judged by intraosseous phlebography, were also demonstrated in the present series.

The significant correlation between intraosseous pressure and carbon dioxide partial tension (pCO_2) in arthrotic bone seems to be indicative of venous engorgement. When oxygen partial tension (pO_2) under such circumstances was increased, it might have been caused by either decreased oxygen consumption or by regional arterial hyperemia. However, the increased amount of subchondral bone does not indicate decreased oxygen consumption, since anaerobic metabolism does not facilitate bone growth (Heppenstall et al. 1976). On the other hand, anaerobic metabolism should provide acidotic pH and hypercapnia, which were not found. The increased pO_2 was therefore assumed to be caused by regional hyperemia at this stage of the process.

The pO_2 of synovial fluid in the arthrotic knee joint did not differ from that of the normal joint, but hypercapnia and acidosis were present. In accordance with earlier studies this suggests anaerobic metabolism (Treuhaft & McCarty 1971, Brighton & Heppenstall 1971, Lane et al. 1977). As the glycosaminoglycans in the present series were found to be totally depleted, the synovial fluid findings probably reflect the metabolism of the degraded cartilage.

The question of which mechanism could have been responsible for degradation of the cartilage arises. Joint incongruity and joint instability, which are both components of the arthrosis model, may affect the synovial membrane and cause joint effusion. This could lead to regional venous stasis, because of the intracapsular localisation of draining veins from the joint and the epiphysis (Brookes et al. 1961). Joint effusion may therefore initiate haemodynamic and metabolic changes. Experimentally, joint effusion has been shown to create increased IOP (Arnoldi et al. 1979) as well as subchondral hypoxia and decreased regional blood flow (Grønlund et al. 1984). At the 3-week stage of the present arthrosis model, there was joint effusion, and hypoxia, hypercapnia and acidity were simultaneously demonstrated in the subchondral bone as well as in the synovial fluid (Kofoed 1984). As cartilage is nourished from the synovial fluid, such an environment might have affected the chondrocyte metabolic processes by changing the pH optimum for enzymatic processes normally protecting the glycosaminoglycans (Mitrovic 1982). This could promote cartilage fibrillation, thus making the cartilage more susceptible to mechanical degradation and possibly new episodes of synovitis and joint effusion, which could perpetuate the process and lead to late results like those presented in the present study.

I therefore suggest that changes in the haemodynamic and metabolic environment, though secondary in nature, may play a role in the development of arthrosis.

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