DICK, W. C. (1972) *Sem. in Arthr. and Rheum.*, 1, 301 (The use of radio-isotopes in normal and diseased joints).
 GIROUD, J. P. (1973) 'Distribution of prostaglandins in inflammatory exudates' in Symposium 'Future Trends in Inflammation'. Verona 28/30 June 1973
 GRENNAN, D. M., ROONEY, P., GILBERTSON, E. AND DICK, W. C. (1974) *Nature*, 249, 368. (The documentation of histamine H2 receptors in peripheral blood vessels)
 LEVINE, L. (1973) *Pharmacolog. Reviews*, 25, 293 (Antibodies pharmacologically active molecules: specificities and some applications of antiprostaglandins)
 NAKANO, J. (1972) 'Cardiovascular actions of prostaglandins' in 'Prostaglandins', ed. P. W. Ramsell and J. E. Shaw. Plenum Press, New York
 WILLIS, A. L. (1969) 'Prostaglandins, Peptides and Amines', ed. P. Montegazza and E. W. Horton, p. 30. Academic Press, London and N.Y.

Wrist Cysts and Fistulae. An Arthrographic Study of the Rheumatoid Wrist. J. M. I. IVESON, A. G. S. HILL, and V. WRIGHT. (Rheumatism Research Unit, The General Infirmary, Leeds, and the Oxford Regional Rheumatic Diseases Research Centre, Stoke Mandeville Hospital, Aylesbury) Published in the *Annals*, 34, 388.

Impairment of Proteoglycan-Collagen Interaction in Early Experimental Osteoarthritis. C. A. McDEVITT, H. MUIR, AND E. M. M. GILBERTSON (Kennedy Institute of Rheumatology, Bute Gardens, London, and the Department of Veterinary Surgery, University of Glasgow)

The early biochemical events in osteoarthritis have been investigated in a disease model (McDevitt and Muir, 1975; McDevitt, Muir, and Pond, 1974). The experimental osteoarthritis was induced by severing the anterior cruciate ligament in the right knee of skeletally mature dogs with the cartilage of the other knee serving as a control. The fibrillation induced in the tibial cartilage of the operated joint represented progressive osteoarthritis by the criteria of Byers, Conteponi, and Farkas (1970) in that it occurred in the area (area A) of the medial tibial condyle not covered by the meniscus, and became more severe with time after surgery as assessed by indian ink staining (Meachim, 1972). The cartilage of the operated joint had a

Table I Total uronic acid extracted sequentially by (1) 0.15 mol/l sodium acetate, (2) 2 mol/l CaCl₂, and (3) 4 mol/l guanidinium chloride. The areas are (A) medial tibial condyle next to the intercondylar notch (B) remainder of medial condyle, and (C) lateral tibial condyle. Grade 1 (Meachim, 1972) represents intact cartilage surface; grade 2, minimal fibrillation; grade 3, over fibrillation

Duration of instability (weeks after surgery)		Tibia					
		OA	Con	OA	Con	OA	Con
3	Area Grade	A+B 2	A+B —	C 1	C —		
		% of total tissue uronic acid					
	Extract 1	6.7	3.8	3.8	3.4		
	Extract 2	44.5	26.6	36.0	34.5		
	Extract 3	11.7	18.2	17.2	20.4		
	Total extracted In residue	62.9 37.1	48.6 51.4	57.0 43.0	58.3 41.7		
48	Area Grade	A 3	A —	B 1	B —	C 2	C —
		% of total tissue uronic acid					
	Extract 1	17.2	7.0	19.8	7.5	19.6	8.8
	Extract 2	51.5	58.0	56.4	48.2	54.7	50.2
	Extract 3	10.6	12.8	8.1	21.1	11.1	15.6
	Total extracted In residue	79.3 20.7	77.8 22.2	84.3 15.7	76.8 23.2	85.4 14.6	74.6 25.4

Table II Galactosamine-glucosamine molar ratios of proteoglycans from osteoarthrotic (OA) and control cartilage. The proteoglycans were sequentially extracted with (A) 0.15 mol/l sodium acetate pH 6.8, and (B) 4 mol/l guanidinium chloride pH 4.5 and purified by both 'associative' and 'dissociative' equilibrium density gradient centrifugation. The 0.15 mol/l sodium acetate extracts of areas A, B, and C of the tibia were pooled. The dog was killed 10 weeks after section of the anterior cruciate ligament—

Tissue	Tibia		OA		OA	
	OA	Control	OA	Control	OA	Control
Area	A	A	B	B	C	C
Grade of OA	3	—	2	—	2	—
Galactosamine-glucosamine molar ratios						
0.15 mol/l sodium acetate	—	—	3.5	3.6	—	—
4 mol/l guanidinium chloride	4.3	4.1	6.3	4.6	6.5	4.4
Cartilage residue	2.6	2.0	2.6	2.5	2.5	2.1

higher water content and galactosamine-glucosamine molar ratio than the control tissue. Periarticular osteophyte formation was also evident very early in the disease process.

Focal sites of tibial cartilage were extracted sequentially with (a) 0.15 mol/l sodium acetate, (b) mol/l calcium chloride, and (c) 4 mol/l guanidinium chloride. A larger proportion of the total proteoglycans was extracted from the cartilage of operated joints than from the corresponding controls and the proportion of the total proteoglycan in each extract changed in such a way as to suggest that the association of proteoglycans with collagen was reduced; thus (a) contained more and (c) less than controls (Table I). These changes, which preceded the appearance of fibrillation as detected by indian ink staining, were confined to area A of the tibial cartilage in the dog killed 3 weeks after surgery, but was evident throughout the whole tibial plateau of the operated joint of the dog killed 48 weeks after surgery.

The purified proteoglycans extracted from osteoarthrotic cartilage had higher galactosamine-glucosamine molar ratios than those from control cartilage. In the cartilage residue this difference was less marked (Table II). Thus, proteoglycans extracted from osteoarthrotic compared with control cartilage contained more chondroitin sulphate. The results suggest that in response to mechanical stress due to the instability of the operated joint, the chondrocytes synthesize a different proteoglycan, relatively rich in chondroitin sulphate, which is less firmly associated with collagen than normal proteoglycans. This might account for the increased hydration of the tissue, because it would increase the swelling pressure of the proteoglycans in the tissue, since at this stage in the disease process the total amounts were unchanged. That the proteoglycans are important in stabilizing collagen fibres is consistent with the report that the shrinkage temperature of human articular cartilage collagen was closely correlated with the hexosamine content of the tissue (Herbage and others, 1972).

References

- BYERS, P. D., CONTEPONI, C. A., AND FARKAS, T. A. (1970) *Ann. rheum. Dis.*, **29**, 15 (Postmortem study of the hip joint)
- HERBAGE, D., HUC, A., CHABRAND, D., AND CHAPUY, M. C. (1972) *Biochem. Biophys. Acta.*, **271**, 339. (Physicochemical study of articular cartilage from healthy and osteoarthritic human hips: Orientation and thermal stability of collagen fibres)
- MCDEVITT, C. A., AND MUIR, H. (1975) 'The proteoglycans of articular cartilage in early experimental osteoarthritis' in 'Protides of Biological Fluids', ed. H. Peeters, Vol. 22, p. 269. Pergamon Press, Oxford
- , —, POND, M. J. (1974) 'Biochemical events in early osteoarthritis' in 'Symposium on Normal and Osteoarthrotic Cartilage', eds. S. Y. Ali, M. W. Elves, and D. H. Leaback, p. 207. Institute of Orthopaedics, London
- MEACHIM, G. (1972) *Ann. rheum. Dis.*, **31**, 457 (Light microscopy of indian ink preparations of fibrillated cartilage)

Graphic Illustration in Handbooks for Patients. J. M. H. MOLL, V. WRIGHT, M. R. JEFFREY, J. D. GOODE, AND P.M. HUMBERSTONE (*Sheffield Centre for the Investigation and Treatment of Rheumatic Diseases, and the Rheumatism Research Unit, University Department of Medicine, Leeds*)

In a previous study of the standard Arthritis and Rheumatism Council 'Handbook on Gout', we found the 9-cartoon booklet to be a satisfactory doctor-patient communication aid (Moll and Wright, 1972). An extension of this study has been undertaken to examine the communication value of increasing the number of illustrations

in such booklets. Two variants of the standard 'Handbook on Gout' were printed specifically for the study. One contained text with 89 cartoons, and the other was purely textual. The text in each booklet was the same as that of the standard handbook.

Fifty patients with gout were studied. On a random basis, 28 were given the booklet with 89 cartoons and 22 the booklet without cartoons. At routine follow-up each patient completed a multichoice questionnaire based on the main points in the handbook. No prewarning of the test was given. The mean overall scores obtained by patients were compared with the mean score of patients tested in the previous study using the standard booklet. Text with 89 cartoons 65.5%; text without cartoons 67.1%; text with 9 cartoons (standard booklet) 70%.

Comparing results obtained in response to individual questions (as opposed to the overall test score), in only one out of 14 questions (that based on 'Lifelong and Preventive Treatment') was there a statistical difference ($P < 0.05$) between the two groups. Text with cartoon 78.7%; text without cartoon 57.1%.

The failure of the illustrated booklet to show better overall test results is not yet understood, but may arise from a 'knowledge saturation effect' inevitable in patients reading material devoted to their own disease. Technical problems to do with presentation of data may also be important.

Reference

- MOLL, J. M. H., AND WRIGHT, V. (1972) *Ann. rheum. Dis.*, **31**, 405 (Evaluation of the arthritis and Rheumatism Handbook on Gout: an objective study of doctor-patient communication)

Osteoporosis in Patients with Rheumatoid Arthritis. A. C. KENNEDY, D. A. SMITH, G. GREY, M. K. JASANI, AND W. W. BUCHANAN (*The Centre for Rheumatic Diseases, University Department of Medicine, Royal Infirmary, Glasgow; the Bone Metabolism Research Unit, University Department of Medicine, Western Infirmary, Glasgow*)

361 patients with 'definite' or 'classical' rheumatoid arthritis were studied, of whom 201 were female and 150 male. The metacarpal indices and femoral indices (Barnett and Nordin, 1960) from these patients were compared with those derived from 119 female and 76 male controls. The source and characteristics of these control subjects have been reported elsewhere (Smith, 1971).

The results of this study show that both male and female patients with rheumatoid arthritis show a significant bone loss in the femur compared with the loss of bone seen in normal subjects with increasing age. There was no evidence to suggest that corticosteroid therapy caused a greater loss of bone from the femur than would have occurred as a result of the rheumatoid arthritis alone. There was a statistically significant relation between the duration of the rheumatoid arthritis and femoral bone loss in women over the age of 45 years ($P < 0.001$) whether or not they had received corticosteroid therapy. There was also a significant relationship between femoral bone loss and the duration of corticosteroid therapy in both male and female patients over the age of 45 years. However, when a correlation excluding disease duration was conducted there was no residual effect of corticosteroid therapy. The metacarpal and femoral indices of the patients were significantly related in both male and female groups ($P < 0.001$).