In 10 patients with classical rheumatoid arthritis indomethacin profiles and articular indices were determined before and after a period of one week's administration of probenecid (1 g daily). There were significant differences between the two indomethacin profile results, and the articular index fell significantly ($P < 0.05$) from a mean value of 17.6 ($\pm$ SEM 2.8) before treatment to a mean value of 12.5 units ($\pm$ SEM 1.1) after probenecid. Despite attaining very high plasma indomethacin concentrations after probenecid no patient complained of side effects. This effect of probenecid on indomethacin levels was noted in further studies after both oral and rectal administration. When frusemide was administered orally with indomethacin the indomethacin profile was reduced. These results are preliminary and based on a small number of patients but do raise the question of the advisability of concurrent administration of diuretics and indomethacin.

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Mark Twain and Rheumatology. G. Juttla and V. Wright (*Rheumatism Research Unit, The University of Leeds*)

The aphorism of Mark Twain that 'the advantage of medicine is the large return of conjecture one gets for such a small investment of fact' has been studied in an analysis of 1 222 articles in 15 journals by 2936 authors! Conjecture has been expressed as a percentage of fact. The journals analysed were from four areas: (1) medicine, (2) 'pure' science, (3) arts, (4) psychology. The medical journals were further subdivided into rheumatology, general medicine, and orthopaedic surgery.

It was found that there was little truth in Mark Twain's aphorism, with the exception of orthopaedic surgery, in that the ranking order of talkativeness was (a) orthopaedic surgery, (b) pure science, (c) arts, (d) general medicine, and (e) rheumatology. It was noted that medical journals required more authors to write an article than arts journals. There was some evidence that Mark Twain (an American) may have been influenced by local observations, in that the Americans were more talkative than those from the United Kingdom in science journals, orthopaedic surgery, and general medicine, whether this was judged by the country of publication, or the country of origin of the authors. In rheumatology, however, the British were the most talkative and were only outstripped (marginally) by authors in psychological literature. This last analysis was by place of publication; in terms of the country of origin the British fared rather better. When the data were analysed by the subject of the article it was found that clinicians and pathologists were more diffuse than surgeons and biochemists.

Generalized Osteoarthritis. A Problem of Definition. T. Benn and P. H. N. Wood (*ARC Epidemiology Research Unit, University of Manchester*)

The epidemiological outlook often appears to confound clinical concepts, particularly in regard to syndromes. Thus primary generalized osteoarthritis (GOA), as conceived by Kellgren and Moore (1952), is regarded clinically as being a separate disease from secondary or pauciarthritic forms of OA. However, a major distinguishing feature, the number of joints affected, failed to differentiate these syndromes clearly in a population survey (O'Brien and others, 1968). The situation is therefore analogous to the old controversy about the distribution pattern of blood pressure levels, and whether essential hypertension is a discrete entity.

We have pursued this question using data on 229 persons with various types of OA who were examined in a collaborative study by rheumatology clinics in England, France, Finland, Czechoslovakia, Bulgaria, and the U.S.S.R. 51 patients with coexisting diagnoses of RA, gout, or ankylosing spondylitis were excluded from the subsequent analysis. The frequency with which a double diagnosis of GOA and RA was assigned in the Finnish and Bulgarian clinics suggests that the concept of GOA may be different in these countries. Examination of the likelihood of particular sites being involved in relation to the total number of involved sites confirmed the clinical concept of separate syndromes of multiple and local OA with preferences for different sites. The results for the hip were consistent with their being more than one syndrome of OA in this joint, as Kellgren and Lawrence (1961) have reported. Multiple joint involvement was associated with raised ESR, serum uric acid, and rheumatoid factor (SCAT). It was concluded that numerical analysis supported GOA as a meaningful concept.

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Discography in Assessment of Lumbar Disc Disease. J. T. Patton (*Department of Radiology, Manchester Royal Infirmary*)

The technique of lumbar discography involves injecting a water-soluble contrast medium into the nucleus pulposus using a posterior midline approach and local anaesthesia under fluoroscopic control. The technique is not new (Lindblom, 1948) but is now made easier by image intensification with television amplification. The technique traditionally relies on two criteria as evidence of disc disease. (a) *Pain reaction.* Injection of the normal disc is painless and pain on injection is good evidence that the disc is diseased. Reproduction of the patient's symptoms is an accurate guide to the level where there is evidence of multiple disc disease. (b) *Radiographic appearances.* The distinction between normal and abnormal discs is so characteristic as to render (a) virtually unnecessary. The contrast medium currently used by the author is virtually painless on injection. The technique demonstrates disc prolapse both anterior and posterior, Schmorl's nodes, degenerative disc disease, etc.

No significant morbidity has been observed in 100 patients examined and the technique, which takes about the same time as a myelogram, has the advantage of not leaving iodized oil in the theca with its attendant long-term hazards. The examination is only valuable in the elucidation of known disc disease and has no part in the diagnosis of any other lesion of the spine. The technique can replace myelography in localizing the level of known herniation before surgery. It is unique in localizing early degenerative disc disease without herniation, thus allowing spinal fusion to be performed without the necessity of multiple disc exploration.

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Biochemical Studies of Individual Lumbar Discs. P. Adams and H. Muir (*Kennedy Institute of Rheumatology, London*)

The quality of articular cartilage proteoglycans is known to change during development (Simunek and Muir, 1972a) and in pathological conditions (Simunek and Muir, 1972b; McDevitt and Muir, 1974), but analogous studies on individual intervertebral discs have not been previously reported. In the present study lumbar spines were obtained at autopsy from 4 individuals between the ages of 8 and 66 years, and each disc was analysed separately. The nucleus pulposus and annulus fibrosus were dissected from each disc and the chemical composition of each determined separately. Proteoglycans were extracted by a step-wise procedure using iso-osmotic sodium acetate, 3 mol/l magnesium chloride and 4 mol/l guanidinium chloride. The proteoglycan content of each extract and of the residue was measured; the molar ratio of glucosamine/galactosamine in the purified extracted proteoglycans was determined, and their hydrodynamic size assessed by gel chromatography on Sepharose 2B.

Significant differences in the overall composition and in the proteoglycans of different discs of the same spine were found. Progressive changes down the spine were evident in the collagen content and the extractability of the proteoglycans of older tissues (Table) and in the keratan sulphate content of total proteoglycan in young discs. The differences were generally most marked between the L5/S1 disc and those above. With increasing age there was a marked general change in the quality of the proteoglycans of both nucleus and annulus in all discs. Both the propor-

tion of inextractable proteoglycan and the amount present in the sodium acetate extract was much higher in older tissues than in juvenile specimens. The proteoglycans extracted by sodium acetate from old nucleus and annulus were of much smaller hydrodynamic size and contained less keratan sulphate than proteoglycans extracted by solutions of higher ionic strength. In young tissues these differences between the proteoglycans in each extract were less marked.

The differences in composition of individual discs and the general changes with age that we have found may both be important in the pathology of the tissue.

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Intervertebral Disc Collagen in Degenerative Disc Disease. C. M. Herbert, K. A. Lindberg, M. I. V. Jayson, and A. J. Bailey (*Department of Medicine, Bristol Royal Infirmary, and Agricultural Research Council, Meat Research Institute, Langford, Bristol*)

Degenerative disc disease and disc prolapse are important causes of low back pain. We have, therefore, initiated an investigation into the nature of the collagen in intervertebral discs and some of the changes occurring during ageing, disc prolapse, and degenerative disc disease.

Normal intervertebral discs covering the age range 0–70 years were obtained from cadavers within 24 hours of death. Although long referred to as fibrocartilage, we have now shown that the nucleus pulposus contains cartilage type collagen (type II) (Miller, 1972), while the annulus fibrosus contains both type II and the skin, tendon type collagen (type I) (Traub and Piez, 1971). Analysis of the nature of the stabilizing crosslinks established that they were similar to cartilage collagen (Robins and others, 1973), that the proportion present varied down the spine, and that the normal (Robins and others, 1973) age-related pattern of changes in these crosslinks occurred. Lumbar spines classified as degenerative by radiological and gross examination were also obtained from cadavers. Although the collagen remaining in the degenerate disc revealed a normal adult crosslink pattern a high proportion of reducible crosslinks were found to be present in the disc above. This clearly indicates the synthesis of new collagen, presumably to compensate for the defective disc below. Based on the type of crosslink present it appears that the new collagen synthesized in both the nucleus and annulus of subjects with degenerative disc disease is type I rather than type II. The proliferation of type I collagen, particularly in the nucleus, could lead to a decrease in the mechanical and biochemical efficiency of the intervertebral disc.

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Table Relationship between collagen content of tissue and proteoglycan extractability in annulus fibrosus (female spine, 44 years old)

Disc	Inextractable proteoglycan ($\times$ of total uronic acid)	Collagen content as % of dry weight of tissue		
		Inner annulus	Middle annulus	Outer annulus
T12/L1	29.8	14.7	30.0	38.0
L1/L2	23.6	15.0	30.0	46.0
L2/L3	25.6	19.0	43.0	46.0
L3/L4	36.8	20.0	35.0	49.0
L4/L5	34.7	30.0	48.0	48.0
L5/S1	36.0	32.0	49.0	58.0