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Post-mortem study of the hip joint

II. Histological basis for limited and progressive cartilage alterations

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Byers, P. D., Contepomi, C. A., and Farkas, T.A. (1976). *Annals of the Rheumatic Diseases*, **35**, 114–121. **Post-mortem study of the hip joint. II. Histological basis for limited and progressive cartilage alterations.** This histological study is based on a macroscopical study of post-mortem hip joints (Byers, Contepomi, and Farkas, 1970) in which two categories of articular cartilage alterations, in addition to osteophytes, were described. One category consisted of 'limited' alterations which occurred frequently, had several subcategories, and rarely led to joint deformity. The other consisted of progressive alterations which caused bone exposure and joint deformity. Histological sections from both groups, including all the subcategories of the first, were studied. Initially the mechanisms that destroy cartilage were determined, and then their prevalence was assessed. Six mechanisms were found, all occurring in the group of limited alterations with varying prevalence and in varying combinations. Only one, fibrillation, occurred in the progressive group.

In a previous paper (Byers and others, 1970) we described three main categories of articular cartilage alterations in the hip joint of a post-mortem population: (1) osteophytic, (2) limited, and (3) progressive. These were defined by site, gross characteristics, and natural history. All the alterations were age-related. The limited group contained a number of subdivisions (Fig. 1), and was the most prevalent, while the progressive group was the least prevalent. One distinction between these two groups was that the limited alterations very rarely led to bone exposure and there was no resulting joint deformity, whereas these always occurred in the progressive group.

It was suggested that limited alterations do not lead to clinical osteoarthrosis. This view has been supported by two other investigations which showed a high incidence of limited alterations in populations in which primary osteoarthrosis of the hip does not occur or is rare (Foss and Byers, 1972; Byers and others, 1974).

The present microscopical study of the limited and progressive groups confirms this classification, which was based originally on macroscopical grounds, with the following evidence. A number of mechanisms operate to destroy cartilage; they all occur in limited alterations but only one is found in the progressive alterations.

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Materials and methods

The detailed macroscopical descriptions of the lesions are given in Byers and others (1970); the age prevalence is recorded there and in Byers (1974). In summary, 365 right hips from a post-mortem population with an age range of a few months to 89 years were studied. 155 left femoral heads were included in the study, but not in the paper. As a result, in the present study and correlation studies (Byers, Contepomi, and Farkas, 1976) the individual lesions have been grouped. These groupings (Fig. 1) and the number of joints affected are (1) the head, showing peripheral/perifoveal limited alterations (PPLA)—303; parafoveal limited alterations (PLA)—123; and superior midregion progressive alterations (PA)—16; (2) the acetabulum, showing horseshoe tip limited alteration (HTLA)—142; outer margin limited alteration (OMLA)—148; inner margin limited alteration (IMLA)—84; dome limited alteration (DLA)—266; and superior midregion progressive alteration

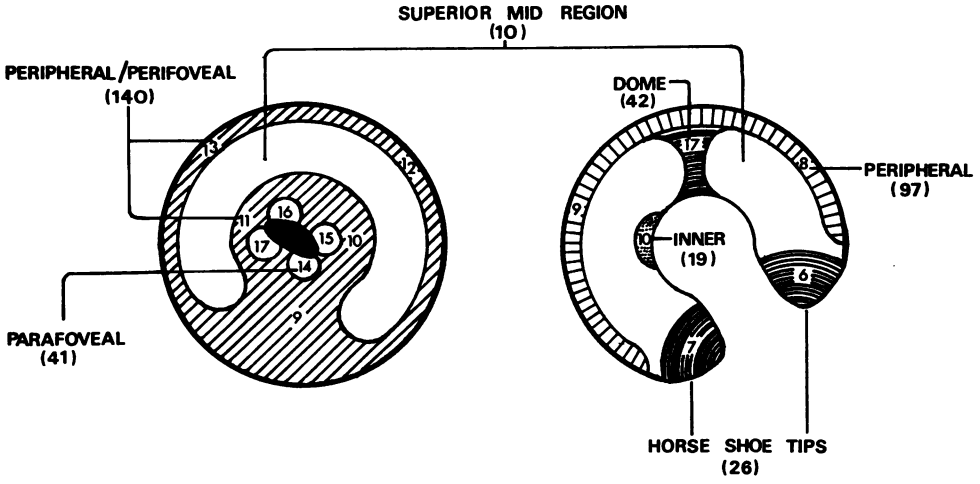


FIG. 1 *Schematic representation of a right hip joint. Classification of sites at which articular cartilage alterations occur. The original numbers (Byers and others, 1970) are shown in the sites for reference. In parentheses are the numbers of affected sites from which histological sections were prepared.*

(PA)—16. Fig. 1 also shows the number of sections studied from affected sites.

Stages of development were established macroscopically for all the lesions. The earlier stages of the limited group were generally more prevalent. The progressive lesions were divided equally between the two stages, *i.e.* with or without bone exposure. All 8 of the first stage progressive lesions and 2 of the second stage were studied histologically.

Each post-mortem specimen, after formalin fixation, was divided coronally and horizontally into 3 mm slices which were radiographed on fine detail film. Additional slices were cut if every alteration in the specimen had not been included. Subsequently, slices were selected for the preparation of decalcified (formic citrate) paraffin-embedded sections, and stained with haematoxylin and eosin.

An initial histological study was made of the mechan-

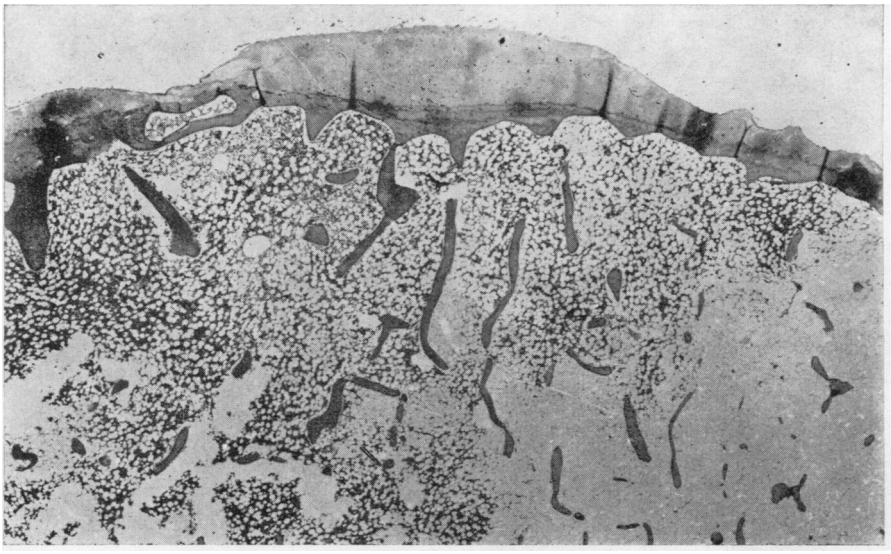


FIG. 2 *Head: perifoveal alteration (subfoveal). There is fraying (superficial tangential clefts) at the surface of the thickest cartilage where the contour is even compared with the other portions with an irregular 'granular' surface texture. See Fig. 3 for details of top right-hand corner. Haematoxylin and eosin.* ×9

isms by which cartilage was removed and the presence of these mechanisms in all the sections was recorded. The sections included over 1100 sites, in about 500 of which alterations were present. The data were transferred to punch cards and the computer listing used to determine the frequency of characteristics in each class of macroscopical alteration.

It was found that articular cartilage was removed in the following ways.

Clefts. The patterns of cleavage were classified by the number, direction, and depth of the clefts. (a) Fraying, *i.e.* many (in the 10s), tangential, superficial (within a few μm of the surface), and deep (Figs. 2, 5, 6). (b) Fibrillation, *i.e.* many vertical, superficial, and deep (Fig. 7).

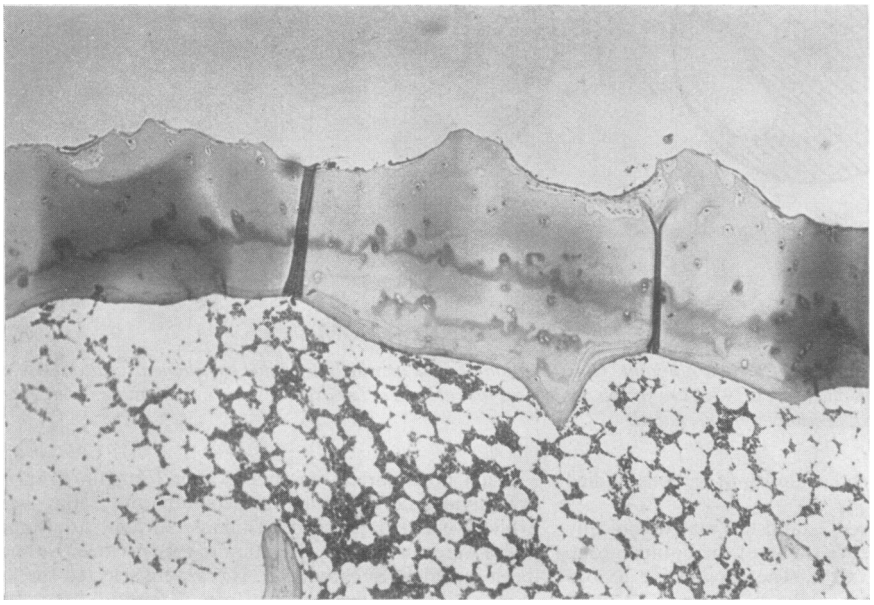


FIG. 3 *Detail of Fig. 2. Chondrocytic matrix resorption: beneath a delicate fibrous layer are pale clear-cut pockets in the matrix containing a few cells. H.E. ×75*

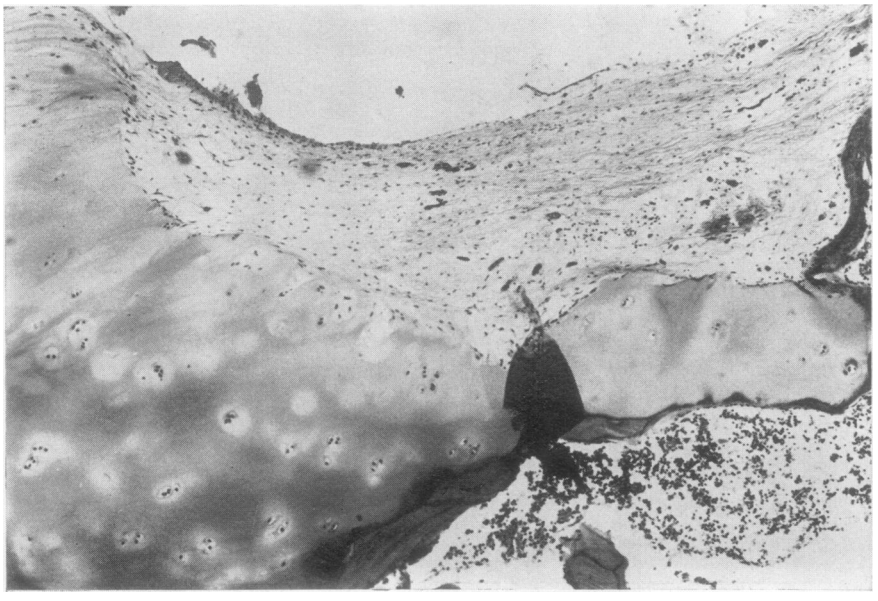


FIG. 4 *Acetabulum: chondrocytic matrix resorption at chondrolabial junction. Similar appearances are found in the capital parafoveal alterations. H.E. ×13*

(c) Splits, i.e., few (less than 10), vertical, and/or tangential, and deep (Figs. 5, 8, 9, 10).

Tangential splits were usually single and extensive, lying in the midzone or deeper. Nearly all communicated with a deep vertical split that reached the surface thereby forming flaps of cartilage. Vertical splits were rarely found alone.

Cellular resorption of surface cartilage was recognized by the presence of single and multiple cells lying in a depression or pocket in the cartilage matrix, the line of demarcation from the normal matrix being sharp and clear (Figs. 2–4). This was found either alone or with an overlying fibrocellular tissue.

Fibrocellular surface tissue. This refers to a layer of varying proportions of cells and collagen on the surface and was associated with loss of cartilage (Figs. 3, 4). The origin of the cells is not known. Vascularization was a feature in up to 25% of instances depending on location; the capital peripheral and parafoveal sites were the most frequently vascularized. No attempt was made to quantify thickness.

Ossification of cartilage. This identifies ossification at sites other than that of osteophytes. It was not associated with cartilage growth and was very localized (Figs. 5, 6).

Results

All the limited alterations showed several destructive mechanisms (Table). This contrasted with the progressive alterations where only fibrillation was found. Nevertheless fibrillation was also to be found among the characteristics of limited alterations. However, fibrillation of the early progressive lesion is very fine and very superficial (Fig. 7). This was not to be seen in any of the limited alterations.

Although it is not the purpose of this paper to go into detail, some aspects are worthy of mention. In the parafoveal alterations extensive chondrocytic resorption of matrix is a striking mechanism which

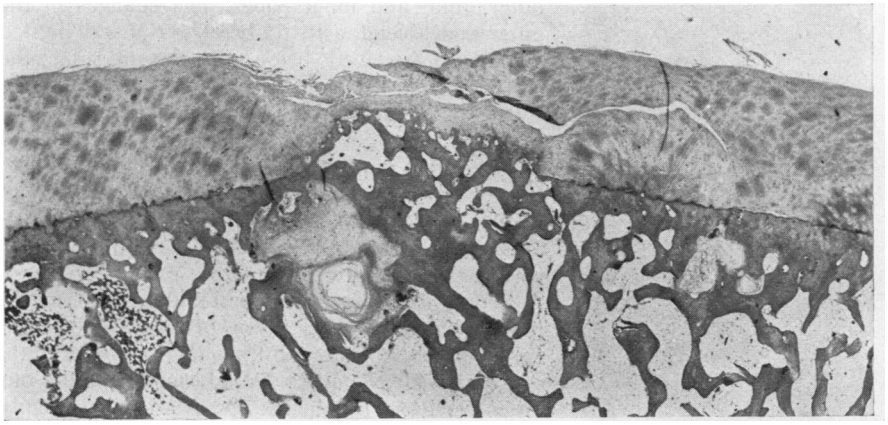


FIG. 5 *Head: perifovial alterations (posterior). There are several splits in the cartilage above and beyond an area of ossification. The cartilage surface is frayed. There is a cystic lesion in the bone that does not communicate with the joint. H.E. ×12.*

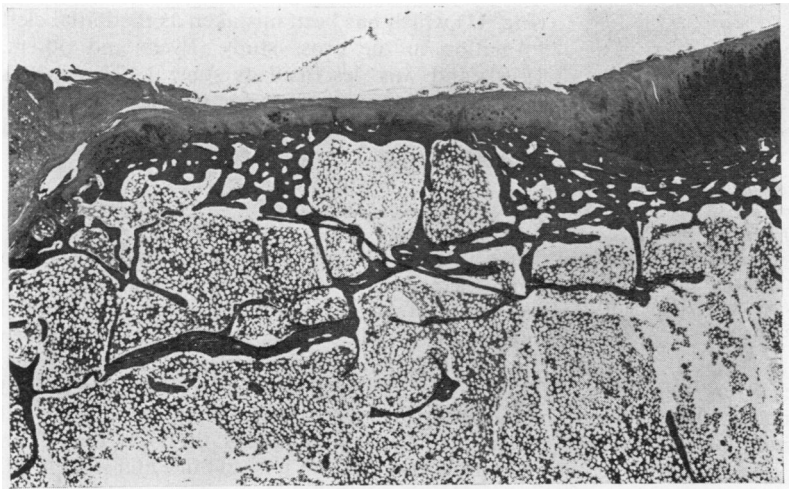


FIG. 6 *Acetabular dome: ossification of inner margin. H.E. ×4*

Table *Percentage prevalence of destructive mechanisms in histological sections prepared from the various articular cartilage alterations in head and acetabulum*

	Limited alterations						*Progressive alterations*
	Head		*Acetabulum*				*Head and acetabulum*
	Peripheral/ perifoveal (PPLA)	*Parafoveal (PLA)*	*Horse-shoe tips (HTLA)*	*Outer margin (OMLA)*	*Inner margin (IMLA)*	*Dome (DLA)*	*Superior midregion*
Fraying	97	75	88	71	16	38	0
Fibrillation	37	0	28	0	5	7	100
Splits	17	16	19	64	20	12	0
Fibrous surface layer	60	75	31	33	67	24	0
Cellular resorption	53	70	19	21	58	0	0
Ossification	25	30	23	10	26	29	0

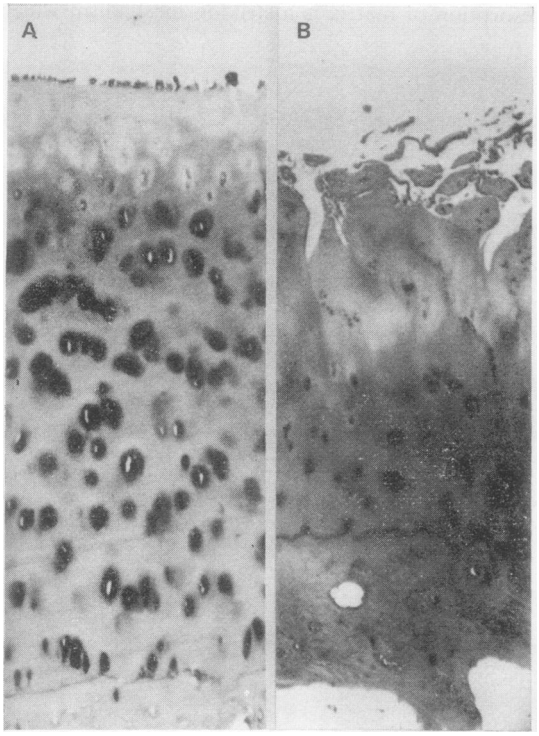


FIG. 7 *Head: fibrillation (numerous vertical clefts, superficial and deep).* A *The earliest progressive lesion found (illustrated in Byers and others, 1970, Fig. 6); the clefts are very fine and the loss of basophilia is superficial.* B *A section from a lesion of limited progression showing much deeper cleft formation, appearances like this are also found in some advanced progressive lesions. H.E.* ×18

can give rise to large lesions (see Byers and others, 1970, Fig. 5). The cartilage which surrounded these nearly always showed an insignificant amount of fraying.

The alterations in the dome of the acetabulum are complex. Description is facilitated by considering outer, mid, and inner zones. The changes in the outer zone blend with those of peripheral limited alteration described below. In the midzone the cartilage may show one or more changes such as splitting, fraying, cellular depletion, cellular proliferation, altered matrix staining, and altered collagen fibre patterns. The inner region may ossify (Fig. 6). The alteration called 'inner margin' is distinct from this anatomically and differs histologically in some respects, mainly in the fibrocellular surface tissue and resorption.

At the outer margin of the acetabulum the principal mechanism at work is a line of cleavage between cartilage and labrum, and the undermining of both, which partially detaches the labrum and splits out large cartilage fragments. Ossification frequently occurs here as in Fig. 10. We do not yet know if this occurs before or after the splits develop. Cysts are not uncommon in the subchondral bone. There is a normal chondrolabial groove in many acetabulae (Fig. 11) which has been mistaken as the initial cleft formation in the gross study (Byers and others, 1970), and was described as stage 1. This means that the prevalence figures for features 8 and 9 in Byers and others (1970), Table IV must be corrected by deleting stage 1.

Discussion

These findings add to the evidence that in the hip joint there are, in addition to osteophytes, two categories of articular cartilage alteration, limited and progressive. The histological distinction between them is not based entirely on specific characteristics. Thus while chondrocytic matrix resorption and surface fraying seem to be confined to limited alterations, fibrillation occurs in both, though in early progressive lesions it is very fine and superficial.

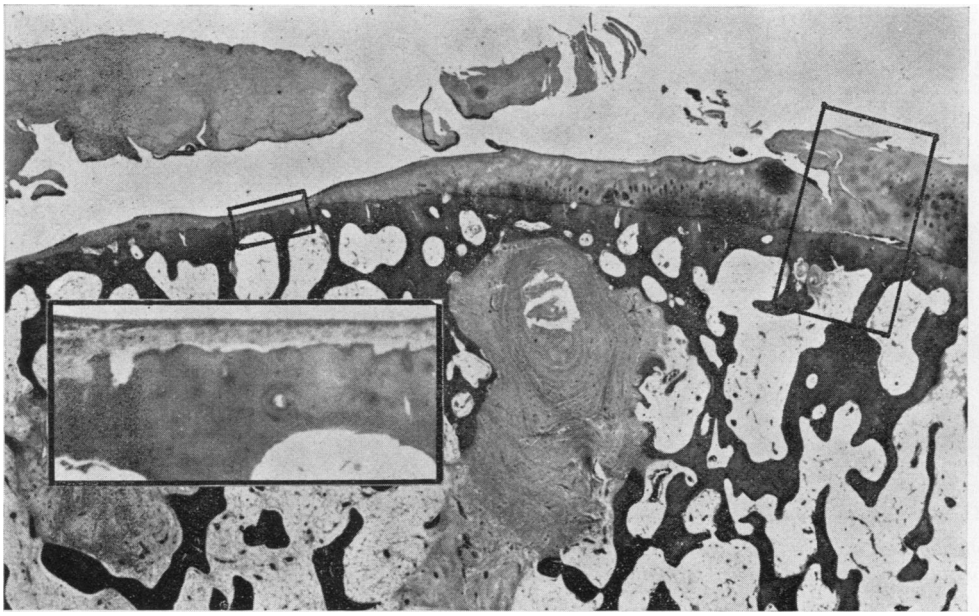
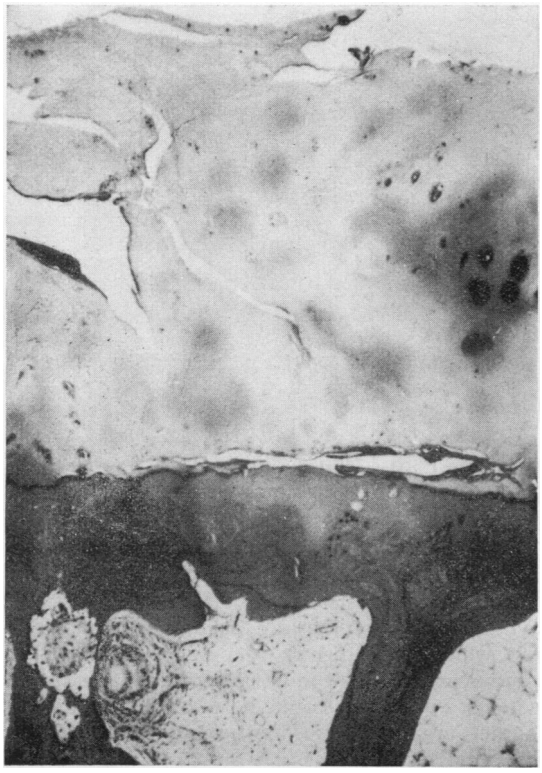


FIG. 8 *Head: perifoveal alterations (subfoveal). An extensive tangential cleft has separated a large flap of cartilage*



This is also found in the cartilage around the margins of exposed bone in the second stage progressive lesions. The coarser fibrillation which is generally illustrated is found beyond this. Meachim and Emery (1973) have drawn attention to these patterns of fibrillation in advanced osteoarthrosis.

A. Maroudas, M. Venn, and G. Weber (personal communication, 1974) have studied the fixed charge density and ^{32}S uptake by cartilage from one histologically studied early progressive alteration supplied through this laboratory and found that only the most superficial portion on the matrix had lost glycosaminoglycan and that there was no increase in cellular activity. Ali and Evans (1973) have found increased enzyme activity in one macroscopically defined early progressive lesion. Clearly more observations in early cases are required. Cellular proliferation was noted histologically by us in later stages of both limited and progressive alterations. Maroudas, Evans, and Almeida (1973) have shown the depth and degree of mucopolysaccharide depletion in limited alterations by measuring fixed charge density.

FIG. 9 *Head: detail of Fig. 6. The cleft in the calcified layer contains a little eosinophilic material; the cartilage above stains poorly, and chondrocytes are few. The microscopical osteolytic lesion, part fibrous tissue and part cyst, has no communication with the joint cavity; some of the surrounding bone is being resorbed. H.E. ×25*

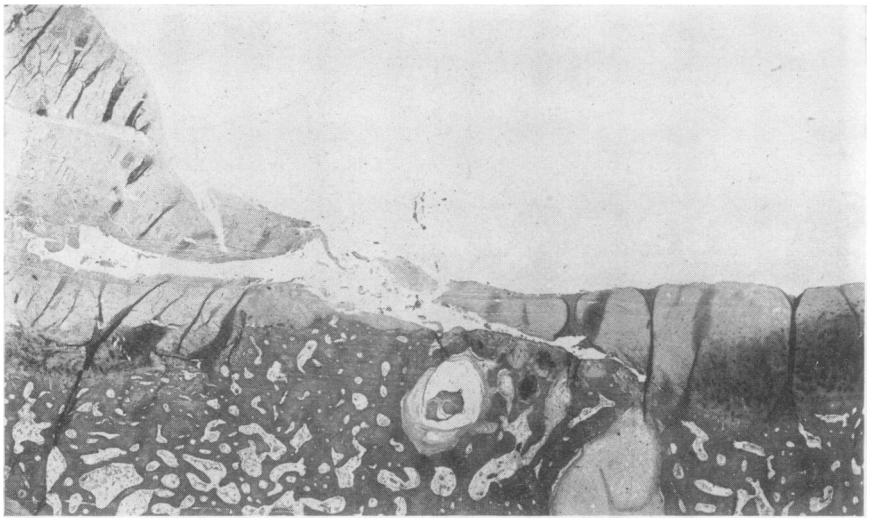


FIG. 10 *Acetabulum: vertical split at the chondrolabial junction, and tangential ones beneath the labrum and cartilage. There has been ossification at some stage and formation of subchondral cysts. H.E.* ×9.

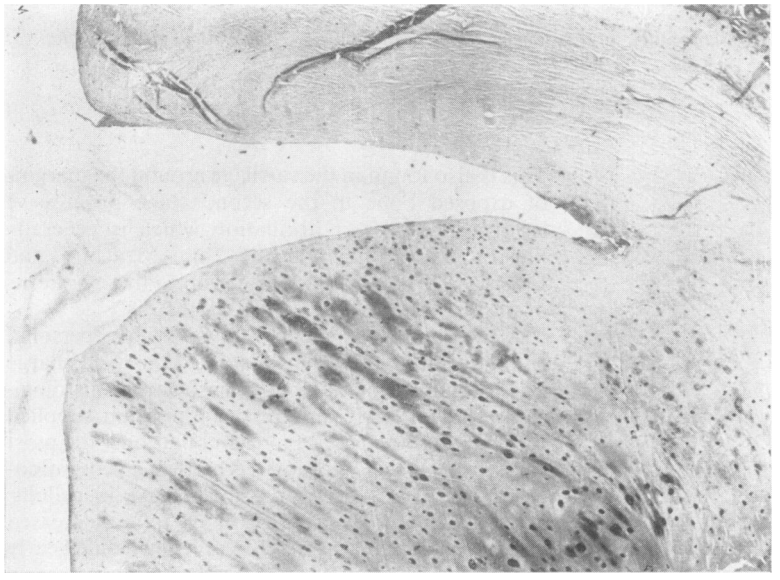


FIG. 11 *Acetabulum: normal chondrolabial groove. H.E.* ×11

From the start of this study one of our assumptions was that ossification of cartilage in limited alterations was a late development. But M. A. R. Freeman (personal communication, 1974) has pointed out that the ossification could well occur first in lesions such as Figs. 5 and 10 illustrate.

Recent work by Day, Freeman, and Swanson (1975) has shown that unusually high loads are borne by the dome in some people; the ossification of the inner zone of the dome may be responsible for this. Indeed the changes at the dome are complex and require further study. We suggested in 1970 (Byers and others) that they had to do with the relationship to the tri-radiate cartilage, but we now agree with Bullough, Goodfellow, and O'Connor (1973) that the pattern of load bearing is the important factor.

Subchondral cysts were found at 85 sites. We favour the idea that they are foci of fibrous proliferation which subsequently become cystic and then communicate with the joint. Nevertheless some of the sections we studied could be used to support the counter argument that the communication is the first event.

The evidence and arguments that have been put forward do not account for the clinical and anatomical osteoarthrosis found affecting sites of limited alterations, especially medial osteoarthrosis, and figures for the prevalence are not readily available. Judging from both post-mortem hip joints and from resected osteoarthrotic heads seen by us, well under 5% of arthritic hips have bone exposure outside the anterosuperior segment, when it is mainly posterior and inferior, in areas ordinarily affected by limited alterations (see Byers and others, 1970, Fig. 3). In contrast with this, when progressive alterations develop in the usual anterosuperior site the limited alterations regress mainly through osteophyte formation, which means that there has been a revival of proliferative and growth activities. Thus the progress of limited alterations is not only variable, but also can undergo a change. Consequently the term nonprogressive introduced by us (Foss and Byers, 1972; Byers, 1974) is inappropriate. 'Limited' is the better term for the simple reason that it conveys the sense of a limit in development of lesions which is not reached by all, but occasionally may be exceeded under special circumstances. An understanding of the basis for this may lead to advances in management and treatment of degenerative disorders of cartilage.

We again express our appreciation to Professor Doniach and his colleagues at the London Hospital for the material. We acknowledge the able assistance of Mrs. Christine King and Mrs. Barbara Glennie, and thank Mr. T. R. Davies, A.R.P.S., for the photomicrographs and illustrations. The work has been possible through the financial support of the Arthritis and Rheumatism Council.

References

ALI, S. Y., AND EVANS, L. (1973) *Fed. Proc.*, **32**, 1494 (Enzymic degradation of cartilage in osteoarthritis)

BULLOUGH, P. G., GOODFELLOW, J. W., AND O'CONNOR, J. (1973) *J. Bone Jt Surg.*, **55B**, 746 (The relationship between degenerative changes and load bearing in the human hip)

BYERS, P. D. (1974) 'What is osteoarthritic cartilage?', *in* 'Normal and Osteoarthrotic Articular Cartilage', eds. S. Y. Ali, M. V. Elves, and D. H. Leaback, p. 131. Institute of Orthopaedics, London

——, CONTEPOMI, C. A., AND FARKAS, T. A. (1970) *Ann. rheum. Dis*, **29**, 15. (A *post mortem* study of the hip joint; including the prevalence of the features of the right side)

——, ——, —— (1976) *Ibid.*, **35**, 122 (Post-mortem study of the hip joint. III. Correlations between observations)

——, HOAGLUND, F. T., PUREWAL, G. S., AND YAU, A. C. M. C. (1974) *Ibid.*, **33**, 157 (Articular cartilage changes in Caucasian and Asian hip joints)

DAY, W. H., FREEMAN, M. A. R., AND SWANSON, S. V. A. (1975) *J. Bone Jt Surg.*, **57B**, 302 (Contact pressures in the loaded human cadaver hip)

FOSS, M. V., AND BYERS, P. D. (1972) *Ann. rheum. Dis.*, **31**, 259 (Bone density and osteoarthrosis)

MAROUDAS, A., EVANS, H., AND ALMEIDA, L. (1973) *Ibid.*, **32**, 1 (Cartilage of the hip joint)

MEACHIM, G., AND EMERY, I. H. (1973) *J. Anat.*, **116**, 161 (Cartilage fibrillation in shoulder and hip joints in Liverpool necropsies)