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OSTEOARTHRITIS IN LUMBAR SYNOVIAL JOINTS

A Morphologic Study

BY

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Introduction

The debate on the morphological background of low back pain has to a large extent been focussed on the lumbar intervertebral discs. To expand our means of seeking conceivable pathophysiological mechanisms capable of explaining low back pain, it was deemed interesting to chart morphologically other lumbar structures. Accordingly the present investigation was devoted to a systematic study of morphological changes in the lumbar synovial joints in a series of spines from autopsy cases of various ages, in order to answer the following questions:

What is the micromorphological picture of osteoarthritis in the lumbar synovial joints?

Are there any sex differences with respect to time of onset, degree and intraspinal distribution of osteoarthritic changes in the lumbar synovial joints?

Which relations exist between ostearthritic changes in the lumbar synovial joints and aging?

Are there any differences in degree of the osteoarthritic changes between ipsiarticular joint facets, ipsisegmental joints and segments in the lumbar spine?

What intrasegmental and intersegmental frequency differences and intercurrences of osteoarthritis in synovial joints, disc degeneration and marginal vertebral osteophytes exist in the lumbar spine?

CHAPTER 1

Survey of the Literature

The Synovial Joints of the Lumbar Spine

*Gross Anatomy**

The synovial joints of the spine are situated between the articular processes of adjacent vertebral arches. Within the lumbar spine, the inferior articular processes have convex and the superior articular processes concave articulating surfaces in the horizontal plane where, therefore, the joint space describes part of the surface of a cylinder whose axis passes near the tip of the spinous process (Fick, 1904). From the craniocaudal aspect the articular surfaces are approximately flat. Osteometric studies have shown that the inclination of the articular surface in the horizontal plane is such that the joint space on the L_{1-2} level forms an angle of about 45° with the sagittal plane and assumes an increasingly frontal attitude farther caudad, until it roughly coincides with the frontal plane on the L_5-S_1 level (Farkas, 1941; Jonck, 1961). On each level, however, the range of nomal variation in the inclination of the articular surface is fairly wide (Fig. 1), especially in the segments L_{4-5} and L_5-S_1 where one commonly distinguishes between frontal and sagittal inclinations (Brailsford, 1929). According to Davis (1955) the inferior articular processes clutch around the superior articular processes rather often in the L_{1-2} segment forming a mortice joint. In the horizontal plane the articular surfaces form an angle of around 90° with a plane through the long axis of the pedicle of the vertebral arch (Junghanns, 1931).

The cartilage covering the joint facet is thickest — about 2 mm — towards the centre of the joint (Fick, 1904). The cartilage surface is smooth, glistening and greyish white in fresh autopsy specimens. The margins of the cartilage often exhibits small indentations into which small fringes from the synovial membrane insinuate themselves (Güntz, 1934).

The joint space extends ventrally as far as ligamentum flavum, which

* Where no source is specified, this description is based on statements in standard anatomy textbooks (Henle, 1855; Rauber-Kopsch, 1955; Gray, 1962).

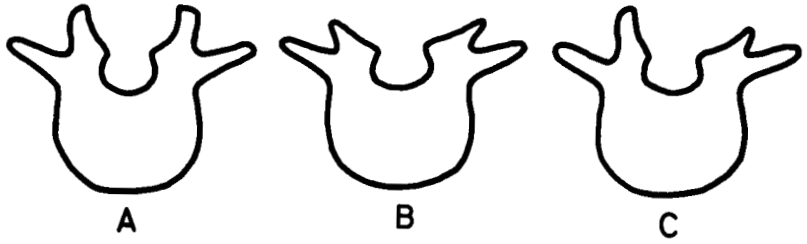


Fig. 1. Typical variants in joint facet inclination: A, "Sagittal"; B, "Frontal"; and C, "Asymmetric" inclination.

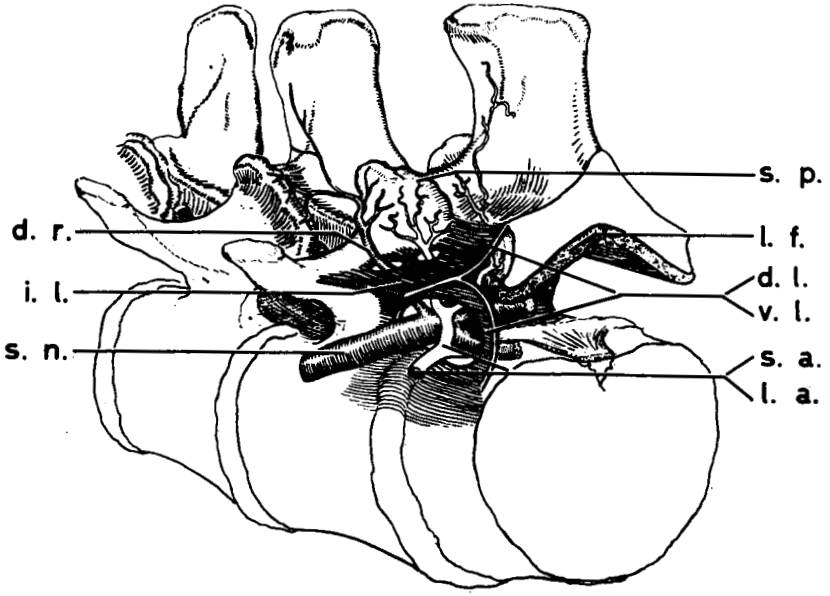


Fig. 2. Topographic relations of lumbar synovial joints. s.p.=Superior articular process. l.f.=Ligamentum flavum. i.l.=Intertransversal ligament. d.l. and v.l.=dorsal and ventral strata of intertransversal ligament. s.n.=Spinal nerve. d.r.=Dorsal ramification of spinal nerve. l.a.=Lumbar artery. s.a.=Arterial branch to synovial joint.

replaces the fibrous layer of a true joint capsule because the synovial membrane is in direct contact with it. The fibrous capsule is very thick in the dorsal portions of the joint (Güntz, 1934), and its outermost fibers are intimately interwoven with the multifidus muscle's insertion on the mamillary process of the vertebra (Lewin, Moffet and Viidik, 1962). In the cranial and caudal ends of the joint the fibrous capsule attaches a few millimetres farther beyond the osteochondral border than it does elsewhere. This gives rise to pocket-like widenings of the joint space. These pockets are the site of a fat pad about the size of a grain of rice and coated with synovial tissue having numerous synovial fringes (Töndury, 1940; Dörr, 1958). The fat pad in the superior pocket is continuous with the adipose tissue ringing the spinal nerve in the intervertebral foramen (Töndury, 1940), while in the inferior pocket it is continuous with the adipose tissue between the multifidus muscle and the dorsal aspect of the lamina of the vertebral arch (Lewin, Moffet and Viidik, 1962).

The lumbar synovial joints are supplied with blood from the lumbar artery which, after passing through the intervertebral foramen, gives off a branch piercing the dorsal half of the intertransverse ligament and then giving off twigs to the joint capsule and neighbouring structures (Lewin, Moffet and Viidik, 1962).

The lumbar synovial joints are innervated by direct offshoots from the spinal nerve (Fick, 1904; Lazorthes and Baubert, 1956; Pedersen, Blunck and Gardner, 1956). As one would expect from their embryonic development (Sensening, 1949), the innervation of these joints is bisegmental (Stillwell, 1956; Lewin, Moffet and Viidik, 1962) in the sense that the nerve branch on each level supplies the lateral portion (superior articular process) of that joint and the medial portion (inferior articular process) of the joint caudal thereto. (Fig. 2.)

Microscopic Anatomy

The writer has failed to find in the literature on the anatomy of the spine any description of the microscopic appearance of the articular cartilage and subchondral bone of the intervertebral synovial joints under normal conditions. But several authors have studied the micromorphology of the joint capsule in the lumbar region. The fibrous layer of the capsule of the lumbar synovial joints includes thick bundles of fibres from ligamentum flavum. These bundles are particularly abundant near the superior and inferior ends of the joint (Keller, 1953).

The synovial membrane in the superior and inferior ends of the joint forms a multiplicity of small villi and as a rule a larger fringe. Meniscoid formations have been reported too (Zaccheo and Reale, 1956; Dörr, 1958). The latter arise from the fibrous capsule and intrude a millimetre or so

between the articular surfaces. These meniscoid formations may be up to about two millimetres thick next to the capsule (Zaccheo and Reale, 1956). They are composed of fibrous connective tissue poor in vessels and with round or oval cells in clusters of 3 or 4 lodged in its meshes (Dörr, 1958).

The dorsocaudal portion of the joint capsule is innervated by fibres from the dorsal branch of the spinal nerve (Stillwell, 1956; Pedersen, Blunck and Gardner, 1956). The complete triad of nerve endings — free fibres, complex endings without a capsule and endings with small capsules — have been demonstrated in supravitally stained synovial—joint capsules, surgically removed from the lumbar spine (Hirsch, Ingelmark and Miller, 1963).

Function

The main function of the synovial joints is presumably to guide and stabilize flexion and extension movements (Fick, 1904). The articular surfaces slide upon one another in craniocaudal direction in flexion and extension of the lumbar spine, the tip of the superior articular process in the former case receding from and in the latter approaching the inferior notch of the overlying vertebra (Dittmar, 1930, 1931). Roentgenographic studies of the range of lumbar spine mobility indicate that in flexion and extension the synovial joints on the L_{4-5} and L_5-S_1 levels have the greatest range of movement (Bakke, 1931; Dittmar, 1931; Allbrook, 1957; Jonck and Niekerk, 1961). In lateroflexion the joint space becomes wedge-shaped, with the narrow end pointing craniad on the concave and caudad on the convex side of the resulting scoliosis (Dittmar, 1930). A limit to the lateroflexion is set by the tip of the inferior articular process on the convex side hitting the superior articular process. The range of movement is then only 5° to 10° at each level except L_5-S1 where little or no lateroflexion is possible (Leger, 1955). Rotation of the lumbar spine seems to be a combination of flexion and lateroflexion, whose limits are set by the synovial joints (Steindler, 1955).

Owing to the lordosis of the lumbar spine gravity will tend to displace ventrad the vertebrae below the vertex of the lordosis (de Cuveland and Feser, 1958). The L_{3-} vertebra constitutes as a rule this vertex (Duhs, 1950; Sullivan and Miles, 1959). It has been postulated, therefore, that the joints on the $L_{4-5}$and L_5-S_1 levels at least in part prevent such displacement (Davis, 1961). Furthermore the frontal inclination of the facets and the dorsally wedge-shaped disc of the L_5-S_1 segment is thought to constitute an anatomical basis for exposing the L_5-S_1 synovial joints to greater stress than the other synovial joints of the lumbar spine (Junghanns; 1933). According to some investigators who have applied a load to spinal columns *post mortem* and measured the resulting expansion of annulus

fibrosus or increase in intradiscal pressure (Brown, Hansen and Yorra, 1957; Nachemson, 1960), the synovial joints take up some of the load borne by the lumbar spine. But other studies, involving intradiscal pressure measurements in postmortal spines carrying a shearing load and intravital spines supporting a vertical load, suggest that the load borne by the synovial joints must be a minute fraction of the whole (Nachemson, 1963).

Osteoarthritis

A detailed survey of the whole literature on osteoarthritis — or as it also is called in many papers, arthrosis deformans, hereinafter termed osteoarthritis — would obviously be beyond the scope of this work. In the present investigation, the morphological observations made in the synovial joints of the lumbar spine were evaluated against the background of our present knowledge about the morphological picture in osteoarthritis of the extremital joints. Hence the gross and microscopic anatomy of these joints in osteoarthritis will be described on the basis of previous workers' morphological observations in autopsy specimens. Furthermore such papers will be surveyed which describe investigations illuminating the pathogenesis and aetiology of osteoarthritis.

Morphology of the Osteoarthritic Joint

Introduction

The morphological alterations characterizing osteoarthritis have long been well established (Ecker, 1843; Weichselbaum, 1877; Nichols and Richardson, 1909; Pommer, 1913). Chondral and subchondral osteoarthritic changes always appear in the same order. The chondral changes set in first and are dominated by degenerative phenomena, in due course leading to necrosis and substance losses in the articular cartilage. The subchondral changes, on the other hand, are far less dominated by such degenerative manifestations as atrophy and necrosis of the cancellous bone trabeculae. Instead they mainly take the form of proliferation of vessels and connective tissue followed by osteoneogenesis, leading to subchondral remodelling and osteophyte formation (Pommer, 1913). The articular cartilage begins to exhibit gross osteoarthritic changes, including necrosis and substance losses, around age 30 (Heine, 1926; Parker, Keefer, Mayers and Irwin, 1934; De Palma, 1950, 1957; Olsson, 1953). At autopsy the frequency of such changes in, say, the hip or knee joint is 20 to 30 per cent in the 40—50 years age group and of the order of 60 per cent around and over age 60 (Heine, 1926). Roentgenographic evidence of osteoarthritis is encountered in about 20 per cent of the hip joints and 40 per cent of the knee joints in large series of normal subjects around the age of 60 years (Kellgren and Lawrence, 1958).

Osteoarthritis shows a marked tendency, in both controls and clinical series, concurrently to affect multiple extremital joints (van der Meer, 1945; Kellgren and Lawrence, 1958). Women are apparently more susceptible to this than men and their knee joints, unlike their hip joints, are also affected more often (Heine, 1926; Holmdahl and Ingelmark, 1946; van der Meer, 1945; Kellgren and Lawrence, 1958). In both sexes the large joints of the lower extremities show a higher frequency of osteoarthritis than those of the upper extremities (Heine, 1926).

Gross Anatomy

The cartilage in the osteoarthritic joint has a greyish white to greyish yellow hue. Its surface seems rough. Here and there it is thinner than elsewhere. If the cartilage is extremely thin it acquires a greyish red tone owing to reflexion from the marrow spaces in the subchondral bone. Eventually a stage is reached where extensive portions of the cartilage are missing entirely, exposing the underlying bone.

Exposed areas of the subchondral bone plate have a more or less eburnated appearance. In sections through the head or socket of a joint the subchondral bone plate and the cancellous trabeculae are thickened and the marrow spaces remarkably small in such exposed regions; but the bone plate and the trabeculae often are abnormally thin in the unexposed regions. (Weichselbaum, 1877; Nichols and Richardson, 1909; Lang, 1924.) Besides these changes, cystic formations occur in the subchondral bone in joints with advanced osteoarthritis (Lang, 1924; Heine, 1926; Harrison, Schajowicz and Trueta, 1953; Grueter and Rütt, 1962).

The synovial membrane in the early stages of osteoarthritis seems more or less marked oedematous and its villi are increased in both numbers and size. In advanced stages the entire joint capsule is tightened and conspicuously thickened, and osteophytes are present adjacent to its attachments. (Weichselbaum, 1877; Nichols and Richardson, 1909; Pommer, 1913; Lloyd—Roberts, 1953.)

Microscopic Anatomy

Microscopic changes in osteoarthritis initially appear in the intercellular substance of the joint cartilage in the form of diffuse fibrillation owing to so-called demasking of the fibrils normally embedded in the ground substance. Concomitantly the chondrocytes vanish from some regions while they remain relatively unaffected, or even become more numerous, in other regions (Pommer, 1913; Lang, 1924; Heine, 1926). Cracks appear at an early stage in the superficial cartilage layer. These cracks develop into deep fissures which in the intermediate zone in vertical sections through the cartilage extend perpendicularly to the cartilage sur-

face. The cartilage thus splits up and takes on a more or less fringed appearance (Ecker, 1843; Weichselbaum, 1877; Nichols and Richardson, 1909). The calcified zone shows irregular thickening and is here and there pierced by vessels from the subchondral marrow spaces. Absorption cavities are often seen in the cartilage around the points of entry of these vessels (Pommer, 1913; Lang, 1924). The cartilage's cellular pattern now is markedly abnormal, in that the ovoid chondrons disposed parallel to the surface are irregularly distributed, have a more rounded shape and/or exhibit necrosis. Although the cell density in the intermediate and radial zones diminishes, any chondrons remaining show cell proliferation leading to the formation of giant chondrons. The chondrocytes in these are enlarged and ultimately destroyed by progressive dilatation. These cellular changes cause regional necrosis of the cartilage in advanced cases (Weichselbaum, 1877; Nichols and Richardson, 1909; Pommer, 1913; Lang, 1924; Heine, 1926).

As the destruction of the articular cartilage progresses, changes appear in the subchondral bone. Initially one sees connective tissue proliferation in the marrow spaces and thickening of the subchondral bone plate as well as of the cancellous bone trabeculae. The thickening of the bone plate and trabeculae is confined to those areas of the subchondral bone which have been exposed by losses of articular cartilage substance. Between such regions of so-called subchondral sclerosis the marrow spaces are often widened, contain a higher proporption of connective tissue and are separated only by thin bone slivers (Weichselbaum, 1877; Nichols and Richardson, 1909; Pommer, 1913; Lang, 1924; Heine, 1926). At the stage when the articular cartilage exhibits necrosis and substance losses, abnormal perforations often appear in the subchondral bone plate. Through these perforations more or less highly vascularized connective tissue from the marrow spaces enters the basal cartilage region, or they may be plugged by cartilage. When proliferating connective tissue from the subchondral marrow spaces has filled an articular cartilage defect, it may be transformed into fibrocartilage in which both calcification and formation of new bone take place (Pommer, 1913; Lang, 1924; Heine, 1926; Harrison, Schajowicz and Trueta, 1953; Grueter and Rütt, 1962).

Cartilage inclusions are encountered more or less deeply within the subchondral bone, either adjacent to defects in the bone plate — when they have more or less distinct contacts with the articular cartilage — or embedded in connective or osseous tissue within the marrow spaces. It has been postulated that these cartilage inclusions may be absorbed, leaving behind them cystic formations (Pommer, 1913; Heine, 1926). Subchondral cysts are almost invariably present in advanced stages of osteoarthritis. They may be anything from one or two up to about ten millimetres in

diameter. These cysts may communicate with the joint cavity. Their contents is very variable. Sometimes it consists of connective tissue foci enclosed in a "bone capsule". In other cases they have a mucoid content encapsulated in osseous or connective tissue. The connective tissue in and around such cysts may be loose and rich in vessels (Harrison, Schajowicz and Trueta, 1953; Rütt, 1958; Grueter and Rütt, 1962).

The subchondral changes are accompanied by bone formation along the margins of the joint. This gives rise to the marginal spurs or osteophytes typical of osteoarthritis. They have marrow spaces and blood vessels communicating with those within the subchondral bone. Only a few vessels give the impression of arising from the synovial membrane and/or the periosteum (Pommer, 1913, 1927; Lang, 1924; Heine, 1926; Harrison, Schajowicz and Trueta, 1953; Lloyd-Roberts, 1955).

The joint capsule exhibits changes confined to the synovial membrane so long as the osteoarthritic changes are exclusively chondral. These early changes in the synovial membrane comprise proliferation of cells in the superficial layer, minor perivascular infiltrations of round cells and a somewhat increased number of vessels. Later, when chondral as well as subchondral osteoarthritic changes are present, the synovial membrane is usually transformed into more or less markedly fibrous and poorly vascularized connective tissue, making it indistinguishable from the fibrous layer of the capsule. The whole capsule concomitantly exhibits thickening (Lloyd-Roberts, 1953; Schmitz, 1955; Rütt, 1958; Grueter and Rütt, 1962).

Pathogenesis and Aetiology

Most of those who have studied the problem of osteoarthritis unreservedly agree that changes in the articular cartilage are primary (Weichselbaum, 1877; Nichols and Richardson, 1909; Pommer, 1913, 1927; Lang, 1924; Heine, 1926; Bennett, Waine and Bauer, 1942; Harrison, Schajowicz and Trueta, 1953; de Palma, 1957; Grueter and Rütt, 1962). These changes are predominantly manifestations of degenerative processes such as fibrillation, necrosis and losses of substance. Certain phenomena, however, like the accumulation of chondrocytes seen around cartilage defects induced experimentally (Bennett and Bauer, 1935) or by the osteoarthritic process itself (Pommer, 1913), should probably be interpreted as restorative processes (Carlsson, 1957).

Aetiologically osteoarthritic changes are ascribed to the actions exerted upon the cartilage by articular function and nutrition (Ecker, 1843; Weichselbaum, 1877; Pommer, 1913; Bennett, Waine and Bauer, 1942; Harrison, Schajowicz and Trueta, 1953; Rütt and Hackenbroch, 1957).

Normal articular function abrades the surface of the joint cartilage (Hammar, 1894; Hultén and Gellerstedt, 1940; Ekholm and Norbäck,

1951). Renewal apparently takes place from the articular cartilage's intermediate zone whose cell density has been shown to rise following increased activity (Sääf, 1950). New cells are formed by amitotic division (Elliot, 1936) and losses of intercellular substance are replaced. The chondrocytes are involved in the latter process to the extent that the interfibrillar ground substance is synthetized intracellularly and their system of α-cytomembranes seem to produce a prestage of the collagen fibrils (Zelander, 1959). The ability to form new cells and to regenerate tissue diminishes with age (Elliot, 1936; Calandruccio and Gilmer, 1962; Hall, 1963).

The articular cartilage is elastic and this property is intimately associated with the state of the intercellular substance (Benninghoff, 1925; Hirsch, 1944; Pauwels, 1959). In the ageing cartilage the composition of the intercellular substance undergoes changes, among other things its chondroitin sulphate content falls, leading to reduced elasticity (Hirsch, 1944; Eichelberger and Roma, 1954). The ability of the articular cartilage to withstand the strains of mechanical movements and of bearing loads accordingly diminishes with age.

The subchondral vascular bed and the synovial fluid constitute the sources of nourishment for the articular cartilage (Ekholm, 1951, 1955; Brodin, 1955). Articular function seems to promote the nutrition: the passage of nutrients into the cartilage from the subchondral vascular bed rises when joint function commences (Ingelmark and Sääf, 1948; Ingelmark, 1950). This passage can longer be maintained on a high level if the joint is exposed to intermittent exercise than a static (Ingelmark and Ekholm, 1948; Ekholm and Ingelmark, 1952). Against this background, it has been adduced that, by interfering with the nutrition of the cartilage, unsuitable articular function is capable of producing alterations of the cell pattern and in the intercellular substance which, in turn, lead to degenerative and regenerative changes in the articular cartilage (Harrison, Schajowicz and Trueta, 1953; Salter and Field, 1960; Trias, 1961).

Undernutrition of the articular cartilage, with attendant osteoarthritic changes, has also been ascribed to impaired circulation, either in the subchondral vessels (Müller, 1924; Phemeister, 1940) or in the vessels of the synovial membrane (Strangeways, 1920; Lacapére and Drieux, 1952). Yet few authors have claimed that vascular disturbances in and around the joint constitute the most common cause of osteoarthritic chondral changes (Wollenberg, 1909; Goldhaft *et al.*, 1930).

Osteoarthritic changes do not appear subchondrally until the chondral ones have progressed to a fairly advanced stage (Weichselbaum, 1877; Nichols and Richardson, 1909; Axhausen and Pels, 1911; Pommer, 1913;

Heine, 1926; Harrison, Schajowicz and Trueta, 1953). Changes in the subchondral bone are consequently interpreted as more or less dependent on, and as a response to, those in the articular cartilage (Pommer, 1913, 1927; Harrison, Schajowicz and Trueta, 1953). This hypothesis receives strong support from the fact that in certain circumstances cartilage defects induced in experimental animals give rise to a subchondral morphological picture typical of osteoarthritis. Superficial defects are healed by tissue regeneration from the surrounding intact cartilage without producing any alterations in the morphological appearance of the subchondral bone. But if the artificial defects extend into the calcified zone of the articular cartilage a more or less profusely vascularized connective tissue appears subchondrally (Carlsson, 1957; Evans, Eggers, Butler and Blumel, 1960).

Connective tissue proliferation in the subchondral bone and hypertrophy of its cancellous trabeculae in osteoarthritis are regarded as its response to increased mechanical stimulation. And the subchondral appearance of osseous atrophy, necrosis and cystic formations are interpreted as degenerative phenomena in osteoarthritis following reduced or completely absent mechanical stimulation (Pommer, 1913, 1927; Müller, 1924; Bennett and Bauer, 1935; Fischer, 1922; Bennett, Waine and Bauer, 1942.) As mentioned, the subchondral bone often displays proliferative and degenerative changes at the same time. It remains to be demonstrated, however, that this is because the presence of chondral osteoarthritic changes redistributes the load on the articular surface, increasing it in some parts and reducing it in others. Nevertheless, it has been shown in animal experiments that the general loading conditions in the joint are of significance for the onset and course of osteoarthritic changes that progress to involvement of the subchondral bone. Joint immobilization alone merely produces degenerative chondral changes, while immobilization combined with compression yields a morphological picture similar to osteoarthritis both in the articular cartilage and in the subchondral bone (Wehner, 1923; Salter and Field, 1960; Trias, 1961; Calandruccio and Gilmer, 1962). Some workers are of the opinion that ingrowth of subchondral vessels into the degenerated articular cartilage is merely an attempt to revitalize the latter having nothing to do with increased loading of the subchondral bone (Harrison, Schajowicz and Trueta, 1953).

The formation of new bone along the margins of the joint is preceded by invasion of connective tissue from the subchondral marrow spaces (Pommer, 1913, 1927; Lang, 1924; Harrison, Schajowicz and Trueta, 1953). During the initial stages of osteophyte development vascularization apparently takes place also from neighbouring synovial tissue and/or periosteum. During the continued development and growth of osteophytes, however, new bone is formed mainly in fibrocartilage produced by the

connective tissue growing in from the subchondral marrow spaces (Harrison, Schajowicz and Trueta, 1953).

The subchondral cysts are, as mentioned, regarded as degenerative phenomena confined to those subchondral bone regions underlying articular cartilage with advanced changes. By overloading the bone this would result in either atrophy or traumatization of the cancellous bone trabeculae (Harrison, Schajowicz and Trueta, 1953; Rhaney and Lamb, 1955; Rütt, 1958; Grueter and Rütt, 1962). Absorption of attendant necrosis would lead to cyst formation. It has alternatively been adduced that synovial fluid pressed into the subchondral bone by way of articular cartilage defects by osteolysis causes the subchondral cysts (Landells, 1953). It does not seem established, however, whether synovial fluid possesses osteolytic activity. Regenerative processes commence within the cysts, especially within those immediately beneath the subchondral bone plate secondary to ingrowth of vascularized connective tissue (Grueter and Rütt, 1962).

Apart from osteophytes adjacent to its attachments, the joint capsule exhibits progressive fibrosis, believed to commence with the proliferation of synovial membrane cells around accumulations of small cartilage fragments. Accumulation of such cartilage fragments is held to be a direct consequence of the increased abrasion of the articular surfaces in an osteoarthritic joint. (Lloyd-Roberts, 1953.)

Osteoarthritis of the Lumbar Synovial Joints

Gross Anatomy

The gross appearance of lumbar synovial joints with osteoarthritis of various degrees is similar in principle to that of osteoarthritis of the extremital joints. The initial manifestations are thus that the articular cartilage exhibits a yellow discolouration and has a rough surface. More or less extensive cartilage defects and osteophytes appear in due course and occasionally one encounters joints with fibrous and/or true ankylosis (Güntz, 1934).

Osteoarthritic changes in the subchondral bone plate and capsular attachments have moreover been studied in skeletons (Güntz, 1934; Shore, 1935; Ingelmark, 1956, 1959). In the early stages the subchondral bone plate displays porosity, which later turns into larger perforations in the bone plate and it also shows uneven thickening. In advanced stages the bone plate has fewer but larger holes, is markedly sclerotic and has eburnated patches. Marginal osteophytes appear concomitantly with these changes, particularly on the dorsal rim of the joints (Ingelmark, 1956, 1959).

A wedge-shaped, or narrowed or widened joint space, more or less pronounced subchondral sclerosis and osteophytes in the roentgenogram have been interpreted as evidence of osteoarthritis of the lumbar synovial joints (Lange, 1933, 1936; Oppenheimer, 1943; Keller, 1953). For roentgenographic studies oblique projections have usually been adopted with an angle of incidence of the central ray on the sagittal plane of around 45° (Dittmar, 1931). But the configuration of the lumbar synovial joints is such that their joint space readily can be destorted in roentgenograms (Reichmann 1963).

Microscopic Anatomy

The microscopic appearance of osteoarthritis in the lumbar synovial joints does not seem to have been followed systematically. Brief accounts have nevertheless been given in conjunction with reports on grossly visible osteoarthritis (Güntz, 1934; Ingelmark, 1956, 1959) or in the course of discussions relating to the mechanical action of intervertebral disc degeneration on the function of the lumbar synovial joints (Keller, 1953; Harris and Macnab, 1954).

Fibrillation and cell proliferation have thus been noted in the articular cartilage in early stages of osteoarthritis when it exhibits gross yellow discolouration and roughening of the surface (Güntz, 1934). As described with respect to extremital joints (p. 12), these chondral changes progress towards fringing of the cartilage with consequent loss of substance, and exposure of the subchondral bone plate (Güntz, 1934; Harris and Macnab, 1954). At this stage the cartilage grossly displays an uneven and course surface, here and there discoloured greyish red. Subchondral sclerosis and formation of new bone are distinctly visible in histological sections (Güntz, 1934). In conformity with the observation on skeletons that one of a joint's articular surfaces may exhibit only minor changes while the other shows sclerosis, perforations in the subchondral bone plate and osteophytes, microscopic examination too sometimes reveals considerable differences between the same joint's articular surfaces. The surface of one cartilage may have a normal cell pattern while its mate may present marked cell proliferation. Indeed, in extreme cases a tolerably well preserved cartilage can touch exposed portions of the opposite subchondral bone plate of the other (Güntz, 1934).

Frequency and Distribution

The frequency and distribution of osteoarthritic changes in the spinal synovial joints has been studied both on skeletons (Shore, 1935; Ingelmark, 1956, 1959) and in autopsy specimens (Güntz 1934; Putti and Logròscino, 1937; Horwitz and Smith, 1940). Shore examined a series of 126 spinal columns from skeletons of unspecified age and sex distribution. Osteo-

arthritis was considered present if osteophytes were found along the margins of the joint's articular surfaces. Such osteophytes were often encountered around the middle of the anatomical regions of the spine. The lumbar spine had the highest frequencies, with an absolute peak incidence for the spine as a whole at the L_{2-3} level where about 65 per cent of the joints had osteoarthritic changes. Caudally of the L_{2-3} level osteoarthritis gradually became less frequent, its incidence being approximately 35 per cent at the L_5—S_1 level. In the cervical and thoracic regions of the spine the peak osteoarthritis frequencies were noted at the C_{3-4} and Th_{4-5} levels, both being of the order of 25 per cent.

Ingelmark studied spinal columns from a series of 138 male and 73 female, mediæval skeletons. The criteria of osteoarthritis were: porosity of the articular surface, sclerosis of the subchondral bone plate, osteophytes in the joint capsule attachment region on the articular process, and ankylosis of the joint. In the series as a whole these types of osteoarthritic changes showed a considerably higher frequency within the cervical and thoracic regions than within the lumbar spine. While in the two former regions 27 and 22 per cent, respectively, of the total number of joints were affected, the same was the case of only 9 per cent of the joints in the lumbar spine. Within complete spines there was a frequency maximum of approximately 35 per cent at the C_{3-4} level and another at the Th_{4-5} level of about 38 per cent. No definite frequency differences between levels could be demonstrated in the lumbar region, but the L_{4-5} level showed the highest relative frequency, namely 10 per cent. No differences were noted between sexes.

The average degree of the osteoarthritic changes, as judged by a point scoring system, was substantially similar in the cervical, thoracic and lumbar regions. Among the lumbar synovial joints those at the L_{4-5} level exhibited the highest average score for osteoarthritic changes. Approximately 5 per cent of the total number of lumbar synovial joints had one articular surface more affected than the other. Only one of the articular surfaces was affected in 2 per cent of the joints. The superior and the inferior articular surface were equally often more affected.

Güntz (1934) studied the thoracic and lumbar synovial joints in 56 autopsy cases of unspecified age and sex. All the joints were opened and grossly examined for the presence of osteoarthritic changes, which were graded according to degree. The gross appearance of some of the joints was, as mentioned elsewhere (p 18), checked by microscopic examination.

Below age 30 all joints were grossly normal. Although Güntz did discuss how the frequency of osteoarthritic changes was related to rising age, he did not state whether his figures were based on complete spines or the total number of joints examined. Accordingly such figures as 30 per cent

at age 45 and 50 per cent at age 65 are ambiguous. Frequencies of affected joints in the series as a whole are, on the other hand, specified for each level and each side. The frequency of joints showing osteoarthritic changes rose rapidly from about 10 per cent in the upper part of the thoracic spine to some 60 per cent at the levels Th_{3-4}, Th_{4-5} and Th_{5-6}, whereupon it once more fell to around 30 per cent in the lower part of the thoracic spine. Then it gradually rose to some 55 per cent at the L_{4-5} and L_5-S_1 levels. A difference between the right and left sides of at most 10 per cent was found only at the L_1-L_2 and L_5-S_1 levels, the right side being preponderant. Ankylotic joints were encountered exclusively in the thoracic region around the Th_{4-5} level.

Putti and Logròscino (1937) studied the occurrence of gross osteoarthritic changes in 42 male and 33 female lumbar spines from autopsy cases. The 4 spines in the 18—30 years age group all had grossly normal joints. All lumbar spines over 30 years of age exhibited gross osteoarthritic changes which became progressively more severe with rising age. More than 50 per cent of the 33 lumbar spines from subjects over 60 years of age exhibited advanced or grave osteoarthritis in one or more joints. The distribution of osteoarthritic alterations within lumbar spine levels showed that in the series as a whole the proportion of affected joints was merely some 60 per cent at the L_{1-2} level *versus* over 80 per cent elsewhere. The highest frequency in the lumbar spine — approximately 90 per cent — was encountered at the L_{4-5} level.

In an investigation designed to seek optimal oblique projections for roentgenographic examination of the lumbar synovial joints, Horwitz and Smith (1940) used an autopsy series from 76 males and 4 females and recorded the frequency of gross osteoarthritic changes. Gross chondral changes and osteophytes were observed in one or more joints of 31 per cent of the spines. No mention is made of the distribution by age or level of these osteoarthitic changes.

Examining roentgenographically 368 subjects, a random sample of every 10th inhabitant of Leigh town, Lancashire, Kellgren and Lawrence (1958) found that the frequency of subjects with osteoarthritic changes in the cervical and lumbar synovial joints was 25 and 30 per cent, respectively, there being no frequency difference between the sexes. The absence of information about the roentgenographic method, however, makes it difficult to assess the value of this investigation.

Aetiology

Apart from being a phenomenon associated with ageing, osteoarthritis has been assumed secondary to congenital deformities, structural scoliosis, disc degeneration and trauma.

In intervertebral disc degeneration increased range of mobility of all moving parts in the segment has been demonstrated (Knutsson, 1944; Friberg and Hirsch, 1949; Jirout, 1959), as well as changes in the mechanical response within the disc itself (Ingelmark and Ekholm, 1952; Hirsch and Nachemson, 1954; Hirsch, 1955; Brown, Hansen and Yourra, 1957; Nachemson, 1960).

Several workers have expressed the view that osteoarthritis more or less often may be secondary to disc degeneration in the lumbar spine (Schmorl, 1931, 1932; Junghanns, 1931, 1933; Hildebrandt, 1933; Severin, 1943; Keller, 1953), the presumed causative factor being functional disturbances of the type mentioned above. Notably, however, nobody has given any information on the degree and frequency of the osteoarthritis accompanying disc degenration to support this view. Conversely, Güntz (1934) adduced that normal and degenerated intervertebral discs are accompanied by osteoarthritic changes equally often. He added, however, that autopsy specimens with disc degeneration of high degree and consequently segmental instability invariably exhibited osteoarthritic changes. No absolute numbers are specified. The same criticism may be raised against Harris's and Macnab's (1954) study of 123 lumbar spines from autopsy cases of all ages. Their most remarkable statement is that osteochondral fractures fairly often accompanied disc degeneration. Ingelmark (1956, 1959), demonstrated that a weak though definitely positive correlation exists between lesions of the vertebral bodies and osteoarthritic changes in the spinal synovial joints. Grave changes in either the vertebral body joints or the synovial joints are usually combined with changes of similar degree in the other type of joint in the same segment.

At roentgenographic examinations Lange (1933, 1936) found that in the lumbar spine osteoarthritis of the synovial joints was closely associated with scoliosis. He supported this statement not with statistical data but with case reports. The same applies to others (Güntz, 1934; Putti and Logròscino, 1937; Täger, 1964) who have postulated that osteoarthritis often is secondary to scoliosis.

Asymmetries in shape, size and inclination of the joint facets have also been regarded as a major factor in the causation of osteoarthritis, especially in the lumbosacral region of the spine (Putti, 1927; Putti and Logròscino, 1937). Studying a series of 80 lumbar spines from autopsy cases, Horwitz and Smith (1940) found that 8 of the 24 with osteoarthritic changes also exhibited asymmetry of the lumbosacral joint facets, contralateral facets being differently inclined towards the sagittal plane. Brailsford (1929) roentgenographically demonstrated asymmetrically inclined joint facets in about 30 per cent of over 3000 subjects although only one of them had roentgenographically manifest osteoarthritis. Among an unspecified

number of patients with various back disorders, Smith (1934) found 55 in whom dorsal displacement of the 5th lumbar vertebra was associated with abnormal inclination of the sacral joint facets. But only a few of them had concommitant osteoarthritis. Southworth and Bersack (1950) reported Putti's (1927) "anomaly of articular tropism" at the L_{4-5} level in 26.5 per cent and at the L_5—S_1 level in 17.4 per cent of 550 subjects without back symptoms who were examined roentgenographically. This anomaly in the lumbar spine was present in 54 of 233 subjects under 40 years of age, although none exhibited either scoliosis or osteoarthritis of the lumbar synovial joints. Distinct asymmetry — a difference of about 15° between the inclinations of the right and left joint facets in relation to the sagittal plane through the vertebra — has a frequency of approximately 10 per cent in large series of skeletons (Badgley, 1941; Jonck, 1961). Similar frequencies have been encountered in comprehensive series of roentgenograms of children's backs (Kuhns, 1935). On the basis of osteometric observations on the thoracic and lumbar vertebrae from 20 entirely normal skeletons between 19 and 86 years of age, Farkas (1941) drew the conclusion that such asymmetries are dependent upon and a normal feature of physiological scoliosis. This conclusion may receive support from the fact that asymmetry of the occipital condyles has been shown to become evident not until the first year of life and to increase in frequency with age (Ingelmark, 1943). Asymmetry of the lumbar synovial joints may also develop on the basis of congenital hypoplasia of the joint facets (Brocher, 1950).

In addition to mechanical abnormalities of the lumbar segments, it has been adduced that rheumatoid arthritis in the spinal synovial joints may precede and induce the osteoarthritic changes (Oppenheimer, 1943). Reporting the results of a roentgenographic study of 1200 subjects with and without back complaints, Gantenberg (1930) stated that intervertebral disc degeneration in many cases was accompanied by rheumatoid arthritis in the lumbar synovial joints.

CHAPTER 2

Material

This investigation is based on observations made in a series of 104 lumbar spines from 86 subjects over and 18 under 20 years of age. All the former and 8 of the latter had been collected by Friberg and Hirsch in the years 1946—1948 at autopsies in Stockholm hospitals, the remaining 10 being taken by this writer from corpses autopsied in Gothenburg hospitals. Every synovial joint and intervertebral disc in the 86 lumbar spines from subjects over 20 years of age was examined systematically for morphological abnormalities. The information thus obtained was used for a statistical analysis of changes in the vertebral body joints as well as in the synovial joints. The age and sex distribution of the 86 adult lumbar spines will be found in Table 1.

The 18 lumbar spines from young persons up to 20 years of age were studied with respect to the microscopic anatomy of the synovial joints, particular attention being paid to any pathological changes therein. The age distribution of the young lumbar spines is presented in Table 1.

TABLE 1

Age and sex distribution of lumbar spines over 20 years of age and age distribution of lumbar spines up to 20 years of age.

Age groups	Women		Men		No.	
20—25 years	4		7		11	
26—35 years	8		8		16	
36—45 years	9		7		16	
46—55 years	7		12		19	
56—65 years	3		11		14	
> 65 years	3		7		10	
No.	34		52		86	
Age, years	0—1	1—5	6—10	11—15	16—20	No.
No.	4	6	2	4	2	18

The series of lumbar spines was unselected in the sense that it did not come exclusively from subjects with or without back disorders during life. No lumbar spine was taken, however, from autopsy cases in which the cause of death was a tumour or tuberculosis, in order to exclude spines with tumour metastases or tuberculous spondylitis. The autopsy report was scrutinized, moreover, for every spine subjected to systematic examination of the synovial joints and intervertebral discs. But the pathological conditions described by the pathologist were in no case such as might have had any direct effects upon the state of the discs and/or joints. Those spines used for microscopic examination of the synovial joints were dissected and prepared for further histotechnical treatment on the same day as, or at the latest the day after, the autopsy. In the latter event the spines were stored in a refrigerator during the interval between autopsy and dissection.

Spondylolysis or spondylolisthesis was seen in 4 cases altogether. None of the spines exhibited evidence of fixed scoliosis in the lumbar region.

None of the spines exhibited evidence of fractures or hypoplasia of the articular processes.

* * *

The association between morphological changes and roentgenologically visible abnormalities in the vertebral body joints in the present series of lumbar spines has been studied by Friberg and Hirsch (1949). It appeared that 17 of the 100 spines examined exhibited roentgenological evidence of intervertebral disc degeneration in the form of reduced disc thickness, osteophytes on the edges of the vertebral bodies and sclerosis of the subchondral bone of the vertebral bodies. The corresponding discs all displayed very advanced morphological changes.

Flexion and extension of the lumbar spine preparations was accompanied by, respectively, ventrad and dorsad diplacement of more than 5 mm — in other words so-called instability, as defined by Knutsson (1944) — of the L_4 vertebra in relation to the L_5 vertebra in 12 of the spines. In these spines the disc in the L_{4-5} segment exhibited total or subtotal ruptures of annulus fibrosus. Prolapse of nucleus pulposus tissue was en countered in the L_{4-5} and/or L_5—S_1 segments of altogether 11 spines. In these discs with nucleus prolapse the morphological changes were in other respects grossly indistinguishable from those presented by other discs with degeneration only.

Both the gross and the microscopic intervertebral disc changes in this series of lumbar spines have been described by Hirsch and Schajowicz (1952). Approximately 40 per cent of the discs in the L_{4-5} and L_5—S_1 segments of spines older than 45 years displayed radiating ruptures of

the annulus fibrosus. Such ruptures were less common in the other discs in the lumbar spine. Below 20 years of age the discs exhibited merely microscopic changes in the form of small ruptures in the innermost lamellae of the annulus fibrosus. Microscopic examination of grossly visible ruptures almost invariably disclosed the presence of more or less richly vascularized connective tissue, growing into and around the ruptures from the connective tissue located marginally in the disc adjacent to the posterior longitudinal ligament.

CHAPTER 3

Methods

Preparation Techniques

All specimens collected 1946—48 and later were treated in the following way. All muscle having been dissected away, the lumbar spine preparation was roentgenographed in the frontal projection with the vertebrae resting normally on top of each other and in the lateral projection in the same position as well as in positions of maximal flexion and extension, as achieved by manual bending of the lumbar spine when the sacrum was fixed in a screw clamp. These roentgenograms were used for studying disc thickness, vertebral bodies and synovial joints. In addition instability, as defined by Knutsson (1944), and subluxation, as defined by Hadley (1936, 1951) and others, were registrered.

The body and arch of each vertebra were now separated by sawing through the pedicles, whereupon the synovial joints were subjected to histotechnical preparation. Each intervertebral disc was divided into two parts of equal thichness, the gross appearance of the cut surfaces being noted, which were photographed and prepared for microscopic examination.

After fixation in 10 per cent formalin solution and decalcification with hydrochloric acid according to Ebner, each synovial joint was devided into three parts of roughly the same size by cuts perpendicular to the craniocaudal axis of the joint in situ. Each such joint portion was embedded in paraffin and 4 or 5 sections approximately 5 μ thick were cut from it on a conventional microtome. In this fashion a "sample" was obtained at about every 4th millimeter of the joint.

For the purposes of the investigation originally performed on these lumbar spines only two sections had in most cases been taken from each joint and stained with Ehrlich's Haematoxylin-eosin. Consequently further sectioning was required for the present investigation, occasionally following renewed decalcification in a mixture of equal volumes of concentrated formic acid and 7 per cent sodium formiate solution. These new sections were stained by either Delafield's or Bock-Hansen's haematoxylin-eosin procedures.

Principles for Gauging Changes of Synovial Joints and of Vertebral Body Joints

Synovial Joints

The microscopic appearance of the synovial intervertebral joints was, as mentioned, studied in sections taken about 4 millimetres apart along the long axis of the joint. This should be adequate in regard to changes in the joint cartilage which show a marked tendency to span the entire craniocaudal extent of the joint facet (Fig. 3). Minimal changes in the subchondral bone and capsular attachments, on the other hand, might occasionally be missed. Any joint with one or more structures showing unmistakeable evidence of damage during histotechnical preparation was discarded, unless its preserved portions presented consistent and pronounced changes.

The morphological appearances of the concave (on superior articular process) and convex (on inferior articular process) surfaces of each joint were examined in the microscope and rated separately, "0" representing normal conditions, "1" mild *to* moderate changes and "2" marked *to* advanced changes. The results of the examination were thus converted to a form suitable for statistical analysis. The following structural details of the synovial joints were taken into consideration.

A. Uncalicified articular cartilage

(a) Cell pattern

GRADE 0: Cells clustered in distinct strata.

GRADE 1: Irregular cell distribution; cells disposed in so-called nests; more or less marked cell enlargement.

GRADE 2: Cell paucity and/or necrosis.

(b) Appearance of intercellular substance

GRADE 0: Unstructured intercellular substance; smooth or only slightly rough cartilage surface.

GRADE 1: Fringing of cartilage surface and fissures of varying depth in cartilage with denudation and fibrillation of intercellular substance; undiminished cartilage thickness.

GRADE 2: Tissue losses and/or necrosis in articular cartilage.

B. Calcified articular cartilage

GRADE 0: Calcification confined to basal portions of cartilage, encompassing approximately one fifth of its total thickness.

GRADE 1: Somewhat thickned and conspicuously irregular calcified zone.

GRADE 2: Markedly thickened calcified cartilage zone.

C. Subchondral bone

GRADE 0: The subchondral bone forms a distinct lamella towards, the articular cartilage; contacts established through this lamella between calcified cartilage zone and bone marrow vessels by vascular budding.

GRADE 1: Here and there thickening of the subchondral bone lamella which exhibits fissures wherein cartilage fragments are lodged; occasional marrow spaces contain connective tissue regions.

GRADE 2: Trabecular thickening and/or large marrow spaces, extending as far as the basal cartilage portions. Marrow spaces wholly or partly filled with more or less richly vascularized connective tissue which via defects in the subchondral bone lamella in places infiltrates the calcified cartilage layer.

D. Capsular attachments

GRADE 0: Smooth transition at joint periphery of hyaline cartilage via fibrous cartilage to fibrous capsular layer; Distinct capsular attachments.

GRADE 1: Minor osseous deposits marginally and synovial tissue fibrosis.

GRADE 2: Pronounced marginal osteophytes and, adjacent to capsular attachments, metaplasia of fibrous capsular layer into cartilage and/or connective tissue.

Coexistence of chondral changes of grade 2 for the cell pattern and the intercellular substance and of subchondral changes of grade 1 or 2 in the same facet was taken as evidence of osteoarthritis (A:a = 2 + A:b = 2 + C = 1 or 2 + D = 1 or 2. See preceding section).

The above rating system was used for coding the morphological appearance of the joint facets, with the criterion that at least three sections from every facet had to attain identical scores. When the entire series had been examined in this manner without knowledge of sex or age, every section was re-examined in the microscope and a statement of the morphological picture of each joint facet was recorded in synoptic form. The statement was always based on those sections exhibiting the most consistent and pronounced degrees of any morphological changes. The results of these two examinations were then collated. It turned out that the numerical code and the synoptic statement were not quite in agreement with respect to a very few joint facets in occasional lumbar spines. To eliminate the few instances of personal bias that had thus become manifest, the whole series was examined a third time and recoded in accordance

with the same rating system as before. This time the results showed adequate agreement with the synoptic statements. The statistical analysis was consequently based on the latter coding. But had it been based on the former the results would not have deviated significantly, for within age groups the mean scores at the first and second numerical coding merely exhibited occasional minor differences. Lastly those joints which, as defined elsewhere (p. 28), were deemed to represent the condition of osteoarthritis were scrutinized a fourth time and found to have a morphological picture well satisfying the criteria adopted for justifying the microscopic diagnosis of osteoarthritis.

Against the background of the observations made in the course of the aforementioned examinations, a general assessment was made of the overall picture presented by all the joint facets in each lumbar spine. This general assessment was used as the foundation for a description of the histological picture of the synovial joints under normal conditions as well as in various degrees of morphological changes.

There is a danger that changes in the capsular attachments will be overrepresented unless some peculiarities of the normal anatomical relations of the synovial joints of the lumbar spine are known. On the dorsal aspect of the superior articular process the capsular attachment extends immediately medial to the mamillary process on which insert the central fibres of the multifidus muscle as well as the outer fibrous layers of the joint capsule (Fig. 4). Changes in those structures inserting on the mamillary process may occasionally give the impression of being osteophytes in the joints. Such changes, however, should rather be interpreted as metaplasia of the transitional zone between bone and fibrous tissue as described by Kneese and Biermann (1958) and others—and are in no way related to any joint changes. To some extends this holds true also for those regions wherein ligamentum flavum attaches to the articular processes with metaplasia to osseous tissue (Fig. 5). The only true osteophytes in the synovial joints are those situated intracapsularly which have marrow spaces communicating with the subchondral ones (Fig. 6).

Considering that the series of lumbar spines had been lying idle in sectioned and/or embedded form for comparatively many years prior to the present investigation, it was felt that improved accuracy of assessment would be achieved by comparing the results with observations in a similar study of the synovial intervertebral joints in 10 fresh lumbar spines. This comparison had the following results. Just as the "stored" specimens exhibited cell proliferation and fibrillation of the intercellular substance in articular cartilages from subjects as young as 20—30 years, the same was the case in articular cartilages in fresh lumbar spines from subjects of similar age. When the latter specimens presented more pronoun-

ced changes in the morphological picture of the synovial joints, it had similar degenerative and restorative features as were encountered in the "stored" lumbar spines. Nor was there any difference with respect to artefacts. Thus the fresh autopsy specimens too included joints in which the articular cartilage, subchondral bone and joint capsule had been damaged during histotechnical preparation. Among commoner artefacts the following may be mentioned: fringing of the articular cartilage in some regions, separation of the cartilage's calcified regions from the subchondral bone, fracture of the cancellous trabeculae with compression of the subchrondal marrow spaces, detachment of the joint capsule or ligamentum flavum from its point of attachment on one of the articular processes.

On the basis of these gradings the following scores were compiled to estimate the degree of osteoarthritic changes in the lumbar synovial joints.

Articular structure	Code	Maximum points		
		Facet score	Joint score	Segment. score
Cell pattern of articular cartilage	A:a	2	4	8
Intercellular substance of articular cartilage	A:b			
Calcified layer of articular cartilage	B			
Subchondral bone	C			
Capsular attachment	D			
Articular cartilage	A—B	6	12	24
Articular bone	C—D	4	8	16
Articular cartilage and bone	A—D	10	20	40

Vertebral Body Joints

The condition of the vertebral body joints was studied by grossly examining the intervertebral discs and by scrutinizing roentgenograms of each lumbar-spine preparation.

The gross appearance of the intervertebral discs was gauged by inspection of photographs, the grades given thereupon being collated with the corresponding grading by Friberg and Hirsch. (In a prior study of intervertebral discs from some 30 fresh corpses of various ages, the writer's experiences had made him thoroughly conversant with different stages of grossly visible disc changes). It turned out that the writer's assessment was in complete agreement with the original one, except for a few instances when one or two of the discs in the photographs were interpreted as exhibiting a lower degree of changes than that originally assessed. The classification of intervertebral disc changes proposed by Friberg, Hirsch and Schajowicz was adopted (Cf. Fig. 7).

GRADE 0: Discs without changes visible to the unaided eye, whose gelatinous shiny nucleus pulposus readily can be distinguished from the grossly unruptured annulus fibrosus.

GRADE 1: Discs with gross changes in the nucleus pulposus which, though somewhat more fibrous, remains clearly distinguishable from the still intact annulus fibrosus.

GRADE 2: Discs with gross changes in both nucleus pulposus and annulus fibrosus, the former being rather fibrotic but still soft and the latter presenting occasional fissures. The two are less clearly yet perceptibly demarcated.

GRADE 3: Discs with marked gross changes in the form of fissures and/or cavities in both nucleus pulposus and annulus fibrosus.

Any score of 2 or 3 was taken as evidence of disc degeneration.

The appearance of any osteophytes occurring on the edges of the vertebral body in roentgenograms of the lumbar spine preparation in frontal and lateral projections was gauged in accordance with the following scale (cf. Nathan, 1962).

GRADE 0: The rim of the vertebral body is clearly demarcated from its cancellous portion in frontal and lateral projections.

GRADE 1: The demarcation between the rim of the vertebral body and its cancellous portion is obscured by small, up to ricegrain-sized osteophytes.

GRADE 2: The edges of the vertebral body exhibit large osteophytes in shape more or less closely resembling bird's beak.

GRADE 3: Osteophytes bridge the gap between and render ankylotic adjacent vertebrae.

The results were checked against the records of the previous investigation by Friberg and Hirsch concerning any osteophytes at dissection on the edges of the vertebral bodies. By so doing, it became possible to make allowance for projection distorsions.

Statistics

Standard statistical methods were used. The significance of differences between means were tested with the aid of Student's *t*. Confidence limits were calculated on the assumption that the series agreed with the t-distribution. The significance of intercurrences of osteoarthritis, disc degeneration and marginal vertebral osteophytes were analysed with the aid of X^2-test. When positiv intercurrences were found the productmoment correlation coefficient was employed.

CHAPTER 4

Microscopic Anatomy of Lumbar Synovial Joints with and without Morphological Changes

Normal Joints

The appearance of the lumbar synovial joints during childhood and adolescence will not be discussed here. The joints have stopped growing by about age 20. The articular process peripheral to the capsular attachment ceases to grow before the joint facet itself does so. Hence the joint facets often seem to curve dorsally beyond the level of the articular processes elsewhere (Figs. 8, 9).

The surface of the articular cartilage is smooth in the adult. In its central region the tangential zone is composed of three or four layers of oval cells with their long axis disposed parallel to the surface. Next comes a hinted transitional zone with chondrons of three or four chondrocytes. Most of the cartilage thickness is occupied by the radial zone where the chondrons are composed of six to eight comparatively large cells. These chondrons have their long axis pedpendicular to the cartilage surface. In the central parts of the cartilage it is thus justified to speak of a radial zone. Not so in the marginal parts, where only a superficial and a deeper zone can be distinguished from the cell pattern. The former is continuous with the central tangential zone, and the latter has its cells disposed as in the aforementioned transitional zone. The transition between cartilage and capsule is gradual in the dorsal parts of the joint but rather abrupt towards ligamentum flavum and in the superior recess. The intercellular substance of the cartilage is light microscopically structureless. (Fig. 10).

Next to the subchondral bone plate comes the calcified zone of the articular cartilage, which uniformly occupies about one-sixth of the whole cartilage thickness (Fig. 10 b). So-called vascular buds on the subchondral bone plate intrude into the calcified zone. The marrow spaces in the subchondral bone are fairly small and uniformly spaced, except that the cancellous trabeculae quite often are a little broader in the ventral portion of the articular process (Figs. 4, 10).

Joints with Morphological Changes

No evidence of specific or unspecific inflammation was observed in any of the lumbar spines. The same applies to tumours and other diseases capable of affecting cartilage, bone or connective tissue. Nor were any fractured synovial joint facets encountered at either the microscopic or the roentgenographic examination.

Changes of degenerative as well as proliferative types were observed, often concurrently, in degrees progressing with age from trifling to profound. In the absence of clearly demarcated stages, the following description is based on an arbitrary classification into degrees that typically are not encountered before the ages of 30, 45 and 60 years, respectively.

Degree 1. Some articular cartilages have a fairly irregular cell pattern either because there are very few cells in some regions or because of marked cell proliferation centrally (Fig. 11). Concomitantly the intercellular substance is fibrous and the cartilage surface splits up by cracks the cells here and there in the tangential layer being lost or replaced by rounder cells in groups of three to five. The cracks may develop into deep fissures in the cartilage. For a short distance in the tangential zone these fissures usually run parallel to the surface and on reaching the transitional zone proceed towards the calcified zone in a direction perpendicular to the surface. In such articular cartilages the thickness of the calcified zone is often increased (Fig. 12). At this stage the chondrons are as a rule large, round or oval and contain up to ten or twelve chondrocytes, which at adequate resolution are seen to be distended and vacuolated and to have a pyknotic, central or eccentric nucleus. Between such chondrons there are necrotic foci more or less distinctly outlining the contours of former chondrons (Fig. 12). A similar cell pattern may be encountered in cartilages with only a few fissures, and similar large chondrons are then situated in the immediate neighbourhood of the fissures. Changes of the type described in the foregoing are seldom accompanied by morphological abnormalities in the subchondral bone. Nor is there appreciable synovial membrane proliferation or round-cell invasion of the capsule.

Degree II. In addition to the changes described under "Degree I", the articular cartilage begins to present regions of circumscribed necrosis and local or extensive substance losses (Figs. 13, 14). The subchondral bone — hitherto at most showing minor thickening of the bone plate and cancellous trabeculae and occasional small regions of connective tissue proliferation—now enters the picture and has conspicuous changes. The marrow spaces are remarkably large in some regions, while in others they are markedly constricted and separated by thick trabeculae. Vascularized connective tissue from the subchondral marrow spaces invades the base of

preserved cartilage portions and, via fibrocartilage, may give rise to formation of new bone so that varying portions of the subchondral bone plate are raised above its original level (Figs. 14, 15, 16).

Opposite necrotic regions or substance losses in the articular cartilage the subchondral bone plate may have large defects which are either penetrated by vascularized connective tissue from enlarged subchondral marrow spaces or plugged by necrotic cartilage or bone (Figs. 14, 15). The synovial and fibrous layers of the joint capsule are no longer clearly demarcated and small deposits of new bone are present in the capsular attachments (Fig. 18 b). Morphological changes of "Degree II" are not accompanied by round-cell invasion of the capsule, nor by anything resembling pannus formation due to synovial tissue proliferation along the cartilage border.

Degree III. In the most advanced stages the micromorphology of the lumbar synovial joints is completely reorganized. The subchondral marrow spaces are almost eradicated and replaced by large cavities containing connective tissue. The latter is avascular centrally and anything from poor in vessels to typically hypervascularized peripherally. The cavities are separated by large regions of closely spaced, thickened bone trabeculae (Fig. 17). Isolated bone pieces are occasionally embedded in the connective tissue. Large regions of the articular cartilage are now completely destroyed or replaced by connective tissue, fibrocartilage or new bone deposited on the original subchondral bone plate. The capsular attachment in the dorsal part of the joint is the site of large osteophytes whose marrow spaces communicate with those in the subchondral bone (Fig. 6). But, as in previous stages, there are only minor abnormalities in the insertion of ligamentum flavum. The changes in ligamentum flavum rather take the form of metaplasia to chondral or osseous tissue locally in the zone where it meets articular cartilage, subchondral bone and synovial tissue (Fig. 5). Here osteophytes having blood vessels and marrow spaces that communicate with those in the subchondral bone are rarely seen.

Comment

In addition to what the literature tells us about the normal microscopic anatomy of the lumbar synovial joints (cf. p. 9), the present investigation disclosed other facts about the micromorphology of the articular cartilage, subchondral bone and joint capsule of these joints which are essential for the grading of any morphological changes in them. Thus only in the central parts of the cartilage can tangential, transitional and radial zones be distinguished from the disposition of the chondrons. The calcified zone next to the subchondral bone plate is of uniform thickness and into it intrude so-called vascular buds on the bone plate (cf. Holmdal and Ingel-

mark, 1950, 1951). In the ventral part of the articular process, the part where ligamentum flavum inserts, the subchondral bone fairly often exhibits somewhat thickened cancellous trabeculae. Owing to non-uniform growth of the articular processes, the capsular attachment along the dorsal aspect of the joint is often more or less heavily marked even when the joint is micromorphologically normal.

The morphological changes exhibited by the lumbar synovial joints could not be ascribed to either specific or unspecific inflammations in any of the examined spines. Nor was there any evidence of other pathological conditions capable of affecting articular cartilage, bone or connective tissue. Moreover the morphological changes in these joints were all compatible with, and included all the features of, the classical picture of osteoarthritis of the extremital joints. The observed morphological changes in the lumbar synovial joints were accordingly interpreted as osteoarthritic manifestations.

The osteoarthritic changes in the lumbar cynovial joints progressed with age from mild to grave and lacked clearly demarcated stages.

Between the ages of 30 and 45 years the osteoarthritic changes were as a rule mild and confined to the articular cartilages. These had an irregular cell pattern owing to local cell proliferation, a fibrillated intercellular substance, and a cracking surface. At higher ages the cartilage surface became more and more broken up by these cracks and fissures appeared deeper in the cartilage, whose calcified zone was thickening. These changes gradually turned into more conspicuous defects in the cartilage such as necrosis and substance losses. At this stage, usually seen only after age 45, degenerative phenomena dominated the morphological picture of the articular cartilage.

From 45 to 60 years of age—when the articular cartilages exhibited necrosis and substance losses comparatively often—osteoarthritic changes also appeared in both the subchondral bone and the joint capsule. As in the extremital joints, the changes now included restorative processes leading to formation of new bone which resulted in remodelling of the subchondral bone plate and the development of marginal osteophytes. Concomitantly the loose synovial tissue in the joint capsule was transformed into fibrous connective tissue.

Around and after the age of 60 years, the osteoarthritic changes often gave the impression of having completely reorganized the micromorphological appearance of the joints. The articular cartilages exhibited extensive necrotic regions, while other regions had been replaced by connective tissue, fibrocartilage or new bone deposited on the original subchondral bone plate. The subchondral bone was now the site of large cavities containing connective tissue with anything from a few to abundant blood

vessels. Between these cavities there were sclerotic regions where the cancellous trabeculae were thickened and closely spaced. In the capsular attachments there were large marginal osteophytes whose marrow spaces were continuous with the subchondral marrow spaces.

Those histological changes which are encountered in the lumbar synovial joints at a systematic histological examination of spines from average autopsy cases of different ages evidently constitute various degrees of osteoarthritic lesions. The micromorphological appearance of these changes in the lumbar synovial joints is in complete agreement with that described in the literature with respect to osteoarthritic changes in the extremital joints (Nichols and Richardson, 1909; Pommer, 1913, 1927; Lang, 1924; Harrison, Schajowicz and Trueta, 1953; Lloyd-Roberts, 1955; etc.). The order of appearance and topography of the changes in the articular cartilage, subchondral bone and joint capsule during the course of osteoarthritis of the lumbar synovial joints are similar to those characterizing osteoarthritis of the extremital joints (Pommer, 1923, 1927; Heine, 1926; Harrison, Schajowicz and Trueta, 1953; etc.). Accordingly osteoarthritis of the lumbar synovial joints cannot morphologically be distinguished from osteoarthritis of the extremital joints.

PLATES

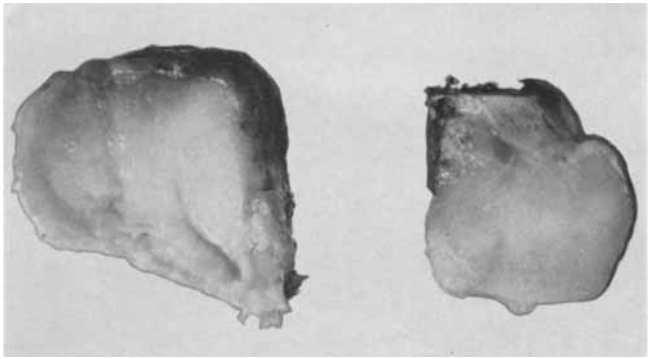


Fig. 3 Synovial joint facets with gross cartilage changes. The left facet shows a cartilage defect over a millimetre broad along its entire length. (Left L_5—S_1 joint, from male, 24 years.)

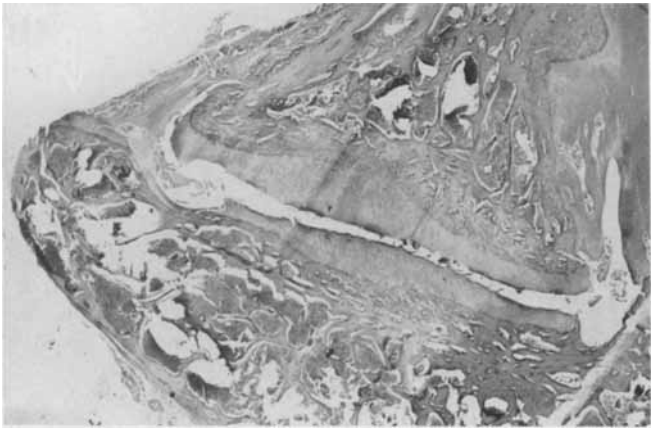
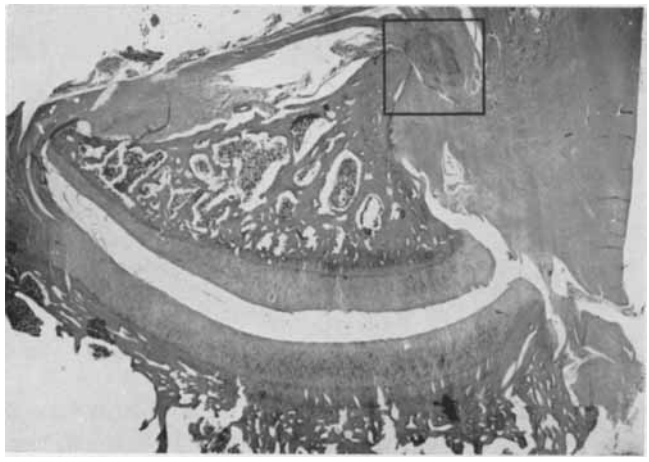
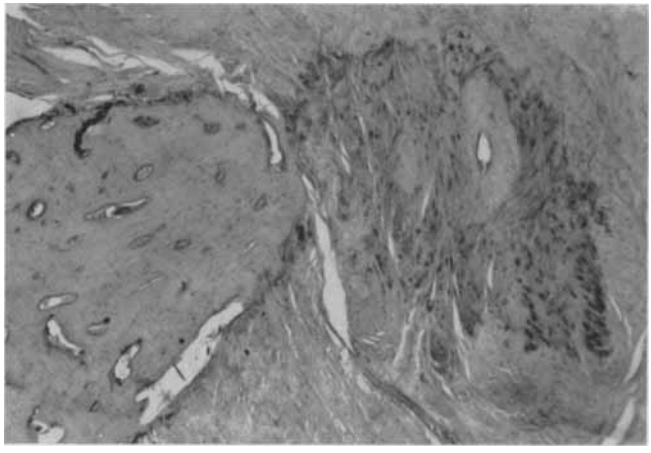


Fig. 4. Relations between joint capsule and mamillary process. Arrow on the left points to superior articular process with mamillary process and capsular attachment thereon. On the right, towards ligamentum flavum, the subchondral bone exhibits somewhat thicker cancellous trabeculae than it does nearer the mamillary process. (Right L_{3-4} joint, Case 8, male, 21 years, x 3.5).



5 a



5 b

Fig. 5. a. New bone formation where ligamentum flavum inserts on inferior articular process. (Right L_{4-5} joint, Case 53, male, 56 years, x 3.5). b. Detail of area marked in Fig. 5. a. Outside the articular process proper one sees a small region with osseous tissue embedded in fibrocartilage (x 100).

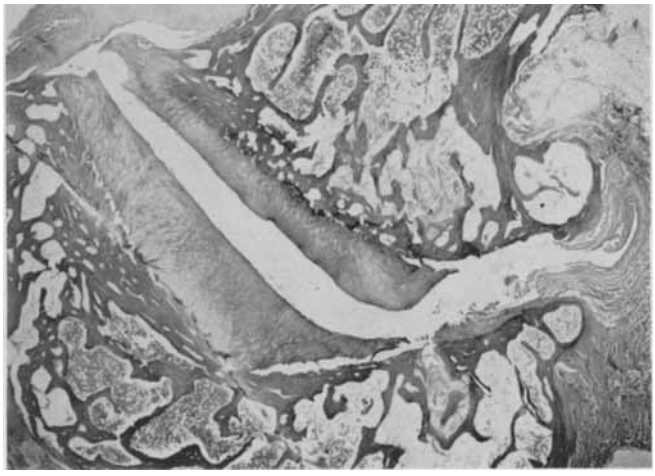
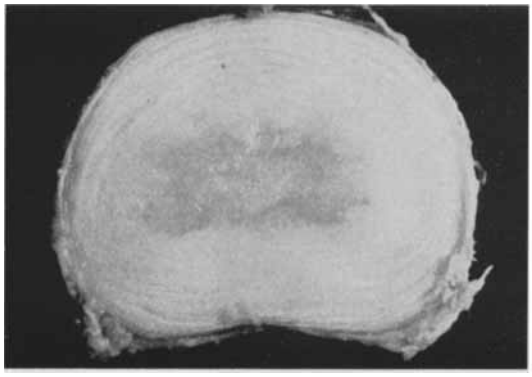
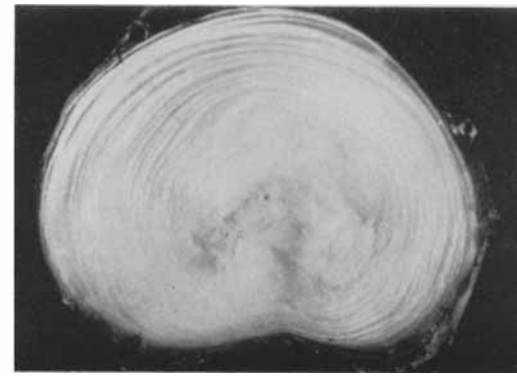


Fig. 6. Joint with osteophytes. On the right, adjacent to the capsular attachments on the dorsal aspect of the joint, osteophytes are present whose marrow spaces communicate with those in the articular processes. The osteophyte on the inferior (convex) articular process is considerably larger than that on the superior (concave) articular process. (Right L_{2-3} joint, Case 68, male, 34 years, x 5).



A



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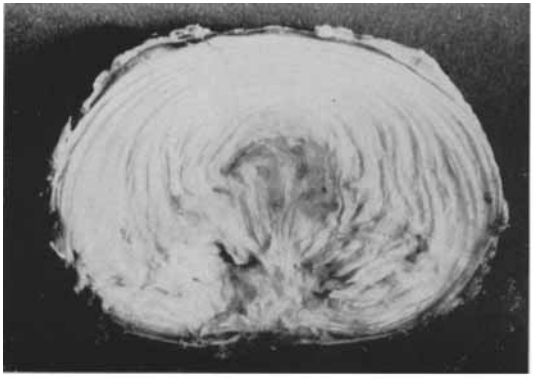

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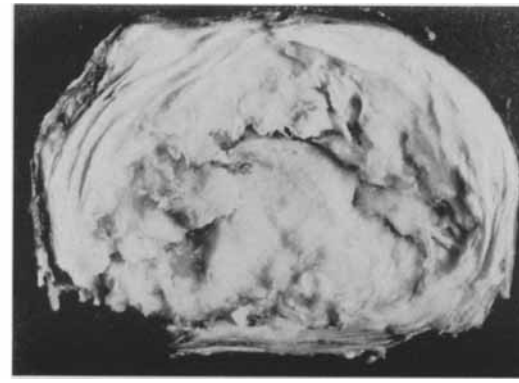


D

Fig. 7. Gross disc changes. A = Grade 0 (Case 95, male, 12 years, L_5—S_1). B = Grade 1 (Case 93, male, 40 years, L_5—S_1). C = Grade 2 (Case 99, male, 62 years, L_{4-5}). D = Grade 3 (Case 69, male, 46 years, L_5—S_1).

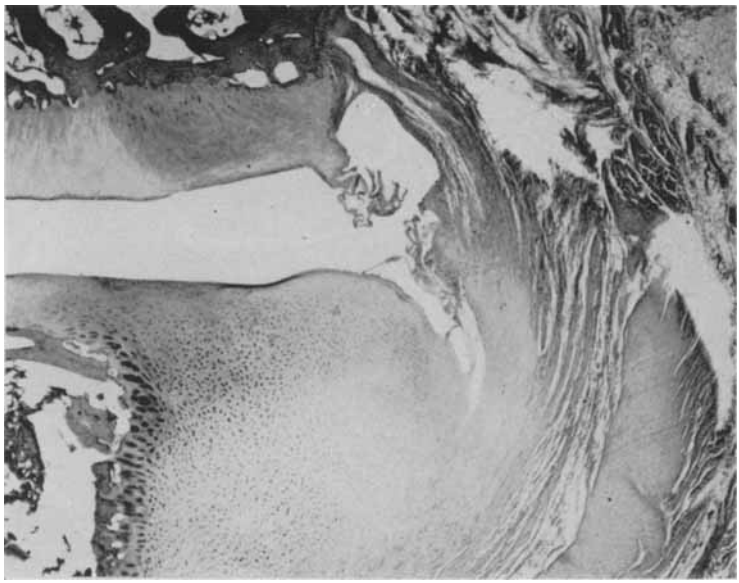


Fig. 8. Ossification of articular processes during growth. The dorsal aspect of the joint with joint capsule appears on the right. The inferior articular process shows enchondral ossification towards the capsular tissue. (Left L_{3-4} joint, from male, 14 years, x 7).

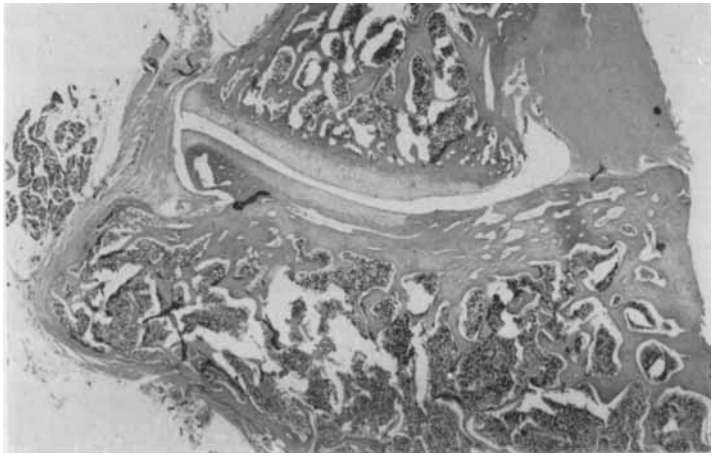
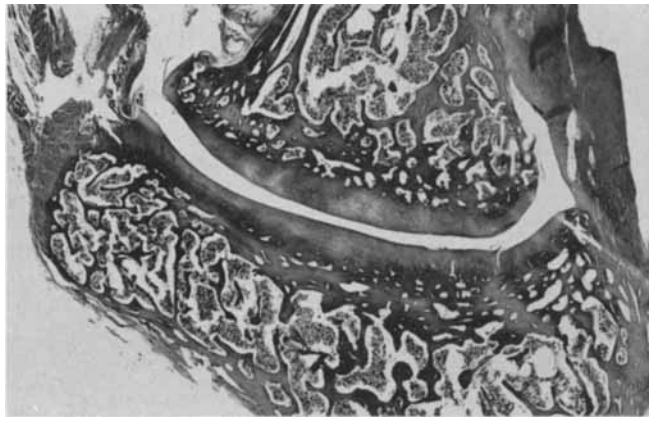
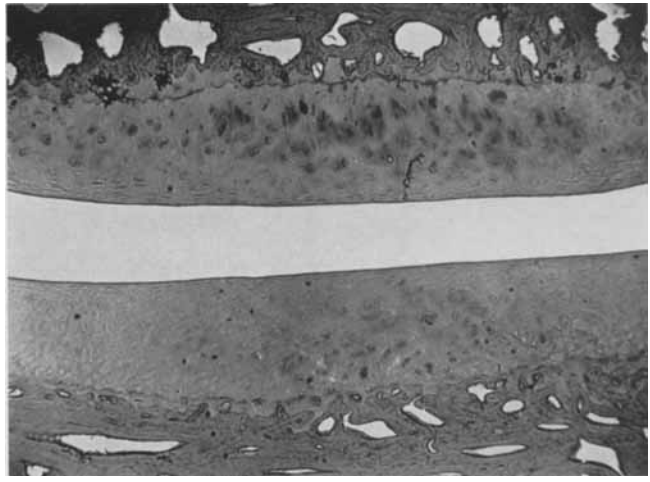


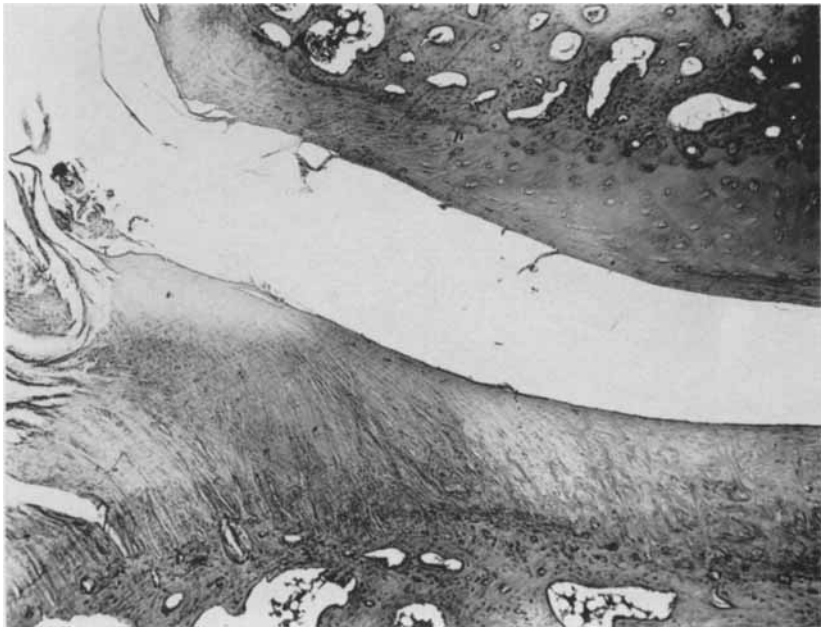
Fig. 9. Joint with "out-turned" facets. In the dorsal part of the joint, facing left, the joint facets seem to be turned outwards owing to the marked indrawing of the capsular attachments. (Right L_{1-2} joint, Case 9, female, 24 years, x 3.5).



10 a

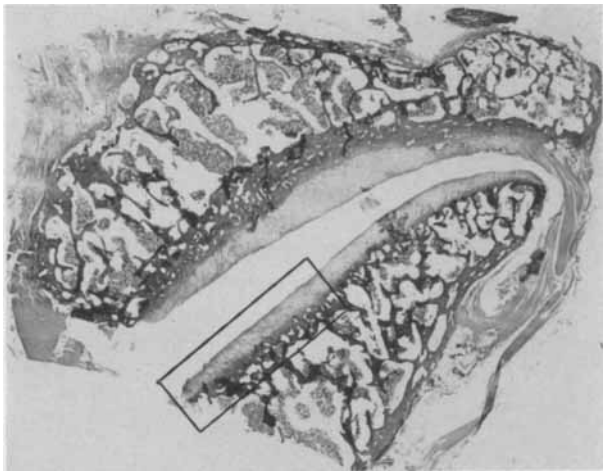


10 b

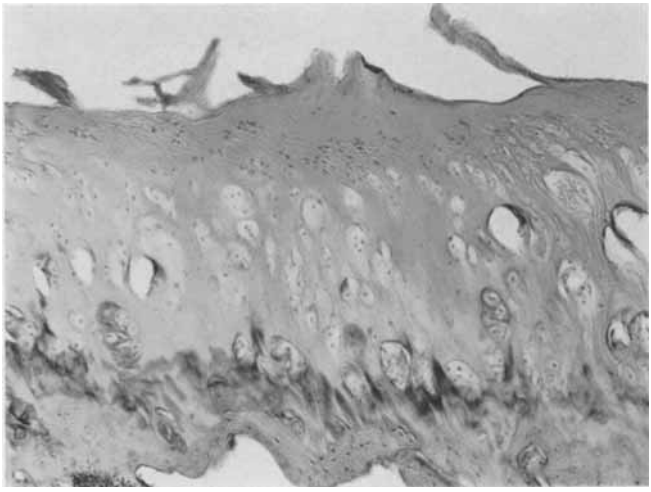


10 c

Fig. 10. a. Survey view of joint without distinct morphological changes. The dorsal aspect of the joint and joint capsule appear on the left, and its ventral aspect with ligamentum flavum on the right. (Left L_{4-5} joint, Case 9, male, 30 years, x 2.5). b. Detail of central joint region (x 16). c. Detail of dorsal aspect where the articular cartilage is seen to lack radially disposed chondrons (x 20).

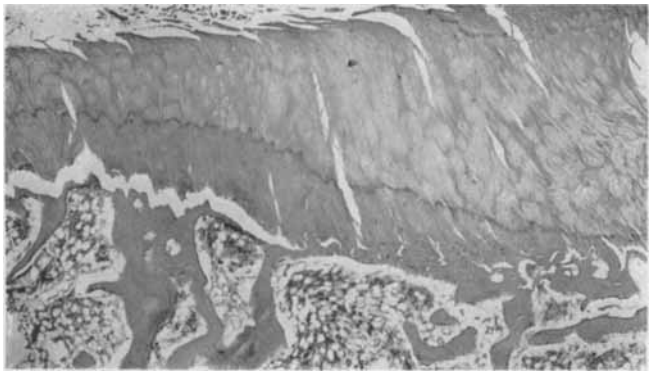


11 a

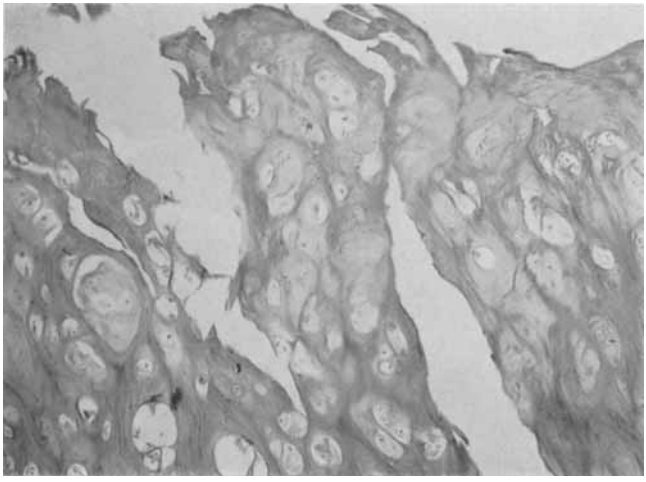


11 b

Fig. 11. a. Survey view of joint with incipient cartilage changes in the inferior joint facet. (Left L_{3-4} joint, Case 11, male, 30 years, x 3.5). b. Detail of area outlined in Fig. 11 a. The cartilage exhibits fibrillation of the intercellular substance and, basally, remarkably large chondrons composed of 10—12 chondrocytes (x 56).

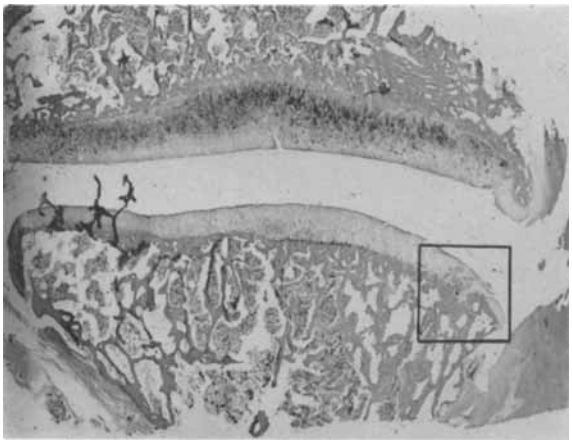


12 a

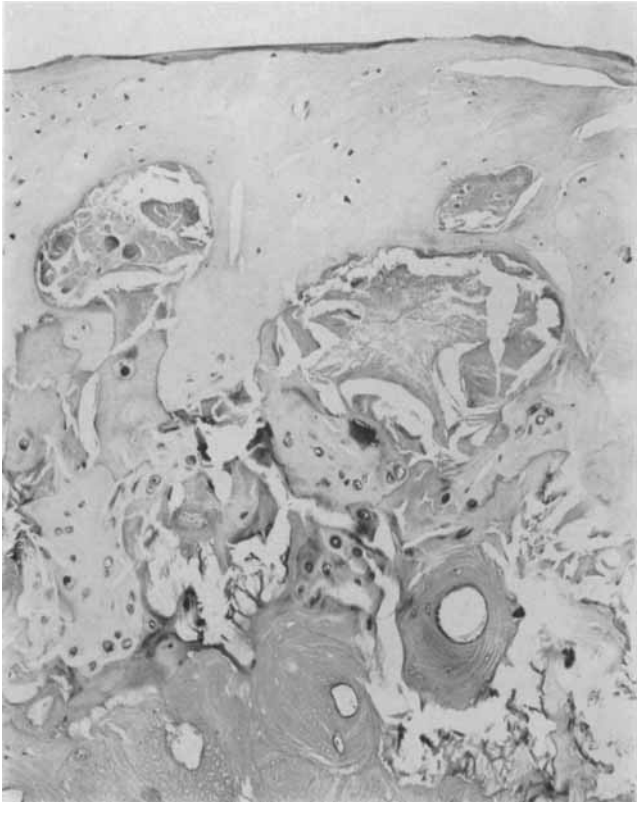


12 b

Fig. 12. a. Articular cartilage with fissure formations; on the left the calcified zone is markedly thickened. (Right L_{4-5} joint, Case 59, male, 37 years, x 20). b. Detail of uncalcified articular cartilage in Fig. 12 a. The chondrons are remarkably closely spaced and the chondrocytes present all transitions between rather distinct demarcations to amorphous or vacuolated appearances (x 100).

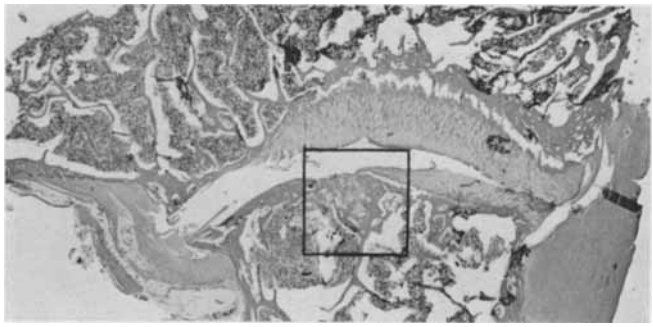


13 a

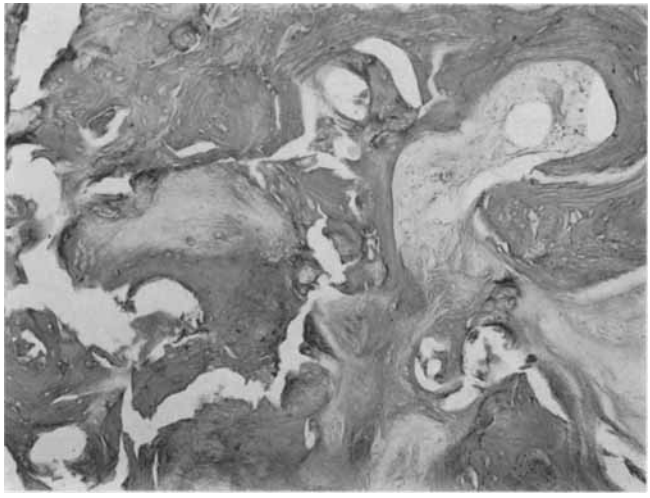


13 b

Fig. 13. a. Survey view of joint whose articular cartilage in marked area seems impressed into the subchondral bone plate. (Right L_{4-5} joint, Case 39, female, 51 years, x 3.5). b. Detail of area marked in Fig. 13 a. Necrotic foci surrounded by comparatively well preserved chondral tissue are seen in the intermediate and deep layers of the cartilage (x 80).

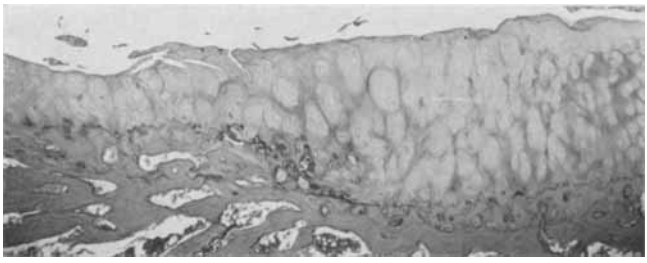


14 a

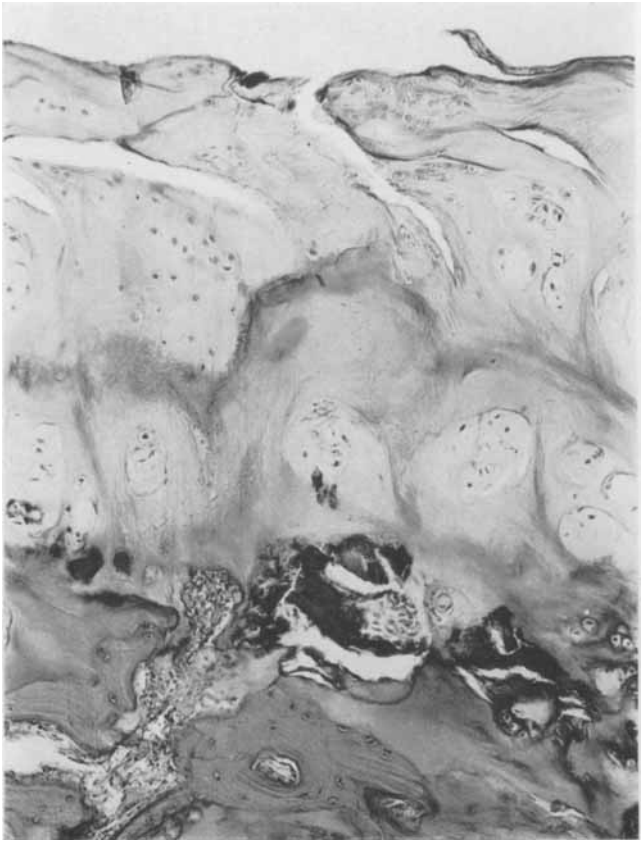


14 b

Fig. 14. a. Survey view of joint whose convex facet has large areas where articular cartilage is missing. Subchondral changes in the area outlined have no counterpart in the subchondral bone of the concave facet. (Right L_{3-4} joint, Case 55, male, 49 years, x 3.5). b. Detail of subchondral bone in area marked in Fig. 14 a. The marrow spaces are filled with rather poorly vascularized connective tissue (x 70).



15 a



15 b

Fig. 15. a. Joint facet with commencing subchondral remodelling. (Left L_5—S_1 joint, Case 55, male, 49 years, x 15). b. Detail of that part of the joint facet in Fig. 15 a where the subchondral bone plate seems elevated. The articular cartilage's basal parts adjacent to the subchondral bone plate include a circumscribed necrotic focus whereto connective tissue from a neighbouring marrow space is passing via a defect in the subchondral bone plate (x 100).

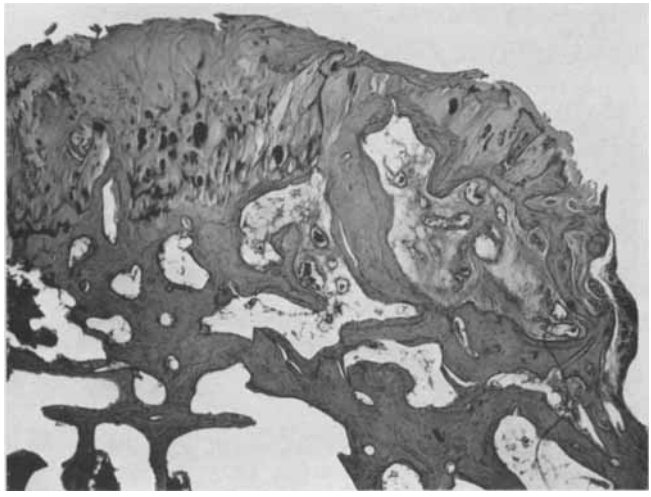
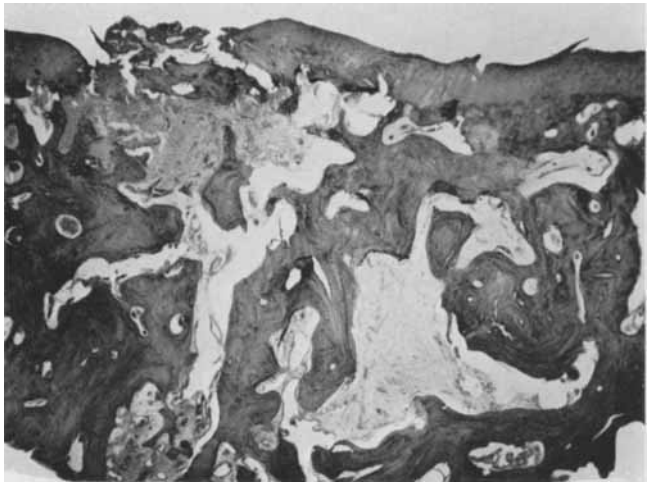
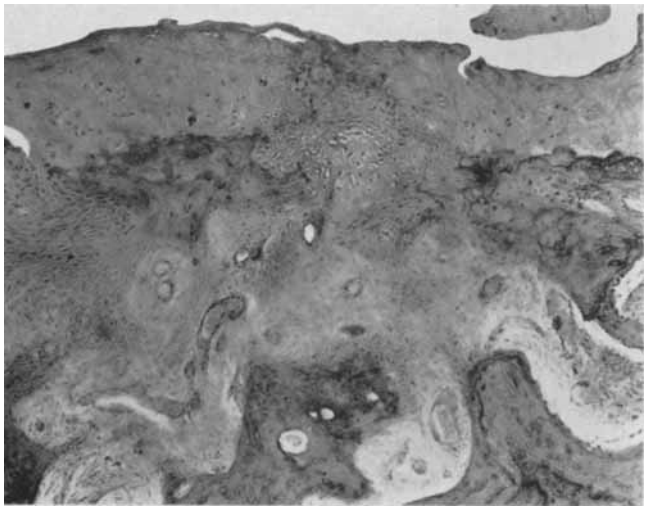


Fig. 16. Joint facet in whose cartilage new bone is forming and with the marrow spaces partly occupied by moderately vascularized connective tissue. (Left L_{4-5} joint, Case 25, male, 69 years, x 16).



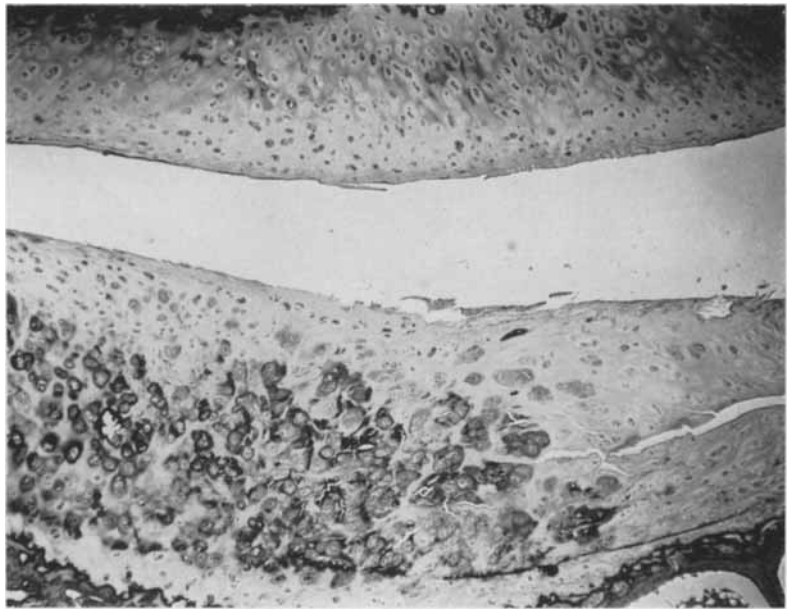
17 a



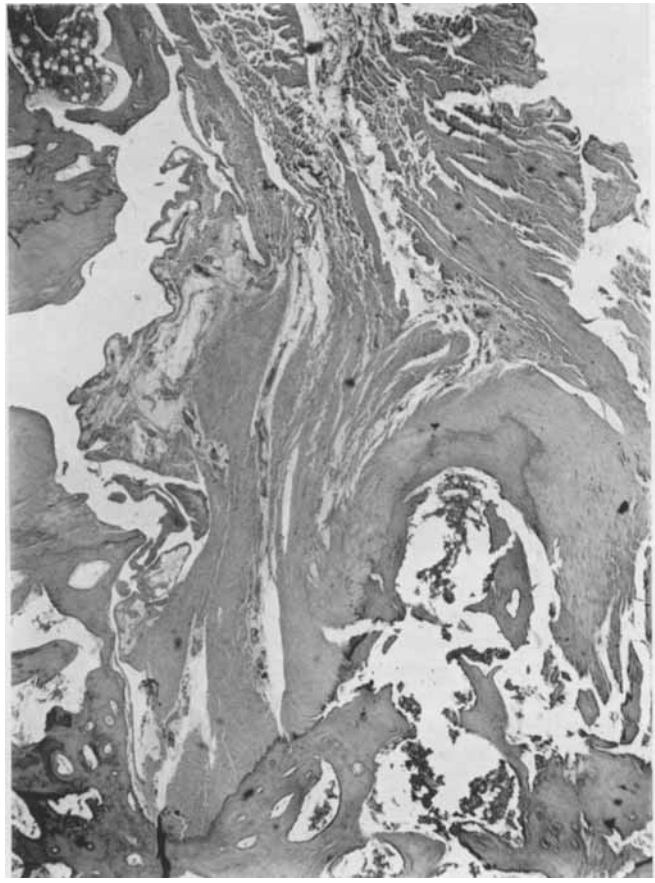
17 b

Fig. 17. a. Joint facet whose subchondral bone exhibits alternately thickened cancellous trabeculae and comparatively large marrow spaces full of connective tissue which in parts is rather rich in vessels. (Right L_5—S_1 joint, Case 60, male, 60 years, x 15). b. Another part of the facet illustrated in Fig. 17 a. Connective tissue from the subchondral marrow space fills a defect in the subchondral bone plate and in the overlying cartilage which is rather like fibrocartilage in appearance (x 72).

Fig. 18. a. Joint with a practically normal chondral cell pattern on the convex facet and marked cell proliferation in the cartilage on the concave facet. (Left L_{2-3} joint, Case 39, female, 51 years, x 20). b. Detail of the capsular attachment on the concave facet of the joint in Fig. 18 a. The synovial and fibrous capsular layers are indistinctly demarcated owing to incipient connective tissue transformation of the synovial membrane.



18 a



18 b

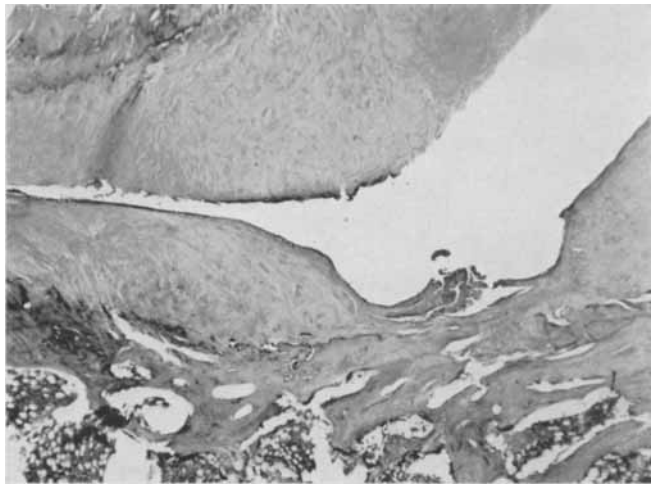
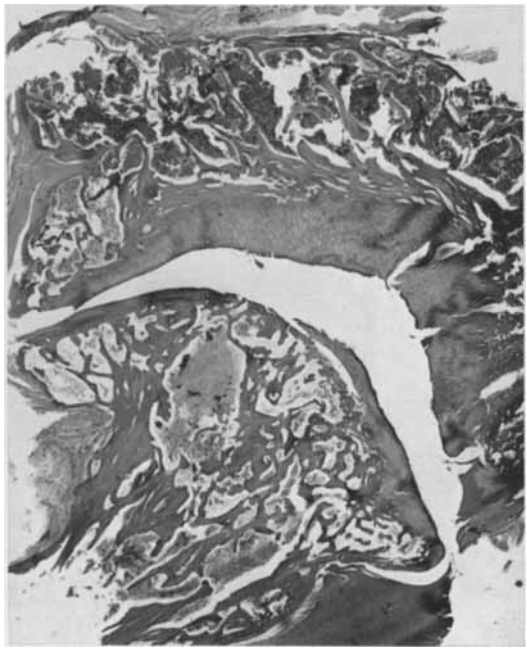
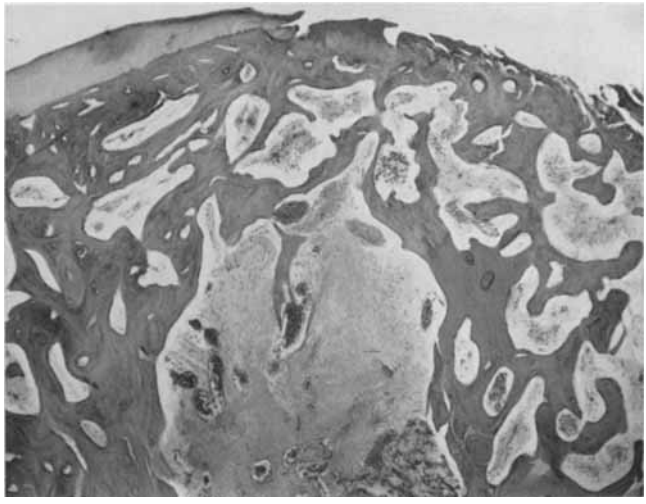


Fig. 19. Joint whose concave facet has a cartilage with an isolated defect. A "discontinuity" in the subchondral bone plate immediately beneath this defect is filled with connective tissue. (Right L_{4-5} joint, Case 32, female, 42 years, x 15).



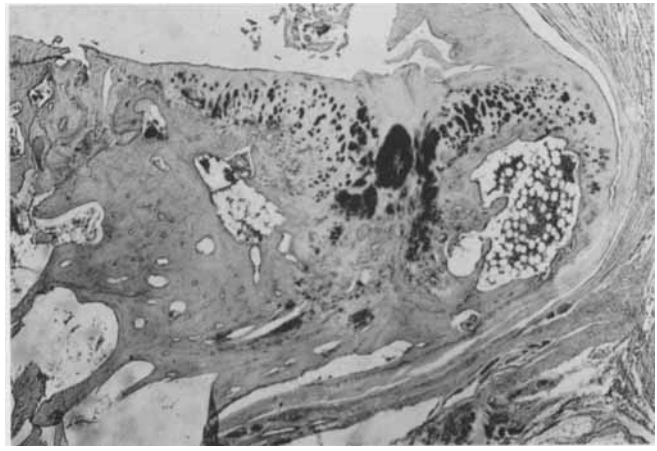
20 a



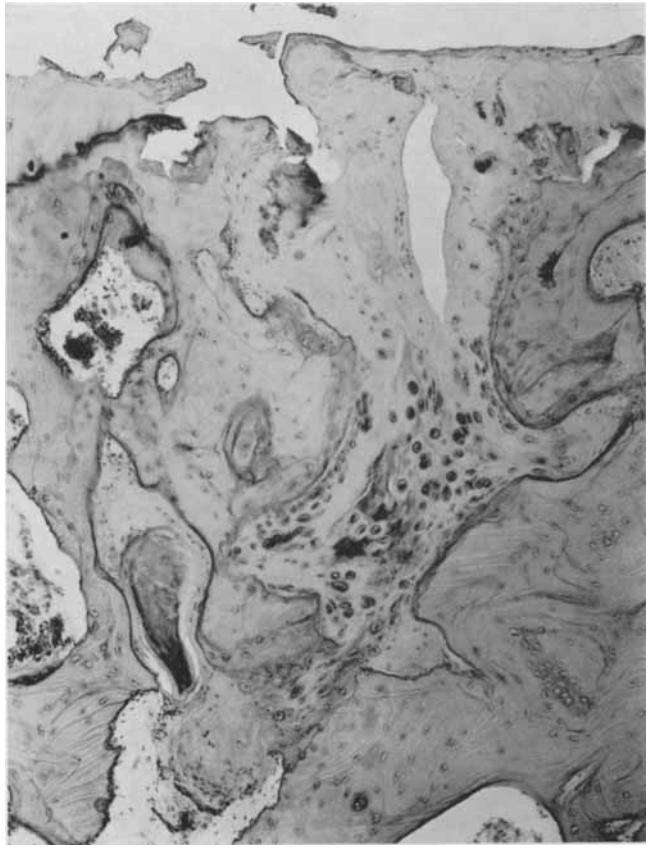
20 b

Fig. 20. a. Survey view of joint with advanced changes in the subchondral bone of the convex facet only. (Left L_5—S_1 joint, Case 91, female, 47 years, x 2.5). b. Detail of the convex facet of the joint in Fig. 20 a. Parts of the articular cartilage show marked thinning, and the marrow spaces in the underlying bone contain remarkably fibrous connective tissue (x 15).

33 a



33 b



33 c

Fig. 33. a. Joint facet with gross osteoarthritic changes. The articular cartilage has a rough surface and exhibits small defects. (Rights S_1 facet from male, 62 years). b. Microscopic detail of the facet in Fig. 33 a. To the left loss of cartilage substance and markedly thickened cancellous trabeculae. To the right formation of new bone towards the capsular tissue (x 15). c. Detail of the left area in Fig. 33 b. The subchondral bone plate exhibits a defect filled with fibrocartilage which is contiguous with the cartilage overlying the subchondral bone plate (x 80). This joint facet is deemed to the following gradings: A:a=2, A:b=2, C=1, D=1.

CHAPTER 5

Osteoarthritic Changes in the Lumbar Synovial Joints Related to Other Factors

Sex (Table 2)

Analysis of sex differences within age groups disclosed that for occasional facets the mean scores for A:a, A:b, B, C and D (cf. p. 30) in a few cases differed significantly (Table 2). These few sex differences were, however, equally often in favour of men and of women. They were also distributed over all lumbar segments and within all age groups. Hence they were considered biologically unimportant. No significant sex differences emerged for the mean scores A—B, C—D and A—D for individual facets, joints or segments. Therefore, as no significant sex differences were found in any age group, during the remainder of the investigation no distinction was made between male and female lumbar spines.

Age (Tables 3, 4, 5, 20, 21, 22)

No osteoarthritic changes were observed before the age of 20 years. Hence only lumbar spines of 20 years or over were included in the statistical analysis.

Cell Pattern of Articular Cartilage (A:a). The cell pattern became increasingly abnormal with rising age. In the age group 20—25 years its segmental mean score already differed significantly from zero in each segment (Fig. 21, Table 20). The segmental mean scores lie between 2 and 4 up to age 45, except on the L_{1-2} and L_{2-3} levels in the 20—25 and 26—35 years age group where they did not exceed 2 points. The 20—45 years groups comprised althogether 696 joint facets. Only 5 of these exhibited cell pattern abnormalities as grave as necrosis in the cartilage, in other words a score of 2 points for each facet. This implies that the large majority of synovial joints exhibited cell proliferation in the cartilages, corresponding to a score of 1 point for each of the two facets (Figs. 11, 27). When the age groups 20—25, 26—35 and 36—45 years were compared, it appeared that the proportion of joint facets with such cartilage changes increased with age. After age 45 the segmental mean score was 3—6 points (Fig. 21). The proportion of joint facets with chondral necrosis,

TABLE 2

Significant mean score differences between corresponding joint facets in male and female lumbar spines within age groups. The sex with the highest mean is denoted by the symbol for that sex. Dashes indicate no significant difference. (Tested by Stundent's t-test.)

A:a. Cell pattern

Age groups		26—35		36—45		46—55		56—65		> 65 years	
Joint facets		Left	Right	Left	Right	Left	Right	Left	Right	Left	Right
L_{1-2}	sup.	—	—	—	—	—	—	—	—	—	—
	inf.	—	—	—	—	—	—	—	—	—	♂
L_{2-3}	sup.	—	—	—	—	—	—	—	—	—	—
	inf.	—	—	—	—	—	—	—	—	—	—
L_{3-4}	sup.	—	—	—	—	—	—	—	—	—	—
	inf.	—	—	—	—	—	—	—	—	—	—
L_{4-5}	sup.	—	—	—	—	—	—	—	—	—	—
	inf.	—	—	—	—	—	—	—	—	—	—
L_5-S_1	sup.	♂	—	—	—	—	—	—	—	—	—
	inf.	—	—	—	—	—	—	—	—	—	—

A:b. Intercellular subtance

Age groups		26—35		36—45		46—55		56—65		> 65 years	
Joint facets		Left	Right	Left	Right	Left	Right	Left	Right	Left	Right
L_{1-2}	sup.	—	—	—	—	—	—	—	—	—	—
	inf.	♀	—	—	—	—	—	—	—	♀	—
L_{2-3}	sup.	—	—	—	—	—	—	—	—	—	—
	inf.	—	—	—	—	—	—	—	—	—	—
L_{3-4}	sup.	—	—	—	—	—	—	—	—	—	—
	inf.	—	—	—	—	—	—	—	—	—	—
L_{4-5}	sup.	—	—	—	—	♀	♀	—	—	—	—
	inf.	—	—	—	—	♀	—	—	—	—	—
L_5-S_1	sup.	—	—	—	—	—	—	—	—	—	—
	inf.	—	—	—	—	—	—	—	—	—	—

scoring 2 points, was considerably higher at these ages than before age 45. Whereas the mean frequency of such facets per spine did not differ significantly from zero before age 45, it amounted to 21.9 ± 7.8 † per cent after that age (Table 5 a).

The age groups 46—55 and over 65 years were the only ones in which the segmental mean score on corresponding joint levels significantly exceeded that in the preceding age group (Table 3), namely on the L_{3-4} and L_{4-5} levels in the former case and on all levels except L_5-S_1 in the latter. The same applied on all joint levels to the 46—55 years group compared with 20—25 years group and also to the group over 65 years compared with the 36—45 years group (Table 4).

† $\pm t \cdot s_{\bar{x}}$

TABLE 2 (cont.)

B. Calcified layer

Age groups	26—35		36—45		46—55		56—65		> 65 years	
Joint facets	Left	Right	Left	Right	Left	Right	Left	Right	Left	Right
L_{1-2} sup.	♀	—	—	—	—	—	—	—	—	—
L_{1-2} inf.	♀	—	—	—	—	—	—	—	—	—
L_{2-3} sup.	—	—	—	—	—	—	—	—	♀	—
L_{2-3} inf.	—	—	—	—	—	—	—	—	—	—
L_{3-4} sup.	—	—	—	—	—	—	—	—	—	—
L_{3-4} inf.	—	—	—	—	—	—	—	—	—	—
L_{4-5} sup.	—	—	—	—	—	—	—	—	—	—
L_{4-5} inf.	—	—	—	—	—	—	—	—	—	—
L_5-S_1 sup.	♂	—	—	—	—	—	—	—	—	—
L_5-S_1 inf.	—	—	—	—	—	—	—	—	—	—

C. Subchondral bone

Age groups	26—35		36—45		46—55		56—65		> 65 years	
Joint facets	Left	Right	Left	Right	Left	Right	Left	Right	Left	Right
L_{1-2} sup.	♀	—	—	—	—	—	—	—	—	—
L_{1-2} inf.	♀	—	—	♂	—	—	—	—	—	—
L_{2-3} sup.	—	—	—	—	—	—	—	—	—	—
L_{2-3} inf.	—	—	♀	—	—	—	—	—	—	—
L_{3-4} sup.	—	—	—	—	♀	—	♀	—	—	—
L_{3-4} inf.	—	—	—	—	—	—	—	—	—	—
L_{4-5} sup.	—	—	—	—	—	—	—	—	—	—
L_{4-5} inf.	—	—	—	—	—	—	—	—	—	—
L_5-S_1 sup.	—	—	♀	—	—	—	—	—	—	—
L_5-S_1 inf.	—	—	—	—	—	—	—	—	—	—

D. Capsular attachment

Age groups	26—35		36—45		46—55		56—65		> 65 years	
Joint facets	Left	Right	Left	Right	Left	Right	Left	Right	Left	Right
L_{1-2} sup.	—	—	—	—	—	—	—	♀	—	—
L_{1-2} inf.	—	—	—	—	—	♀	—	♀	—	—
L_{2-3} sup.	—	—	—	♀	—	♀	—	♀	—	—
L_{2-3} inf.	—	—	—	—	—	—	—	—	—	—
L_{3-4} sup.	—	—	—	—	—	—	—	—	—	—
L_{3-4} inf.	—	—	—	—	—	—	—	—	—	—
L_{4-5} sup.	—	—	♂	—	—	—	—	—	—	—
L_{4-5} inf.	—	—	—	—	—	—	—	—	—	—
L_5-S_1 sup.	♂	—	—	—	—	—	—	—	—	—
L_5-S_1 inf.	—	—	—	—	—	—	—	—	—	—

Intercellular Substance of Articular Cartilage (A:b). The development of changes in the intercellular substance with rising age was in its main features similar to that of the cell pattern (Figs. 21, 22, 27, Tables 3, 4). Merely 10 of the 662 joint facets in the 20—45 years groups exhibited losses of cartilage substance, the intercellular substance scoring 2 points. Facets with losses of cartilage substance became a comparatively frequent phenomenon only after age 45, their mean frequency per spine then being 28.1 ± 9.2 † per cent (Table 5 a).

Calcified Cartilage Zone (B). Before age 45 the calcified cartilage was changed considerably less often than the non-calcified cartilage (Figs. 23, 27, Table 20). The segmental mean score thus did not exceed 2 points. Only about a third of the joint facets in the 20—45 years groups had changes in the calcified zone in the form of moderate thickening, that is a facet score of 1 point (Fig. 12 a). After age 45 the segmental mean score rose rather rapidly from about 2 points in the 46—55 years group to approximately 4 points over age 65. The mean frequency per spine of facets with markedly thickened calcified zone, scoring 2 points, was 9.5 ± 6.6 † per cent after age 45 (Table 5 a). The corresponding mean frequency of advanced changes, such as necrosis and/or substance losses, in the non-calcified cartilage was as high as 34.7 ± 8.2 † per cent (Table 5 c).

Changes in the calcified zone within segments were only on a few segments of significantly higher degree than in the preceding age group (Table 3). On the other hand, the corresponding mean segmental score differences on most segments were significant for all ages over 45 compared with all ages up to 45 (Table 4).

It was not deemed justified to analyse statistically the associations between the articular cartilage's cell pattern (A:a), intercellular substance (A:b) and calcified zone (B), owing to the risk that their gradings might be incommensurable quantities. Some idea of these correlations may be obtained, however, by combining the points scored for A:a, A:b and B into a three-digit number for each joint facet. The fact that only a few of the possible 27 combinations occurred and the percentages of facets having the same combinations (Fig. 26) suggested that the osteoarthritic changes in the cartilage often were confined to its non-calcified portion. Moreover, changes in the cell pattern were usually associated with changes in the intercellular substance. Rather more than 85 per cent of the facets had equal scores for cell pattern and intercellular substance, approximately 10 per cent had a higher intercellular substance score and about 4 per cent a higher cell pattern score.

† $\pm t \cdot s_{\bar{x}}$

Of those joint facets with cartilages scoring more points for intercellular substance than for cell pattern, about half occurred on the L_{1-2} and L_{2-3} levels. The basic scoring sheets for these facets disclosed that practically all had displayed fibrillation of the intercellular substance, while a slightly deviating cell distribution in the cartilage was deemed normal for the cartilages on these levels (cf. p. 27). Roughly 5 per cent of the facets exhibited losses of cartilage substance without concomitant necrosis (Fig. 19).

Subchondral Bone (C). Up to the age of 45 years there was a rising frequency of minor changes, such as small areas with thickened cancellous trabeculae and occasional marrow spaces with connective tissue proliferation (Fig. 14), in other words a score of 1 point for the joint facet (Fig. 27). At these ages the segmental mean score on the L_{1-2} level did not differ significantly from zero, but it did so in the L_{3-4} level in the 36—45 years group as well as on the L_{2-3}, L_{4-5} and L_5-S_1 levels in the 26—35 years group (Fig. 24, Table 20). Before age 45 no segmental mean score exceeded 2 points. Thereafter joints occurred with more advanced changes in the subchondral bone, for example extensive sclerosis, marrow spaces containing connective tissue, and ingrowth of more or less vascularized connective tissue into the basal parts of the articular cartilage from neighbouring marrow spaces by way of abnormal defects in the subchondral bone plate (Fig. 17). The mean frequency per spine of facets with such grave changes in the subchondral bone, scoring 2 points, differed significantly from zero at ages over 45 years and was 7.6 ± 3.6 † per cent (Table 5 a).

The segmental mean score for the L_{4-5} level of the lumbar spine in all age groups was significantly higher than for the corresponding level in the preceding age group (Table 3), the 36—45 years group being an exception to this rule. The mean scores for the other levels were only in the age groups 36—45, 46—55 or >65 years significantly higher than for the corresponding levels in the preceding age group. At ages over 55 years the segmental mean scores for all levels significantly exceeded the corresponding mean scores at ages up to 35 years (Table 4).

Capsular Attachments (D). Along the joint margin on the transition from hyaline cartilage to fribrocartilage and where the capsule attaches to adjacent bone, only minor changes such as fibrosis of synovial tissue or small osteophytes were encountered before age 45. Between 20 and 45 years of age, therefore, the segmental mean score was at most 2 points on

† $\pm t \cdot s_x$

each level (Fig. 25, Table 20). More advanced changes, i.e. large osteophytes, began to appear only after age 45 (Fig. 27), but a segmental mean score exceeding 2 points at higher ages was found only on the levels L_{3-4}, L_{4-5} and L_5-S_1 (Fig. 25). Significant segmental mean score differences was first encountered on all levels when the 46—55 years group was compared with the 20—25 years group, and after age 65 all segmental mean scores significantly exceeded the corresponding mean scores up to age 45 (Tables 3, 4). Over age 45 the mean frequency per spine of joint facets with large osteophytes, i.e. facets scoring 2 points for the capsular attachment, differed significantly from zero and was 9.3 ± 3.2 † per cent (Table 5 a), the corresponding figures for facets with advanced changes in the subchondral bone and/or capsular attachment being 13.4 ± 4.4 † per cent (Table 5 c).

Changes in Ligamentum Flavum (E). Being contiguous with the synovial membrane and forming part of the joint capsule over the ventral part of the joint, ligamentum flavum was also examined for the presence of any morphological changes in the shape of osteophytes next to its periarticular insertion (Fig. 5). Such osteophytes were seen on one or two levels in 3 of 40 spines up to 45 years and in 8 of 38 over 45 years of age. In no case did these osteophytes cause ligamentum flavum to bulge ventrad; but, as mentioned (p. 29), such changes should be interpreted as metaplasia of ligament tissue via cartilage to bone rather than as manifestations related to any osteoarthritic changes.

† $\pm t \cdot S_{\bar{x}}$

TABLE 3

Segments with significantly higher mean segmental score for osteoarthritic changes (denoted "+") than the corresponding segment in the next younger group. (cf. Table 22).

	A:a Cell pattern		A:b Intercellular substance			B. Calcified layer			C. Subchondral bone					D. Capsular attachment	
Age groups	46–55	> 65	26–35	46–55	> 65	26–35	46–55	56–65	26–35	36–45	46–55	56–65	> 65	46–55	> 65 year
Segments															
L_{1-2}	–	+	+	+	–	+	–	–	–	–	+	–	–	–	–
L_{2-3}	–	+	+	+	–	–	+	–	–	+	–	–	–	–	–
L_{3-4}	+	+	–	+	+	–	–	+	–	+	–	–	+	–	+
L_{4-5}	+	+	–	–	–	–	–	+	+	–	+	+	+	+	–
L_5–S_1	–	–	–	–	–	–	–	–	–	–	+	–	–	–	–

TABLE 4

Segments (denoted "+") with significantly higher mean segmental score for osteoarthritic changes than the corresponding segment in any lower age group. (cf. Table 22).

(1 = L_{1-2}, 2 = L_{2-3}, 3 = L_{3-4}, 4 = L_{4-5}, 5 = L_5–S_1)-

	A:a Cell pattern					A:b Intercellular substance					B. Calcified layer					C. Subchondral bone					D. Capsular attachment				
Compared age groups:	1	2	3	4	5	1	2	3	4	5	1	2	3	4	5	1	2	3	4	5	1	2	3	4	5
36–45 and 20–25 years	–	–	–	–	–	–	–	–	–	–	+	+	+	+	–	+	+	+	+	+	–	+	–	–	–
46–55 and 20–25 years	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+
46–55 and 26–35 years	–	+	+	–	+	–	+	+	–	–	+	+	+	+	–	+	+	+	+	+	–	–	–	–	+
56–65 and 26–35 years	–	+	–	+	–	–	–	+	–	–	+	+	+	+	–	+	+	+	+	+	–	+	+	–	+
> 65 and 26–35 years	–	+	+	+	+	–	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+	+	+
56–65 and 36–45 years	–	–	–	+	–	–	–	+	+	–	–	+	+	+	+	+	–	–	+	+	–	–	–	+	+
> 65 and 36–45 years	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	–	+	+	+	+	+	+	+	+
> 65 and 46–55 years	–	+	+	–	–	–	–	+	+	–	–	–	+	+	–	–	–	+	+	–	+	–	+	+	–

TABLE 5 a

Mean frequency per lumbar spine of joint facets showing osteoarthritic changes of grade 2.

		Age 20—45 years		Age > 45 years	
		N	$M \pm t \cdot S_{\bar{x}}$	N	$M \pm t \cdot S_{\bar{x}}$
Cell pattern	(A:a)	40	0.7 ± 0.8 %	38	21.9 ± 7.8 %
Intercellur substance	(A:b)	40	1.3 ± 0.7 %	38	28.1 ± 9.2 %
Calcified cartilage	(B)	40	0.5 ± 0.3 %	38	9.5 ± 6.6 %
Subchondral bone	(C)	40	0.2 ± 0.4 %	38	7.6 ± 3.6 %
Capsular attachment	(D)	40	0.3 ± 0.6 %	38	9.3 ± 3.2 %

TABLE 5 b

Frequency of lumbar spines above 45 years with some joint facets showing osteoarthritic changes of grade 2.

		Number of lumbar spines					
Number of joint facets on each spine with grade 2		0	1—2	3—6	7—8	9—12	> 12
Cell pattern	(A:a)	12	10	10	0	4	2
Intercellur substance	(A:b)	10	7	9	2	6	4
Calcified cartilage	(B)	26	5	4	0	3	0
Subchondral bone	(C)	21	9	7	1	0	0
Capsular attachment	(D)	21	10	6	1	0	0

TABLE 5 c

Mean frequency per lumbar spine above 45 years with joint facets showing extensive cartilage changes and with joint facets showing extensive bone changes.

	N	$M \pm t \cdot S_{\bar{x}}$
Extensive cartilage changes (a = 2 and b = 1, a = 1 and b = 2 or a = 2 and b = 2)	38	34.7 ± 8.2 %
Extensive bone changes (C = 2 and D = 1, C = 1 and D = 2 or C = 2 and D = 2)	38	13.4 ± 4.4 %

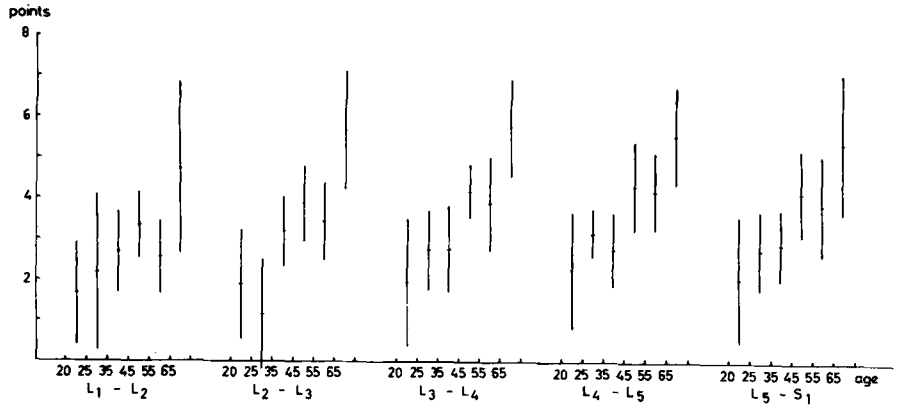


Fig. 21. Mean segmental scores with confidence limits within age groups for osteoarthritic changes in the cell pattern of the articular cartilage of lumbar synovial joints (cf. Table 20).

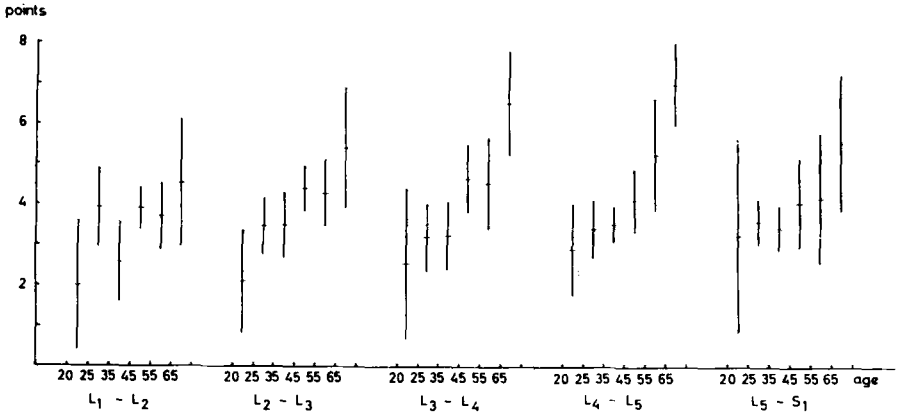


Fig. 22. Mean segmental scores with confidence limits within age groups for osteoarthritic changes in the intercellular substance of the articular cartilage of lumbar synovial joints (cf. Table 20).

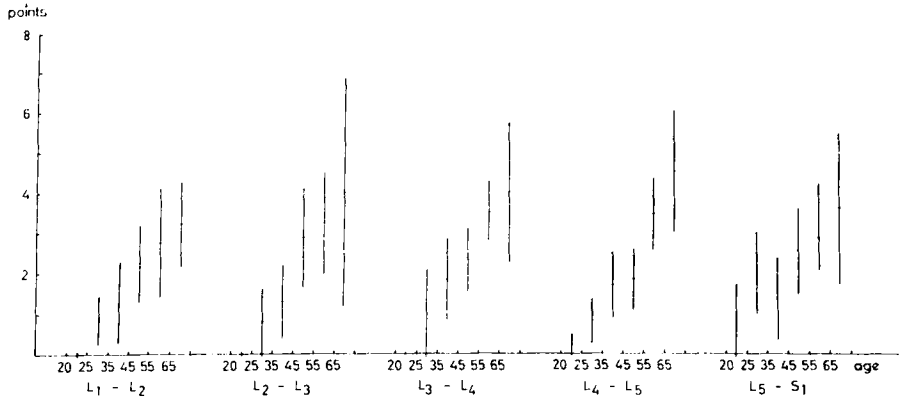


Fig. 23 Mean segmental scores with confidence limits within age groups for osteoarthritic changes in the calcified portion of the articular cartilage of lumbar synovial joints (cf. Table 20).

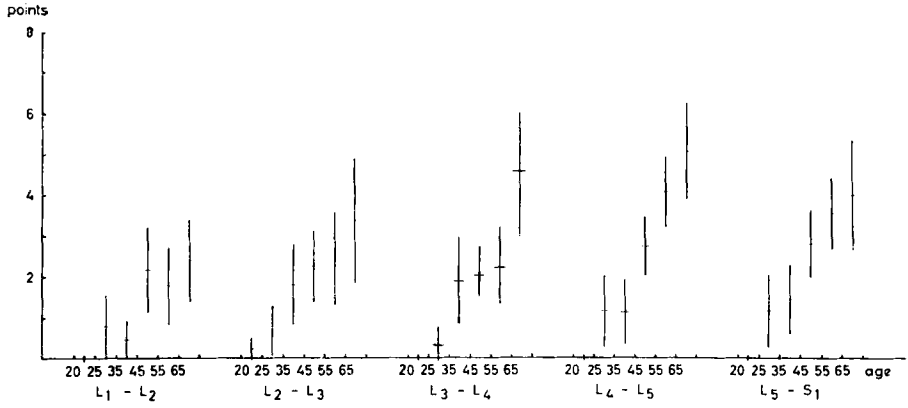


Fig. 24. Mean segmental scores with confidence limits within age groups for osteoarthritic changes in the subchondral bone of lumbar synovial joints (cf. Table 20).

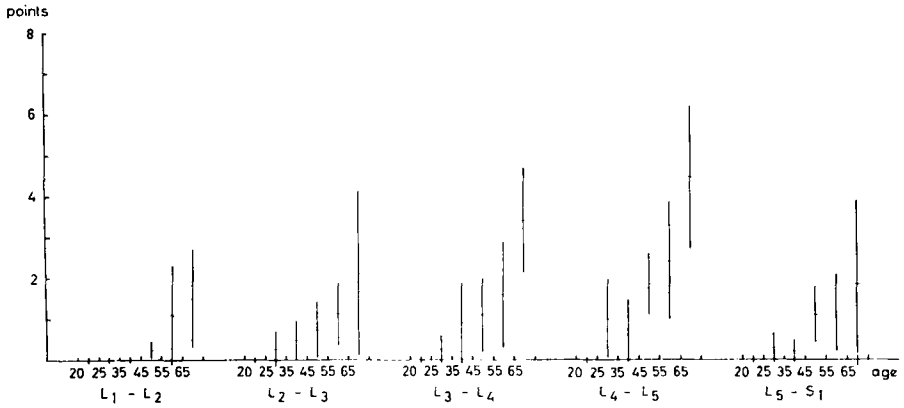


Fig. 25. Mean segmental scores with confidence limits within age groups for osteoarthritic changes in the capsular attachments of lumbar synovial joints (cf. Table 20).

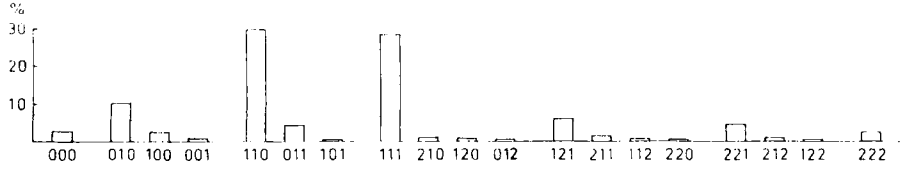


Fig. 26. Relative frequencies of joint facets with different combinations of the three-digit number for the degree of osteoarthritic changes in cell pattern (A:a), intercellular substance (A:b) and calcified portion (B) of the articular cartilage.

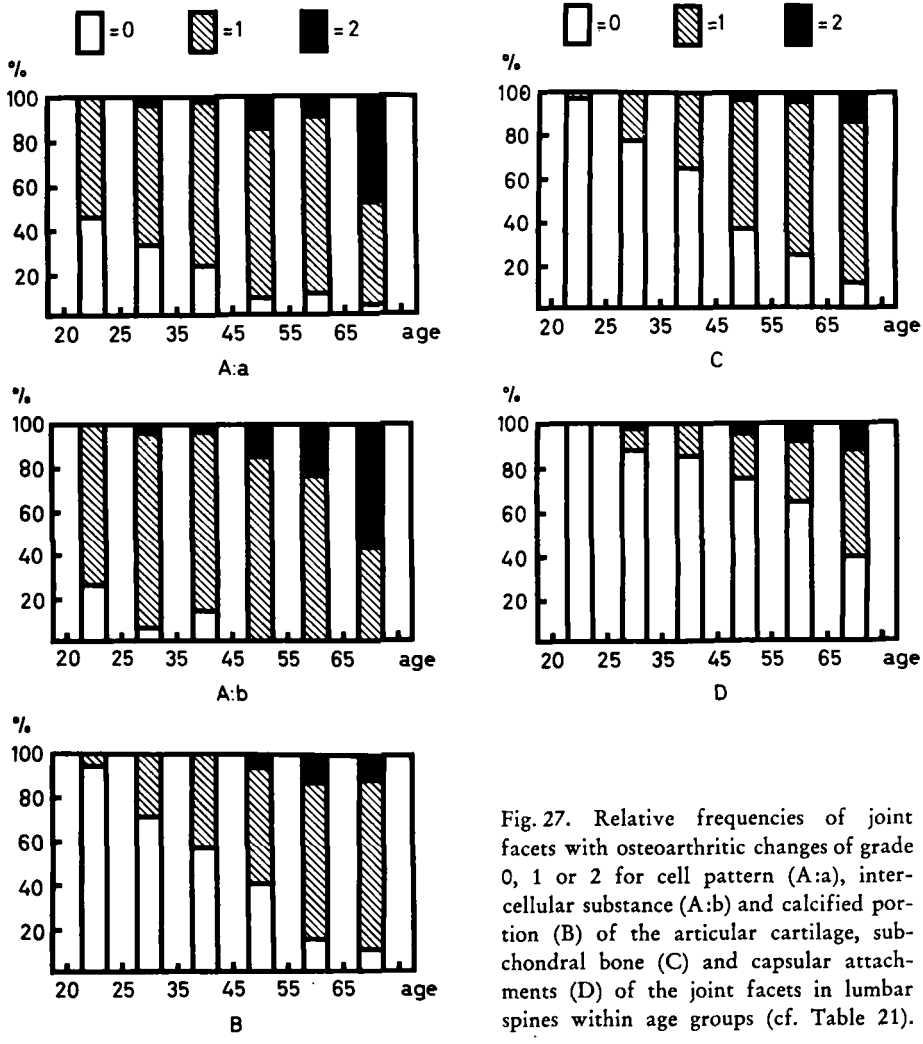


Fig. 27. Relative frequencies of joint facets with osteoarthritic changes of grade 0, 1 or 2 for cell pattern (A:a), intercellular substance (A:b) and calcified portion (B) of the articular cartilage, subchondral bone (C) and capsular attachments (D) of the joint facets in lumbar spines within age groups (cf. Table 21).

Topographic Relations (Table 6)

Intrasegmental differences

The two facets of the same synovial joint occasionally exhibited differences in the degree of osteoarthritic changes. Indeed, one facet might exhibit a sensibly normal cell pattern in the articular cartilage and the other pronounced cell proliferation (Fig. 18 a). A higher degree of cell pattern abnormality was shown by one of the facets in 4.4 ± 2.2 per cent of the examined joints. The corresponding difference for the intercellular substance was 6.7 ± 2.7 per cent. The usual difference in the latter case was that one of the cartilages displayed fringing only and the other fringing plus extensive substance losses (Fig. 19). There were even substantial differences in the appearance of the calcified cartilage zone between the superior and inferior surfaces of 3.5 ± 2.0 per cent of the joints. In 5.1 ± 2.4 per cent of the joints one facet had negligible subchondral changes and the other facet displayed markedly thickened cancellous trabeculae and marrow spaces filled with connective tissue (Figs. 19, 20). The most common discrepancy was that osteophytes were lacking or negligible on one facet and comparatively large on the other (Fig. 6). This was so in 10.8 ± 3.3 per cent of the joints. These differences between the two facets in the same joint were distributed rather uniformly on the lumbar levels and on the right and left sides. The superior joint facet had the higher degree of osteoarthritic changes as often as the inferior. Furthermore examinations of the confidence limits for mean facet scores within age groups revealed no systematic topographic differences between facets.

Intersegmental differences

Considering that the osteoarthritic changes tended to affect the synovial joints on the lower levels of the lumbar spine sooner than the joints on the upper levels (cf. p. 57), differences in the degree of osteoarthritic changes were analyzed between segments without paying regard to age or sex but including only such spines in which all facets could be examined.

Articular cartilage. The cell pattern exhibited significant intersegmental mean differences when scores for the three lower segments were compared with those of the two upper segments of the lumbar spine. Significant mean differences for intercellular substance were found between the L_{1-2} segment and each of the segments below it. Conversely, the calcified zone displayed no significant intersegmental mean differences between the segmental scores in the degree of osteoarthritic lesions (Table 6, Figs. 28, 29, 30).

The maximum mean differences for cell pattern and intercellular substance were 0.87 ± 0.56 and 0.78 ± 0.55 points, respectively, both occur-

TABLE 6

Mean differences between segmental scores (cf. p. 30) for osteoarthritic changes.
(The differences apply to all lumbar spines over 20 years of age with complete sets of synovial joints.)

	A:a *Cell pattern*		A:b *Intercellular-substance*		B. *Calcified layer*		C. *Subchondral bone*		D. *Capsular attachment*	
Segments compared	N	$M \pm t \cdot S_{\bar{x}}$	N	$M \pm t \cdot S_{\bar{x}}$	N	$M \pm t \cdot S_{\bar{x}}$	N	$M \pm t \cdot S_{\bar{x}}$	N	$M \pm t \cdot S_{\bar{x}}$
$L_{2-3}-L_{1-2}$	53	0.26 ± 0.45	57	0.53 ± 0.45	58	0.19 ± 0.75	63	0.56 ± 0.50	61	0.40 ± 0.30
$L_{3-4}-L_{2-3}$	53	0.55 ± 0.44	57	0.23 ± 0.36	58	0.19 ± 0.42	63	0.22 ± 0.40	61	0.31 ± 0.44
$L_{4-5}-L_{3-4}$	53	0.06 ± 0.41	57	0.03 ± 0.58	58	0.05 ± 0.40	63	0.43 ± 0.41	61	0.61 ± 0.47
$L_5-S_1-L_{4-5}$	53	−0.07 ± 0.41	57	−0.19 ± 0.50	58	0.10 ± 0.47	63	−0.08 ± 0.45	61	−0.85 ± 0.47
$L_{3-4}-L_{1-2}$	53	0.81 ± 0.64	57	0.75 ± 0.49	58	0.38 ± 0.50	63	0.78 ± 0.48	61	0.82 ± 0.23
$L_{4-5}-L_{1-2}$	53	0.87 ± 0.56	57	0.78 ± 0.55	58	0.43 ± 0·50	63	1.21 ± 0.52	61	1.38 ± 0.50
$L_5-S_1-L_{1-2}$	53	0.80 ± 0.56	57	0.56 ± 0.54	58	0·53 ± 0.56	63	1.13 ± 0·58	61	0.56 ± 0.39
$L_{4-5}-L_{2-3}$	53	0.60 ± 0.38	57	0.26 ± 0.44	58	0.24 ± 0.55	63	0.65 ± 0.52	61	0.93 ± 0.54
$L_5-S_1-L_{2-3}$	53	0.54 ± 0.52	57	0.07 ± 0.46	58	0.33 ± 0.51	63	0.57 ± 0.58	61	0.05 ± 0.46
$L_5-S_1-L_{3-4}$	53	0.02 ± 0.56	57	−0.16 ± 0.50	58	0.12 ± 0·51	63	0.35 ± 0.56	61	−0.26 ± 0.46

= number of lumbar spines examined.

= mean difference of segmental scores.

ring between L_{4-5} and L_{1-2} segments. Notably, however, only 27 of the 53 spines examined had higher cell pattern scores for the lower than for the upper segments. The latter spines included 8 with a score difference of 1 point, 12 with a score difference of 2—3 points and 7 with a score difference of 4 or more points between the lower and the upper segments. These 7 spines had cartilage necrosis confined to joint facets only in the three lower segments.

The intercellular substance score for the three lower segments exceeded that for the two upper segments in 36 of 57 spines, a difference of 2 points or more being present in 15 of these lumbar spines. In 6 of these 15 spines the difference was due to the fact that facets in the three lower segments exhibited losses of cartilage substance (i.e. a score of 2 points per facet) whereas the facets in the two upper segments merely presented intercellular substance fibrillation (i.e. a score of 1 point per facet).

Subchondral Bone. Significant intersegmental mean differences for the degree of osteoarthritic changes in the subchondral bone were found when segmental scores of L_{1-2} were compared with those for each segment

below it. Moreover, segment L_{4-5} exhibited significant mean differences from segments L_{2-3} and L_{3-4} (Table 6, Fig. 31).

The highest intersegmental mean difference was present between L_{4-5} and L_{1-2} segments with 1.21 ± 0.52 points, and the next highest between L_5-S_1 and L_{1-2} segments with 1.13 ± 0.58 points.

The scores for any of the three lower segments exceeded that for the two upper segments in 45 of the 63 lumbar spines examined with respect to the degree of osteoarthritic changes in the subchondral bone. In the majority of these 45 spines 2 or three facets in the lower segments had higher scores than the facets of the two upper segments. In 8 spines a difference of 2 points or more was recorded between the lower and the upper segments, the cause being that one or a few facets in the three lower segments exhibited extensive subchondral sclerosis and marked connective tissue proliferation in the marrow spaces (a facet score of 2 points) while the facets in the two upper lumbar segments merely showed minor subchondral changes (i.e. a facet score of 1 point).

Capsular Attachments. In regard to the degree of osteorathritic changes in the capsular attachments the L_{4-5} segment exhibited significant mean differences from any other segment in the lumbar spine except that for the L_5—S_1 segment. Furthermore significant mean differences were found between each of the segments L_{2-3}, L_{3-4} and L_5-S_1 on the one hand and the L_{1-2} segment on the other. (Table 6, Fig. 32).

The maximum intersegmental mean difference was 1.38 ± 0.50 points and occurred between L_{4-5} and L_{1-2}.

A segmental score difference of 3 points or more was noted in 10 of 61 spines for the L_{4-5} segment compared with other segments. In these 10 spines the L_{4-5} segments either was the only ones in the lumbar spine with osteophytes in the capsular attachments or it had conspicuous osteophytes while the joints in the other segments had only small osteophytes.

None of the spines with intersegmental score differences for articular cartilage, subchondral bone or capsular attachments exhibited evidence in the roentgenograms of marked joint asymmetry in the lower segments.

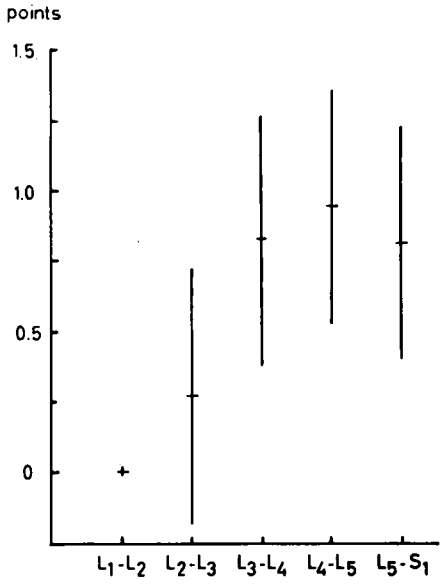


Fig. 28. Mean differences between segmental scores for osteoarthritic changes in the cell pattern (A:a) of the articular cartilage in the synovial joints.

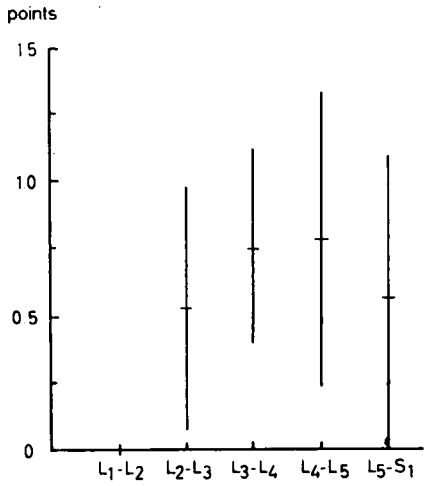


Fig. 29. Mean differences between segmental scores for osteoarthritic changes in the intercellular substance (A:b) of the articular cartilage in the synovial joints.

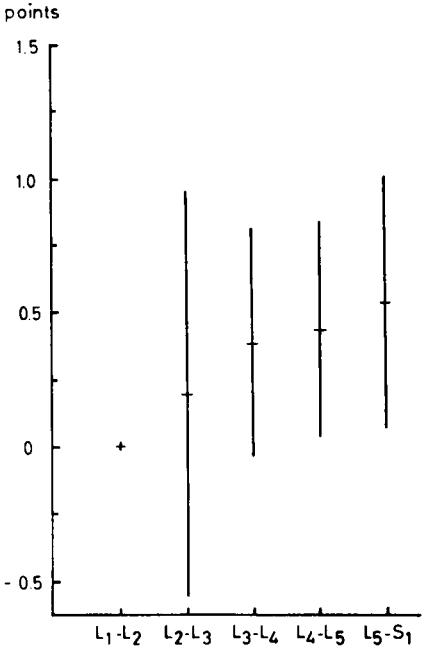


Fig. 30. Mean differences between segmental scores for osteoarthritic changes in the calcified portion (B) of the articular cartilage in the synovial joints.

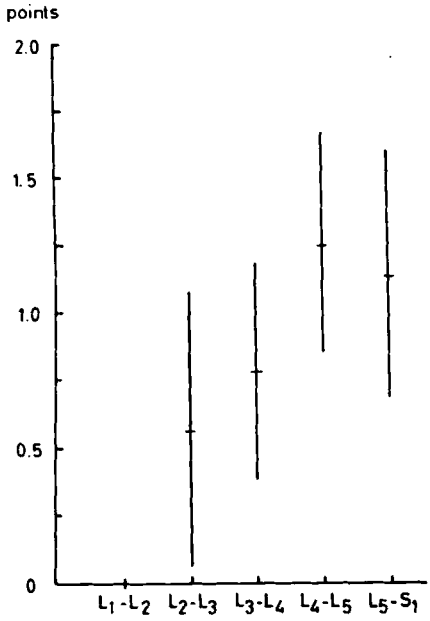


Fig. 31. Mean differences between segmental scores for osteoarthritic changes in the subchondral bone (C) of the synovial joints.

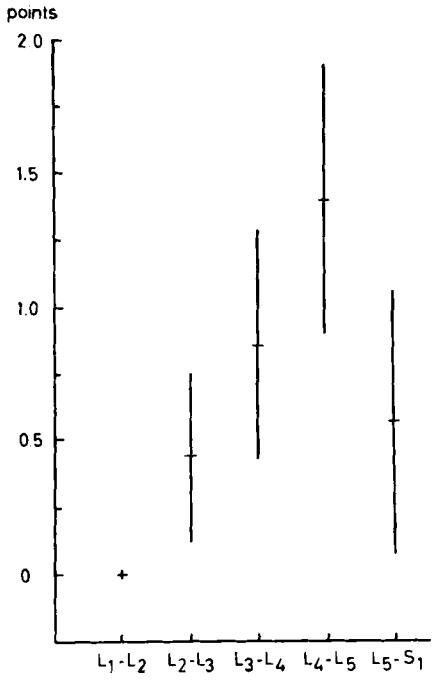


Fig. 32. Mean differences between segmental scores for osteoarthritic changes in the capsular attachments (D) of the synovial joints.

Fig. 28—32. Mean differences between segmental scores for osteoarthritic changes in all lumbar spines over 20 years of age with complete sets of synovial joints. Interpolation for any two segments gives their mean difference. The confidence limits refer to the differences obtained by comparing any segment with the next higher segment (cf. Table 6).

Segmental Instability

In principle the flexion and extension mobility pattern of the lumbar spine preparations was characterized by increasing mobility of the vertebrae in relation to the one above from segment L_{1-2} through segment L_{4-5} and then somewhat less mobility of the L_5—S_1 segment.

Twelve of the lumbar spines exhibited instability of the L_{4-5} segment as defined by Knutsson (1944) during flexion and extension of the preparation. Eight ot them occurred before age 45, all having only minor osteoarthritic changes confined only to the articular cartilages. The remaining 4 spines over 45 years all displayed both chondral and subchondral osteoarthritic changes. These observations, however, permit no conclusions to be drawn regarding the prodromal significance, if any, of segmental instability for the development of osteoarthritis in lumbar synovial joints.

Comment

No significant sex differences in the degree of osteoarthritic changes in the lumbar synovial joints were found within any age group between any joint facets, any joints or any segment. The osteoarthritic changes were in other words similarly distributed in the lumbar spines of men and women. Consequently age and the position of the joint within the lumbar spine must be equally important in men and women as factors in the aetiology of osteoarthritis of the lumbar synovial joints.

Before age 45 the articular cartilages usually exhibited only minor changes such as cell proliferation, intercellular substance fibrillation and slight hypertrophy of the calcified zone. Necrosis, substance losses and marked thickening of the calcified zone became frequent only after that age. The mean frequency per spine of joint facets having such advanced chondral changes after age 45 was 21.9 ± 6.8 † per cent, 28.1 ± 9.2 † per cent and 9.5 ± 6.6 † per cent (Table 5a). The mean degree of osteoarthritic changes after age 65 significantly exceeded that in any age group up to 45 years, as did that in the 46—55 years group compared with the 20—25 years age group. Chondral osteoarthritic changes showed significant differences in degree between consecutive age groups only within certain segments (Tables 3, 4).

Advanced osteoarthritic changes within the subchondral bone — such as extensive sclerosis and marrow spaces filled with more or less highly vascularized connective tissue — occurred only sporadically before age 45. But thereafter it became an increasingly common phenomenon, especially in the three lower segments of the lumbar spine. The mean frequency per spine of facets exhibiting these advanced subchondral changes at ages from 46 years was 7.6 ± 3.6 † per cent (Table 5a). On all levels of the lumbar

† $\pm t \cdot s_{\bar{x}}$

spine the mean degree of subchondral osteoarthritic changes was higher after age 55 than before age 35 (Tables 3, 4).

Osteophytes in the capsular attachments exhibited the same association with age as the subchondral changes. Large osteophytes became fairly common only around age 60, when they had their highest relative frequency in the L_{4-5} joints. The mean frequency per lumbar spine of joint facets with large osteophytes in the capsular attachment at ages over 45 years was 9.3 $\pm$ 3.2 per cent (Table 5a).

Changes in cell pattern and intercellular substance were intercurrent in most articular cartilages. But a normal or negligibly thickened calcified zone was often combined with even advanced changes in the cell pattern and/or intercellular substance of the non-calcified cartilage. This is responsible for the fact that at ages over 45 years the mean frequency per spine of facets with chondral necrosis and/or substance losses significantly exceed that of facets with a markedly thickened calcified zone (34.7 ± 8.2 † per cent versus 9.5 ± 6.6 † per cent. See Table 5c).

In accordance with the adopted scoring system, the corresponding degrees of advanced osteoarthritic changes would be extensive sclerosis and marked connective tissue proliferation in the subchondral bone and/or large osteophytes in the capsular attachments. Such manifestations over age 45 showed a mean frequency per spine of 13.4 ± 4.4 † per cent of the facets (Table 5c). Similarly, the division of mild osteoarthritic changes upon the articular cartilage on the one hand and the subchondral bone or capsular attachment on the other at ages up to 45 years shows that the cartilage had the higher frequency. Accordingly, although the observations all were based on a quantitative assessment that might not be directly comparable for the separate articular structures, it is justified to conclude that the osteoarthritic changes in the subchondral bone and capsular attachments are secondary to those in the articular cartilage in order of appearance.

Osteoarthritic changes in the lumbar synovial joints were thus strongly dependent on one or more factors related to age. But this statement, based as it is on morphological grounds, permits no conclusions to be drawn concerning either the nature or the degree of any such factors. It seems justified to point out, however, that degenerative changes seem to appear around the age of 30 years and are followed by restorative phenomena at about the age of 45 years.

No systematic differences in osteoarthritic changes were found between joint facets nor between joints within lumbar spines. Hence in the lumbar spine as a unit there exist no local conditions that would promote the development of osteoarthritic changes. Nevertheless the articular cartilage

† $\pm t \cdot s_{\bar{x}}$

and subchondral bone of one facet exhibited changes of higher degree than the other in some 5 per cent of the joints examined, while the capsular attachment did so in about 10 per cent of the joints. Such differences between ipsiarticular facets were distributed on all the lumbar synovial joints without showing any predilection for the superior or inferior facet, the left or right joint in the same segment or any of the lumbar segments. For some reason, therefore, the development of the osteoarthritic changes in one facet may lag behind that in the other facet of the same joint.

When all the lumbar spines regardless of age and sex were analyzed with respect to intersegmental differences in the degree of osteoarthritic changes significant differences appeared. This was the case for the cell pattern of the articular cartilage between the three lower lumbar segments on the one hand and the two upper segments in the other. The degree of changes in the intercellular substances differed significantly for the three lower segments only compared with the L_{1-2} segment. These significant intersegmental differences in cell pattern and intercellular substance could be accounted for mainly by necrosis and substance losses in the articular cartilage of one or more facets in the three lower segments, while the L_{1-2} and L_{2-3} facets had articular cartilages exhibiting merely cell proliferation and fibrillation of the intercellular substance. No intersegmental differences appeared for the calcified zone of the articular cartilage.

In principle the degrees of osteoarthritic changes in the subchondral bone displayed similar intersegmental differences as the articular cartilage, except that the differences were more accentuated for the subchondral bone. Thus the mean score for subchondral osteoarthritic changes for the facets in the L_{4-5} segment was significantly higher than the corresponding score for any segment craniad to it. Extensive subchondral sclerosis and an abundance of more or less highly vascularized connective tissue in the marrow spaces confined to the facets in the three lower lumbar segments constituted the main contributory factor to these differences.

Changes in the form of osteophytes in the capsular attachments showed a higher mean degree in the L_{4-5} segment than in any other lumbar segment. This predominance can be accounted for to a large extent by the fact that every fifth spine had markedly larger osteophytes here than elsewhere.

The level of the joints within the lumbar spine is thus a factor of significance for the degree of osteoarthritic changes. This contention is borne out by the fact that the more extensive the changes in the structures of the joint, the greater were the intersegmental differences. In the lower segments of the lumbar spine, especially the L_{4-5} segment, the osteoarthritic changes consequently seem to be dependent on one or more factors in addition to age.

CHAPTER 6

Osteoarthritis in Synovial Joints, Disc Degeneration and Marginal Vertebral Osteophytes in the Lumbar Spine

Osteoarthritis (Tables 7, 8, 9, 10)

Osteoarthritis in lumbar synovial joints was considered present in any segment where at least one synovial joint facet exhibited both chondral and subchondral changes (Fig. 33). Only necrosis and substance losses were accepted as reliable chondral changes; but even minor sclerosis and connective tissue proliferation in the subchondral bone as well as small osteophytes in the capsular attachments were regarded as reliable subchondral changes (A:a = 2, A:b = 2, C = 1 or 2, D = 1 or 2, cf. p. 27).

The complete series of lumbar spines included none with osteoarthritis before the age of 25 years. Between 26 and 45 years 40.0 ± 11.0 per cent (8 of 20) lumbar spines exhibited osteoarthritis. In 3 of these spines the synovial joints in the L_{1-2} segment were affected, in 4 those in the L_{2-3} segment and in one those in the L_5—S_1 segment (Tables 7, 8).

Over 45 years 90.3 ± 5.4 per cent (28 of 31) lumbar spines exhibited osteoarthritis of the synovial joints (Table 7). The frequency of spines with osteoarthritis on a particular level rose gradually from the L_{1-2} segment to the L_5—S_1 segment, the respective frequencies being 32.3 ± 8.4 and 64.3 ± 9.1 per cent (Table 8). The frequencies of L_{4-5} and L_5—S_1 segments with affected synovial joints were significantly higher than the frequencies of affected L_{1-2} and L_{2-3} segments. The same applies to the L_{3-4} segment compared with the L_{1-2} segment (Table 8).

TABLE 7

Absolute and relative frequencies of lumbar spines with osteoarthritis in at least one segment.

	Osteoarthritis				
Age	N	n	%	S %	S % × 1.96
20—25 years	6	0	0	—	(38.6 %)*
26—45 years	20	8	40.0	± 11.0	± 21.6
> 45 years	31	28	90.3	± 5.4	± 10.6

TABLE 8

Absolute and relative frequencies of osteoarthritis in separate lumbar spine segments

	Age 26–45 years					Age > 45 years				
	Osteoarthritis					Osteoarthritis				
Segments	N	n	%	S %	S % × 1.96	N	n	%	S %	S % × 1.96
L_{1-2}	23	3	13.0	± 7.0	± 13.7	31	10	32.3	± 8.4	± 16.5
L_{2-3}	27	4	14.8	± 6.9	± 13.5	36	14	38.9	± 8.1	± 15.9
L_{3-4}	21	0	0	—	(13.3 %)*	35	19	54.3	± 8.4	± 16.5
L_{4-5}	25	0	0	—	(11.3 %)*	33	19	60.6	± 8.4	± 16.5
L_{5-S_1}	23	1	0	—	(19.3 %)*	28	18	64.3	± 9.1	± 17.8

TABLE 9

Absolute and relative frequencies of lumbar spines over 45 years of age with osteoarthritis in at least two adjacent segments.

	Osteoarthritis				
Segments	N	n	%	S %	S % × 1.96
L_{1-2} and L_{2-3}	28	5	17.9	± 7.3	± 14.3
L_{2-3} and L_{3-4}	32	11	34.4	± 8.4	± 16.5
L_{3-4} and L_{4-5}	30	14	46.7	± 9.1	± 17.8
L_{4-5} and L_5-S_1	25	13	52.0	± 9.7	± 19.0

TABLE 10

Absolute and relative frequencies of lumbar spines over 45 years of age with osteoarthritis in at least three segments.

	Osteoarthritis				
Segments	N	n	%	S %	S % × 1.96
L_{1-2}, L_{2-3} and L_{3-4}	28	4	14.3	± 6.6	± 12.9
L_{2-3}, L_{3-4} and L_{4-5}	27	7	25.9	± 8.4	± 16.5
L_{3-4}, L_{4-5} and L_5-S_1	24	15	37.5	± 9.8	± 19.2
Joint segments not adjacent	35	17	48.6	± 8.4	± 16.5

N = number of spines examined

n = number of examined spines showing osteoarthritis

* = estimated upper limit

Whereas osteoarthritis of the synovial joints was confined to a single segment in the ages up to 45 years, more than one segment was affected from the age of 46 years. Thus of the total number of examined L_{1-2} and L_{2-3} segment pairs, 17.9 ± 7.3 per cent were affected. The corresponding figures for the segment pairs L_{2-3} and L_{3-4}, L_{3-4} and L_{4-5} as well as L_{4-5} and L_5—S_1 were 34.4 ± 8.4, 46.7 ± 9.1 and 52.0 ± 9.7 per cent, (Table 9). Osteoarthritis in 3 or more segments occurred in 48.6 ± 8.4 per cent of the lumbar spines over 45 years of age (Table 10).

All segments could be examined in 14 of the 28 lumbar spines over 45 years of age with osteoarthritis of the synovial joints. A mere 6 of them (41.9 ± 12.4 %) exhibited osteoarthritis of the synovial joints in the L_{1-2} and/or L_{2-3} segments, while 13 of them (92.9 ± 24.4 %) exhibited osteoarthritis in at least two of the segments L_{3-4}, L_{4-5} and L_5—S_1.

Disc degeneration (Tables 11, 12).

In the present context disc degeneration was regarded gross changes of grades 2 and 3.

Gross disc changes involving both nucleus pulposus and annulus fibrosus began to appear in the 20—25 years group (Table 11). Disc degeneration

TABLE 11

Frequency of intervertebral discs with gross changes of grades 0, 1, 2 or 3 (cf. p. 31) in separate lumbar spine segments.

Age	20—25 years				26—35 years				36—45 years			
Grade	0	1	2	3	0	1	2	3	0	1	2	3
Segments												
L_{1-2}	3	6	1	0	3	10	2	0	1	16	0	0
L_{2-3}	4	4	2	0	4	11	0	0	2	13	2	0
L_{3-4}	4	5	1	0	6	7	2	0	3	11	3	0
L_{4-5}	3	2	4	1	4	8	2	1	3	7	7	0
L_5—S_1	4	3	3	0	1	8	4	2	0	9	6	2
Age	46—55 years				56—65 years				> 65 years			
Grade	0	1	2	3	0	1	2	3	0	1	2	3
Segments												
L_{1-2}	0	14	2	0	0	7	3	2	0	3	4	1
L_{2-3}	1	13	2	0	0	7	6	0	2	1	3	1
L_{3-4}	1	13	2	0	1	4	6	2	1	3	2	2
L_{4-5}	1	7	4	4	1	1	7	4	0	4	3	1
L_5—S_1	0	6	5	5	0	2	8	3	0	3	3	2

in one or more segments was exhibited by 24 of the 42 lumbar spines examined in the 20—45 years group, i.e. 57.1 ± 7.1 per cent. Only 3 spines were entirely free from apparent disc degeneration. In the age groups over 45 years 10 of 37 spines exhibited gross changes of grade 1, while 27 spines — 72.8 ± 8.9 per cent — had disc degeneration in one or more segments.

Significant intersegmental mean differences in the degree of gross disc changes occurred between either of the L_{4-5} and L_5—S^1, on the one hand, and any of the three upper segments on the other (Table 12, Fig. 34). In 26 of 77 spines, 33.3 ± 9.6 per cent, the three upper discs exhibited merely nucleus pulposus changes, while the two lower discs exhibited nucleus pulposus as well as annulus fibrosus changes.

TABLE 12

Mean differences between segmental scores for gross changes in the discs. The differences apply to all lumbar spines over 20 years of age with complete sets of intervertebral discs.

Segments compared	N	M	$\pm t \cdot S_{\overline{X}}$
$L_{2-3}-L_{1-2}$	77	−0.10	± 0.11
$L_{3-4}-L_{2-3}$	77	0.05	± 0.14
$L_{4-5}-L_{3-4}$	77	0.33	± 0.19
$L_5-S_1-L_{4-5}$	77	0.19	± 0.18
$L_{3-4}-L_{1-2}$	77	−0.06	± 0.05
$L_{4-5}-L_{1-2}$	77	0.33	± 0.05
$L_5-S_1-L_{1-2}$	77	0.51	± 0.06
$L_{4-5}-L_{2-3}$	77	0.42	± 0.07
$L_5-S_1-L_{2-3}$	77	0.61	± 0.32
$L_5-S_1-L_{3-4}$	77	0.43	± 0.18

N = number of lumbar spines examined
M = mean difference of segmental scores

Marginal Osteophytes (Table 13)

Marginal osteophytes regarded as X-ray changes of grade 1 or higher on the vertebral body margins began to be a reasonably common phenomenon only after age 45 (Table 13). Thus only 8 (18.6 ± 6.5 %) of the 42 spines in the 20—45 years group exhibited osteophytes, non over grade 1. Over 45 years this was the case of 24 of 37 spines (64.1 ± 3.1 %). 7 of 8 spines over 65 years had osteophytes in at least two segments.

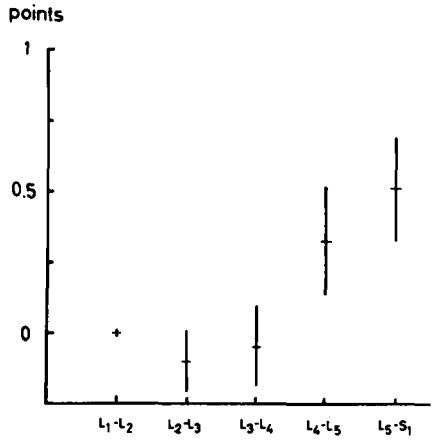


Fig. 34. Mean differences between segmental scores for gross changes of the intervertebral discs in all lumbar spines over 20 years of age with complete sets of discs. Interpolation for any two segments gives their mean difference. The confidence limits refer to the differences obtained by comparing any segment with the next higher segment (cf. Table 12).

TABLE 13

Frequency of lumbar segments with osteophytes of grades 0, 1, 2 or 3 (cf. p. 31) on either one or both of the vertebral body edges in the separate segment.

Age	20–25 years				26–35 years				36–45 years			
Grade	0	1	2	3	0	1	2	3	0	1	2	3
Segments												
L_{1-2}	10	0	0	0	15	0	0	0	17	0	0	0
L_{2-3}	10	0	0	0	15	0	0	0	16	1	0	0
L_{3-4}	10	0	0	0	14	1	0	0	12	5	0	0
L_{4-5}	10	0	0	0	15	0	0	0	15	2	0	0
L_5-S_1	10	0	0	0	15	0	0	0	13	3	1	0
Age	46–55 years				56–65 years				> 65 years			
Grade	0	1	2	3	0	1	2	3	0	1	2	3
Segments												
L_{1-2}	14	1	1	0	6	2	2	2	3	2	1	2
L_{2-3}	14	1	1	0	5	5	1	1	3	2	2	1
L_{3-4}	11	3	1	0	5	6	1	0	1	3	2	2
L_{4-5}	15	1	1	0	6	4	1	1	2	5	1	0
L_5-S_1	11	3	0	2	8	2	1	1	2	6	0	0

Significant intersegmental mean differences in the degree of osteophyte formation occurred between the L_{3-4} and L_{2-3} segments (Fig. 35). Of 36 lumbar spines with osteophytes 5 had large osteophytes (grade 2 or 3) in the former segment and insignificant or no osteophytes (grade 0 or 1) in the latter.

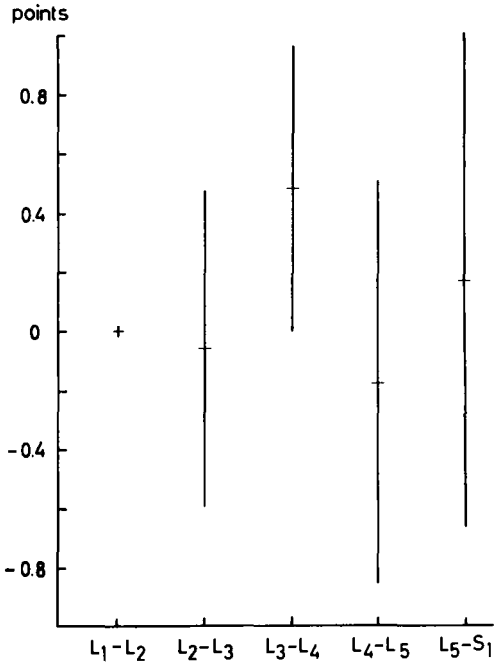


Fig. 35. Mean differences between segmental scores for marginal osteophytes on the vertebral bodies in all lumbar spines over 20 years of age with osteophytes in at least one segment. Interpolation for any two segments gives their mean difference. The confidence limits refer to the differences obtained by comparing any segment with the next higher segment.

* * * * *

Isolated Osteoarthritis (Table 14)

Regardless of age 25 of 46 lumbar spines with 5 complete segments had osteoarthritis in at least one segment. 9 of them (36.4 ± 9.6 %) had at least one segment with osteoarthritis as the sole pathological change, 5 being up to 45 years and 4 over 45 years.

Isolated Disc Degeneration (Table 14)

Regardless of age 28 of 46 lumbar spines with 5 complete segments had disc degeneration in at least one segment. In 8 of them (28.6 ± 8.6 %) all 20—45 years old, at least one segment exhibited disc degeneration as the only pathological condition.

Isolated Marginal Osteophytes (Table 14).

Regardless of age 24 of 46 lumbar spines with 5 complete segments had osteophytes in at least one segment, but the condition was isolated in only one spine. This occurred in the L_{3-4} segment and took the form of sharpening of the vertebral body margins.

TABLE 14

Absolute and relative frequencies of lumbar spines with and without isolated disc degeneration, osteoarthritis or marginal osteophytes in at least one segment. The frequencies apply exclusively to complete lumbar spines with disc degeneration, osteoarthritis and/or marginal osteophytes in at least one segment.

Age	20—45 years	> 45 years	> 20 years
Disc degeneration only	8	0	8 (28.6 ● 8.6 %)
Disc degeneration and marginal osteophytes or osteoarthritis	8	12	20 (71.4 ± 8.6 %)
Osteoarthritis only	5	4	9 (36.4 ± 9.6 %)
Osteoarthritis and disc degeneration or marginal osteophytes	3	13	16 (63.6 ± 9.6 %)
Marginal osteophytes only	1	0	1 (0 18.2 %*)
Marginal osteophytes and disc degeneration or osteoarthritis	4	19	23 (95.7 ± 4.2 %)

* * * * *

* = estimated upper limit

The following analysis included only lumbar spines with 3 or more complete segments. In the 20—45 years group this means that only 33 of the original 43 and over 45 years 31 of 43 spines could be included. (Cf. Table 15).

Intrasegmental Frequency Differences and Intercurrences (Tables 15, 16, 17, 18)

Significant frequency differences between osteoarthritis, disc degeneration and marginal osteophytes occurred only in the 20—45 years group. In this age group the L_{4-5} and L_5—S_1 segments exhibited higher disc degeneration frequencies than frequencies of the other two conditions. In the L_{4-5} segment 11 of 31 spines (35.5 ± 16.9 %) had disc degeneration, while only one had marginal osteophytes and none osteoarthritis. In the L_5—S_1 segment 11 of 29 spines exhibited disc degeneration (37.9 ± 17.6 %), the figures for marginal osteophytes and osteoarthritis being 2 and 1 spines respectively. (Table 15).

In all segments disc degeneration and marginal osteophytes on the one hand as well as marginal osteophytes and osteoarthritis on the other were intercurrent oftener than one would expect of a random distribution, the respective (product moment) correlation coefficients both varying between 0.3 and 0.5 (Tables 16, 17). Conversely, only the L_{2-3} and L_5—S_1 seg-

TABLE 15

Absolute and relative frequencies of disc degeneration, marginal osteophytes and osteoarthritis in separate lumbar segments.
The frequencies apply exclusively to complete spinal joints.

	Segment	N	Disc degeneration				Marginal osteophytes				Osteoarthritis			
			n	%	S % S	% × 1.96	n	%	S %	S % × 1.96	n	%	S % S	% × 1.96
Age 20—45 years	L_{1-2}	28	3	10.7	±5.8	±11.4	0	0	0	(10.2%)*	3	10.7	±5.8	±11.4
	L_{2-3}	30	3	10.0	±5.5	±10.8	1	3.3	0	(14.2%)*	4	13.3	±5.9	±11.6
	L_{3-4}	27	5	18.5	±7.4	±14.5	3	11.1	± 6.2	±12.2	0	0	0	(10.5%)*
	L_{4-5}	31	11	35.5	±8.6	±16.9	1	3.2	0	(13.8%)*	0	0	0	(9.2%)*
	L_5-S_1	29	11	37.9	±9.0	±17.6	2	6.8	± 4.7	± 9.2	1	3.4	0	(14.6%)*
Age > 45 years	L_{1-2}	28	8	28.6	±8.6	±16.9	10	35.9	± 9.1	±17.8	10	35.9	±9.1	±17.8
	L_{2-3}	31	10	32.3	±8.4	±16.5	9	29.1	± 8.2	±16.1	12	38.9	±8.8	±17.2
	L_{3-4}	31	10	32.3	±8.4	±16.5	16	51.6	± 9.0	±17.6	16	51.6	±9.0	±17.6
	L_{4-5}	29	19	65.5	±8.8	±17.2	10	34.1	± 8.8	±17.2	18	62.1	±9.0	±17.6
	L_5-S_1	25	16	64.0	±9.6	±18.8	13	52.0	±10.0	±19.6	15	60.0	±9.8	±19.2

* = estimated upper limit

ments exhibited intercurrence of disc degeneration and osteoarthritis oftener than one would expect of a random distribution, the (product moment) correlation coefficient being 0.35 and 0.33 respectively (Table 18).

TABLE 16

Segmental intercurrence of disc degeneration and marginal osteophytes in the lumbar spine.

	Segments				
	L_{1-2}	L_{2-3}	L_{3-4}	L_{4-5}	L_5-S_1
No. of cases studied	56	67	56	60	54
No. with disc degeneration	11	13	15	30	27
No. with marginal osteophytes	10	10	19	11	15
No. with intercurrent disc degeneration and marginal ostophytes	7	10	10	10	11
No. with intercurrence expected from the nullhypothesis	1.97	3.81	4.41	5.50	7.22
X^2 ($X^2_{0.05} = 3.84$)	15.90	14.95	11.40	7.11	6.35
Correlation coefficient r (product-moment)	+ 0.54	+ 0.47	+ 0.45	+ 0.34	+ 0.35

TABLE 17

Segmental intercurrence of marginal osteophytes and osteoarthritis in the lumbar spine.

	Segments				
	L_{1-2}	L_{2-3}	L_{3-4}	L_{4-5}	L_5-S_1
No. of cases studied	56	57	56	60	54
No. with marginal osteophytes	10	10	19	11	15
No. with osteoarthritis	13	16	16	18	16
No. with intercurrent marginal osteophytes and osteoarthritis	6	9	12	7	10
No. with intercurrence expected from the null hypothesis	1.97	3.81	4.41	3	4.44
X^2 ($X^2_{0.05} = 3.84$)	9.74	10.10	14.40	7.80	11.30
Correlation coefficient r (product-moment)	+ 0.42	+ 0.42	+ 0.51	+ 0.36	+ 0.46

TABLE 18

Segmental intercurrence of disc degeneration and osteoarthritis in the lumbar spine.

	Segments				
	L_{1-2}	L_{2-3}	L_{3-4}	L_{4-5}	L_5-S_1
No. of cases studied	56	67	56	60	54
No. with disc degeneration	11	13	15	30	27
No. with osteoarthritis	13	16	16	18	16
No. with intercurrent disc degeneration and osteoarthritis	5	9	7	8	12
No. with intercurrence expected from the null-hypotesis	2.55	4.18	4	9	8
X^2 ($X^2_{0.05} = 3.84$)	2.40	8.05	2.92	0.20	5.90
Correlation coefficient r (product moment)	+ 0.21	+ 0.35	+ 0.23	+ 0.01	+ 0.33

Intersegmental Frequency Differences and Intercurrences (Tables 15, 19)

Intersegmental significant frequency differences between osteoarthritis, disc degeneration and marginal osteophytes occurred exclusively between 20 and 45 years of age. Thus the L_{4-5} segment displayed a higher frequency of disc degeneration than the $L_5—S_1$ segment of marginal osteophytes or osteoarthritis. The L_{4-5} segment displayed disc degeneration in 11 of 31 spines (35.5 ± 16.9 %), while the $L_5—S_1$ segment showed marginal osteophytes in 2 and osteoarthritis in 1 of 29 spines. The latter segment had disc degeneration in 11 of 29 spines (37.9 ± 17.6 %) while the former exhibited marginal osteophytes in 1 and osteoarthritis in none of the 31 spines. In addition to these significant differences, the frequency of disc degeneration on each of the two lower segments exceeded the frequency of marginal osteophytes in the L_{1-2} or L_{2-3} segments (0 of 28 and 1 of 30 spines respectively), and the osteoarthritis (0 of 27) frequency in the L_{3-4} segment (Table 15).

A diffuse pattern of positive correlations appeared between disc degeneration in one segment and marginal osteophytes or osteoarthritis in another segment. This should be considered in the light of the fact that each of the conditions osteoarthritis, disc degeneration and marginal osteophytes is present in adjacent segments more often than one would expect of a random distribution (Table 19). Owing to the aforementioned intrasegmental correlations, this pattern should therefore be interpreted as the result of mere numerical coincidences without biological significance.

TABLE 19

Number of lumbar spines with disc degeneration in two segments.

Segments	n	No. expected from the null-hypothesis	X^2 ($X^2_{0.05} = 3.84$)
L_{1-2} and L_{2-3}	10	3.0	28.0
L_{2-3} and L_{3-4}	10	4.2	12.5
L_{3-4} and L_{4-5}	13	9.5	1.3
L_{4-5} and L_5-S_1	26	16.7	21.2
L_{3-4} and L_5-S_1	15	8.9	10.0

Number of lumbar spines with marginal osteophytes in two segments.

Segments	n	No. expected from the null-hypothesis	X^2 ($X^2_{0.05} = 3.84$)
L_{1-2} and L_{2-3}	10	2.4	26.2
L_{2-3} and L_{3-4}	11	4.6	13.4
L_{3-4} and L_{4-5}	11	4.0	20.0
L_{4-5} and L_5-S_1	8	3.6	7.0

Number of lumbar spines with osteoarthritis in two segments.

Segments	n	No. expected from the null-hypothesis	X^2 ($X^2_{0.05} = 3.84$)
L_{1-2} and L_{2-3}	7	3.2	6.27
L_{2-3} and L_{3-4}	9	3.7	6.23
L_{3-4} and L_{4-5}	13	4.6	16.0
L_{4-5} and L_5-S_1	12	5.0	17.6

n = number of spines with disc degeneration, marginal osteophytes or osteoarthritis

The significant intercurrence of osteoarthritis in the L_{4-5} segment and disc degeneration in the L_{3-4} segment (9 intercurrences versus 6.4 expected, $x^2_{0.05} = 4.16$) cannot be thus explained. For (i) osteoarthritis and disc degeneration in the L_{4-5} segment and (ii) disc degeneration in L_{3-4} and L_{4-5} segments were not correlated (Tables 18, 19).

CHAPTER 7

Discussion

The examined series of spines came from a random sample of autopsy cases (Table 1), except that subjects with malignant tumours or chronic tuberculosis were eliminated. The morhological changes noted in the lumbar spines were unlikely to be related to the causes of death. Subjects over 20 years of age were residents of Stockholm and subjects under 20 residents of Stockholm or Gothenburg.

The assessment of the morphological changes in the synovial joints might of course have been affected by various sources of error. The most obvious of these have been mentioned in Chapter 3 (p. 00) and are: (i) variations in the normal anatomy of the joint, (ii) artefacts due to the histological procedures, and (iii) lack of uniformity in grading the morphological changes.

These sources of error are unlikely to have influenced gravely the assessement of advanced osteoarthritic changes, but they could have affected the grading of minor changes in particular joints. However, the means and mean differences would then be randomly affected by positive and negative influences that would tend to cancel out.

In principle the assessment of the gross disc changes and the roentgenological vertebral body changes were affected by similar sources of errors. But any errors would also have fallen randomly. Hence the results with respect to the gross changes in the vertebral body joints should be no less reliable than those with respect to the synovial joints.

* * *

The present investigation was carried out on a series of lumbar spines sufficiently comprehensive to illuminate the micromorphology of the lumbar synovial joints in osteoarthritis. The pattern of osteoarthritis agrees in all respects with what has been reported concerning osteoarthritis of the extremital joints (Pommer, 1913; Bennett, Waine and Bauer, 1942; Harrison, Schajowicz and Trueta, 1953; Grueter and Rütt, 1962). Thus in the lumbar synovial joints, too, the earliest microscopic changes are seen in the

articular cartilages (Fig. 11), while those in the subchondral bone and joint capsule set in later.

Like osteoarthritic extremital joints, the lumbar synovial joints with osteoarthritic changes exhibit a mixture of degenerative and restorative processes. Remodelling of the subchondral bone plate and osteophyte formation next to the capsular attachment constitute the most conspicuous restorative processes in osteoarthritis of the lumbar synovial joints (Figs. 6, 15, 16). The outstanding manifestations of degeneration are cartilage necrosis and defects in the subchondral bone plate (Figs. 13, 14).

The order of appearance of degenerative and restorative processes in the articular cartilage and subchondral bone impart the same impression of the mode of development of the morphological changes in the subchondral bone as reported by other workers on the basis of the microscopic appearance of osteoarthritis in the extremital joints. Defects in the subchondral bone plate and alternately narrowed and thickened trabeculae in the subjacent cancellous bone combined with marked cartilage changes in the lumbar synovial joints are common (Figs. 14, 19). The passage of vascularized connective tissue from the subchondral marrow spaces into an articular cartilage that exhibits necrosis and substance losses (Fig. 17) bears out the hypothesis that also subchondrally proliferation takes place in an attempt to restore and repair the degenerated articular cartilage (Harrison, Schajowicz and Trueta, 1953).

Synovial tissue proliferation with so-called pannus formation or extensive perivascular round cell infiltrations were in no case seen in the present series of lumbar spines. This fact contradicts the view that osteoarthritis of the lumbar synovial joints more or less often is a sequel to arthritis (Gantenberg, 1930; Oppenheimer, 1943).

No sex differences were demonstrated with respect to the time of onset, intraspinal distribution and degree of the osteoarthritic changes in the lumbar synovial joints (Table 2). Nor did Kellgren and Lawrence (1958) encounter any sex differences in the frequency of lumbar spines with X-ray evidence of osteoarthritis in a representative sample of an urban population between 55 and 64 years of age. Hence it seems likely that the same main factors are responsible for the development of osteoarthritic changes in the lumbar synovial joints in men and vomen.

Osteoarthritic changes in the lumbar synovial joints in principle show the same relation to aging as in the extremital joints (Heine, 1926; Bennett, Waine and Bauer, 1942; Olsson, 1953; De Palma, 1950, 1957). Thus in both types of joint they increase in frequency and degree with rising age (Figs. 21—25, Fig. 27, Tables 3, 4, 5, 20, 21, 22). Morphologically

this is reflected by the fact that restorative processes in the form of remodelling of the subchondral bone plate and osteophyte formation adjacent to the capsular attachments begin to appear around the age of 45 (Figs. 16, 17).

In about 5 per cent of all the lumbar synovial joints examined there was, regardless of level, a marked difference between the superior and inferior facets of the same joint in the degree of chondral and subchondral osteoarthritic changes (Figs. 18, 19, 20). Approximately 10 per cent of the joints exhibited similar differences with respect to osteophyte formation in the capsular attachements (Fig. 6). Corresponding dissimilarities between the degree of osteoarthritic changes in ipsiarticular joint components were reported by Güntz (1934) in an unspecified proportion of cases. Ingelmark (1956, 1959) encountered such discrepancies between the facets of approximately 5 per cent of the lumbar synovial joints in a large series of mediaval skeletons. And the same thing in principle was reported by Heine (1926) in knee joints of autopsy cases with microscopic osteoarthritic changes. None of the latter authors attempted to explain this phenomenon. Yet it seems reasonable to assume that these differences reflect the correspondence between the two facets of a synovial joint and the ball and socket of an extremital joint with their somewhat different load distributions. This might cause the osteoarthritic changes in the two facets to lose synchronism in their development, at least in a proportion of the lumbar synovial joints. Ossification disturbances during the growth of one of the facets might also account for this phenomenon.

Osteoarthritic changes confined to particular synovial joints were not seen in the present series of lumbar spines. This suggests that local causes acting on isolated synovial joints cannot be a common cause of lumbar osteoarthritis.

Osteoarthritic changes in the lumbar synovial joints exhibited a distinct tendency to be associated with particular segments of the lumbar spine (Table 6, Figs. 28—32). In the present series of lumbar spines it was thus quite a common observation that the articular cartilages in the L_{4-5} and L_5—S_1 segments exhibited necrosis and substance losses without those in the L_{1-2} and L_{2-3} segments doing so. The same applied to such advanced changes in the subchondral bone as extensive sclerosis of the cancellous bone and abundant connective tissue in the subchondral marrow spaces. The capsular attachments showed a higher degree of changes in the L_{4-5} segment than in the segments higher up (Fig. 32). This observation agrees with what previous workers have noted regarding osteoarthritic changes in the lumbar synovial joints (Güntz, 1934; Putti and Logròscino, 1937; Ingelmark, 1956, 1959).

Putti and Logròscino (1937) ascribed these intersegmental differences to asymmetries of the synovial joints in the lower lumbar segments. The corresponding differences in the present series of lumbar spines are not susceptible of such an explanation. For perusal of the frontal and lateral X-ray films of spines exhibiting such differences yielded no evidence of such asymmetries. It shold be pointed out, however, that the presence of synovial joint asymmetry in the lumbar spine cannot be based on X-ray examinations alone, for the configuration of these joints is such that their joint space readily can be distorted (Reichmann, 1963). In the present investigation this potential source of error was to some extent compensated by the fact that none of the spines showed the combination commonly associated with asymmetry of hypoplasia with malformation of the joint facets on one side compared with those on the opposite side (Putti, 1927; Putti and Logròscino, 1937; Brocher, 1950). But this is not to say that it may not be correct in a particular case of marked joint asymmetry to hold it partly responsible for any osteoarthritis that may be present (cf. Horwitz and Smith, 1940). Joint asymmetry seems to have contributed little to the development of osteoarthritis in the lumbar synovial joints in large roentgenological series (Brailsford, 1929; Soutworth and Bersack, 1950). The results of the present investigation seem to bear this out, as does the fact that the frequency of osteoarthritis in the L_{4-5} and L_5—S_1 segments far exceeded the approximately 10 per cent of lumbar spines which, according to osteometric investigations (Badgley, 1941; Jonck, 1961), could have been affected with primary synovial joint asymmetry. Moreover, such asymmetry seems to be a functional adaption to mechanical stresses to which the joints are exposed (Farkas, 1941; Ingelmark, 1943) rather than an anomaly that constitutes a **locus minoris resistentiae** in the lumbar spine.

The gradual increase in the average degree of osteoarthritic changes in the synovial joints from the L_{1-2} segment through the L_{4-5} segment, followed by a distinct tendency to decrease in the L_5—S_1 segment, suggests that these intersegmental differences reflect anatomical and functional associations between the separate lumbar segments. For, among other things, the anatomical relations in the lumbar spine are such that the synovial joints in the L_{4-5} segment as a rule constitute that pair of joints which support the vertebra at the vertex of the lumbar lordosis (Duhs, 1950; Sullivan and Miles, 1959). It has been demonstrated that the force of gravity is capable of displacing ventrad those vertebrae below the vertex of the lumbar lordosis (deCuveland and Feser, 1958). It is believed that this ventrally directed force is withstood, at least partly, by the synovial joints in the L_{4-5} and L_5—S_1 segments. Consequently the anatomical relations in the lumbar spine expose the synovial

joints in these segments to increased stress more often than the synovial joints in the three segments above them. Functionally the lumbar spine is characterized by increasing mobility of the vertebrae in relation to the one above from segment L_{1-2} through segment L_{4-5} and then somewhat less mobility of the L_5—S_1 segment (Bakke, 1931; Dittmar, 1931; Allbrook, 1957). In principle the same mobility pattern was displayed by the lumbar spine preparations in the present investigation. Thus the functional relations in the lumbar spine also favour the synovial joints in the upper segments over those in the lower segments from the point of view of mechanical stresses.

Osteoarthritis of the lumbar synovial joints was here considered present only when the articular cartilage exhibited both necrosis and substance losses at the same time as the subchondral bone and capsular attachments displayed more or less extensive changes (Figs. 6, 17, 20). This delimitation of the microscopically observed osteoarthritic changes was adopted because it would provide some idea of the presence of grossly manifest osteoarthritis of the lumbar synovial joints (Fig. 33) in a comparable series of lumbar spines. Osteoarthritis was encountered already in the age group 26—45 years (Table 7), as previous workers also have done (Güntz, 1934; Putti and Logròscino, 1937). Notably, however, neither of the latter authors specified either the number of segments affected or their site.

Consequently the observation made in the present investigation to the effect that osteoarthritis tended to appear initially in the synovial joints in the two upper segments of the lumbar spine (Table 8) cannot be compared with the results of previous studies. In a series of skeletons of unspecified age distribution Shore (1935) found the highest incidence of osteoarthritis in the upper segments of the lumbar spine. The observation made in the present investigation concerning the level of osteoarthritis in young subjects suggests that Shore's series included a fairly high proportion of young skeletons. The anatomical variations described by Davis (1955) in the articular processes forming the so-called thoracolumbar mortice joint might be predisposing to early osteoarthritis in some cases. According to Davis, a mortice joint — where the inferior articular process cluthes around the superior articular process dorsally — may give rise to a locally increased mechanical strain on the synovial joints in this segment.

After age 45 osteoarthritis was exceedingly common in the present series of lumbar spines (Tables 9, 10). Thus at least one of the synovial joints exhibited osteoarthritis in approximately 90 per cent of the lumbar spines over age 45. The corresponding frequencies reported by Güntz (1934) and Putti and Logròscino (1937) were of the order of 50 to 60 per cent. The comparatively high frequency observed in the present investigation

is probably due to the fact that it represents microscopically grave osteoarthritis while those of the aforementioned workers represent grossly grave osteoarthritis. In the present investigation the intrasegmental frequencies of osteoarthritis were about 60 per cent. As a comparison may be mentioned that osteoarthritis manifested by necrosis and substance losses in the articular cartilage combined with subchondral remodelling and connective tissue proliferation has a frequency of 50 to 60 per cent in the knee and hip joints in large autopsy series around age 50 (Heine, 1926).

Osteoarthritis is seen isolated in either of the two upper segments of the lumbar spine before age 45 as often as it is seen in the three lower segments simultaneously after age 45 (Tables 7, 10). It may be of interest to compare the frequency of this phenomenon, 38 per cent, with the frequency of 30 per cent Kellgren and Lawrence (1958) reported for osteoarthritis in the lumbar spine found at X-ray examination of 368 subjects between 55 and 64 years of age. Considering that these workers recorded roentgenologically demonstrable osteoarthritis, osteoarthritis localized to one of the three lower segments of the lumbar spine should have had fairly good chances of remaining undetected owing to the difficulty of visualizing the synovial joints in all segments simultaneously without overlapping. When allowance is made for this fact, the frequency of osteoarthritis found in the present investigation would seem to fall within the range of variation of the frequency of roentgenologically demonstrable osteoarthritis of the lumbar synovial joints.

The comparison made between the vertebral body joints and the synovial joints in the present series of lumbar spines demonstrates that disc degeneration dominates the morphological changes in the 20—45 years age group (Table 15). At higher ages both osteoarthritis and marginal osteophytes are as common as disc degeneration. This agrees with the conclusion that can be drawn by collating previous morphological investigations on the lumbar intervertebral discs (Schmorl, 1931; Hirsch and Schajowicz, 1952; etc.) and on the lumbar synovial joints (Güntz, 1934). Intrasegmentally disc degeneration occurred as an isolated phenomenon unaccompanied by either marginal osteophytes or osteoarthritis only in the 20—45 years age group (Table 14), whilst it invaryably was associated with either or both the latter conditions above age 45. Similar observations are probably responsible for the current view that osteoarthritis of the lumbar synovial joints in most cases is secondary to disc degeneration (Schmorl, 1932; Gantenberg, 1930; Hildebrandt, 1933; Harris and Macnab, 1954). Yet in the present investigation it was a fact that intrasegmentally osteoarthritis occurred unaccompanied by either disc degeneration or marginal osteophytes just as often as isolated

disc degeneration (Table 14), and such isolated osteoarthritis was seen both before and after age 45.

A greater than random intercurrence of osteoarthritis and disc degeneration was seen solely in the L_{2-3} and L_5—S_1 segments (Table 18). Because disc degeration has a much earlier onset than osteoarthritis in the L_5—S_1 segment, this intercurrence could here be accounted for by a tendency of disc degeneration to predispose to osteoarthritis. If so, this would primarily be due to the anatomical relations in the L_5—S_1 segment, where the intervertebral disc differs in shape from the other lumbar discs and the joint facets are comparatively more frontally inclined (Junghanns, 1933). For if the intervertebral disc is degenerated in this segment, these anatomical relations would cause its synovial joints to be exposed to greater stress than the synovial joints in the other lumbar segments. But if the length of time during which disc degeneration exposes the synovial joints to increased functional demands was the sole factor determining whether osteoarthritis would be secondary to disc degeneration, the association between osteoarthritis and disc degeneration should have been positive in the L_{4-5} segment too. For the disc in the latter segment exhibited early degeneration as often as the L_5—S_1 disc (Table 15). Actually, however, there was no positive association between osteoarthritis and disc degeneration in the L_{4-5} segment (Table 18).

The greater than random intercurrence of osteoarthritis and disc degeneration in the L_{2-3} segment is not susceptible to a similar explanation, for the onset of osteoarthritis took place as early as disc degeneration in this segment (Table 15).

Furthermore, osteoarthritis in the L_{4-5} segment was positively correlated to disc degeneration in the L_{3-4} segment. It should be kept in mind, however, that when a large number of correlation coefficients are calculated some of them may happen to become numerically positive although the positiveness has no biologically significant background. Moreover, this writer is convinced that our knowledge of the anatomical and functional relationships of the lumbar spine is so superficial that attempts to interprete associations between different segments would run grave risks of leading to unjustified simplifications. Accordingly, suffice it to state here that osteoarthritis in the L_{4-5} segment exhibited a positive correlation to disc degeneration in the L_{3-4} segment, but this statement makes no pretensions to explain whether or how the two processes are related causally. Therefore, apart from the L_5—S_1 segment, disc degeneration seems to be neither the sole nor the dominant factor predisposing to the onset and development of osteoarthritis of the lumbar synovial joints.

In the present investigation marginal osteophytes on the vertebral bodies seemed to be a condition essentially induced by disc degeneration inter-

acting with ageing (Tables 14, 15, 16), which is in good agreement with opinions expressed by previous authors (Schmorl, 1931, Hildebrandt, 1933; Severin, 1943). Intrasegmentally, moreover, there was a greater than random intercurrence of marginal osteophytes and osteoarthritis (Table 17). Similarly, in the series of mediaeval skeletons studied by Ingelmark (1956, 1959) there was also a positive correlation between changes on the vertebral bodies and changes in the synovial joints. This might equally well be due to interdependence of marginal osteophytes and osteoarthritis or to both these conditions having a common predisposing factor. In the latter case disc degeneration might be considered in the first place. However the present investigation no more than previous morphological studies justifies any attempts to interprete such complex fuctional interactions in the lumbar spine.

CHAPTER 8

Summary

The relevant literature is surveyed. It appears that comparatively little is known about the micromorphology of the lumbar synovial joints in osteoarthritis. Nor do we fully understand the age, sex and intraspinal distribution of lumbar osteoarthritis or its association with other lumbar abnormalities. Hence the present investigation was designed.

This investigation was carried out on a series of 104 lumbar spines from autopsy cases of both sexes — 18 below and 86 over 20 years of age. The specimens were examined grossly and at X-ray. The synovial joints were also examined in the light microscope after sectioning and staining, any morphological changes encountered being graded according to a coding system. Gross disc changes in nucleus pulposus and annulus fibrosus and marginal osteophytes on the vertebral bodies were similarly graded. All the observations were subsequentely subjected to statistical analysis.

The results revealed that all morphological changes in the synovial joints were compatible with the known picture of osteoarthritis in the extremital joints. Thus the lumbar synovial joints as well exhibited a mixture of degenerative and restorative processes: cartilage necrosis and defects in the subchondral bone plate with remodelling of the plate and osteophyte formation in the capsular attachments constituted the most conspicuous and advanced varieties of these processes.

The frequency and degree of osteoarthritic changes in the lumbar synovial joints increased with age equally in both sexes. Before age 45 only minor chondral changes such as cell proliferation, intercellular substance fibrillation and hypertrophy of the calcified zone were the common features in the morphological picture. After that age more advanced chondral changes such as necrosis and substance losses as well as subchondral manifestations like sclerosis, cystic formations with connective tissue proliferation and osteophytes became rather common phenomena. The mean frequency per lumbar spine of joint facets with such extensive chondral and subchondral changes after age 45 amounted to 34.7 ± 8.2 per cent and 13.4 ± 4.4 per cent respectively.

Occasionally the inferior and superior facets of the same synovial joint

exhibited marked differences in the degree of osteoarthritic changes regardless of level in the lumbar spine. But within age groups there were no systematic differences between facets. Both chondral and subchondral osteoarthritic changes exhibited intersegmental differences in degree — the lower segments of the lumbar spine more often were affected with necrosis and substance losses of the cartilage as well as extensive subchondral sclerosis with connective tissue proliferation and osteophytes than the two upper segments.

Manifest osteoarthritis of the synovial joints was considered present in any segment where at least one joint facet exhibited extensive chondral changes coexistent with conspicuous subchondral changes. With this delimitation of the microscopically observed osteoarthritic changes lumbar synovial osteoarthritis was seen in the age group 26—45 years with a segmental frequency of at most about 15 per cent. This initial incidence of osteoarthritis tended to occur in the two upper lumbar segments. After age 45 about 30 per cent of the examined spines exhibited osteoarthritis in these segments, while in the lower lumbar segments this was the case in about 60 per cent. For about 50 per cent of the examined lumbar spines above age 45 osteoarthritis occured in three or more segments simultaneously.

Intrasegmentally regardless of age osteoarthritis occasionally occured unaccompanied by either disc degeneration or marginal vertebral osteophytes. Disc degeneration considered as gross changes of nucleus pulposus and annulus fibrosus was seen as the sole pathological change in a lumbar segment only in the 20—45 years age group. Up to age 45 disc degeneration dominated the segmental frequency of morphological abnormalities. Thus in the L_{4-5} and L_5—S_1 segments about 35 per cent of the examined spines exhibited disc degeneration, while only a few cases showed synovial osteoarthritis and/or marginal vertebral osteophytes. After 45 years of age both synovial osteoarthritis and marginal vertebral osteophytes were as common as disc degeneration with segmental frequencies of at most about 60 per cent.

While positive intrasegmental correlations occured between synovial osteoarthritis and marginal vertebral osteophytes in all segments of the lumbar spine this was the case for synovial osteoarthritis and disc degeneration only in the L_{2-3} and L_5—S_1 segments.

The present investigation shows that one must take into account the lumbar synovial joints in any discussion on morphological basis of low back pain, especially after age 45. For the past two or three decades there has been a tendency to concentrate upon the role of the morphology of disc degeneration and marginal osteophytes in studies of the aetiology of lumbar pain with and without radiation. This is understandable in view

of the relative ease of X-ray detection of disc and marginal osteophyte changes, but it has obscured the importance of the synovial joints. In the light of the present investigation, it is evident that more emphasis should be placed on the radiologic diagnosis of osteoarthritic changes in the lumbar synovial joints. Moreover attempts should be made to define specific clinical entities that can be attributed to osteoarthritic changes in the lumbar synovial joints.

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Gothenburg, August 1964

Thord Lewin

TABLE

APPENDIX

TABLE 20.

Mean segmental scores and confidence limits for osteoarthritic changes of lumbar spines within age group (cf. Figs. 21–25).

A:a. Cell pattern

Segments	N	M	$\Sigma(X-\overline{X})^2$	$\pm t \cdot S_{\overline{X}}$	Max.	Min.	N	M	$\Sigma(X-\overline{X})^2$	$\pm t \cdot S_{\overline{X}}$	Max.	Min.
	Age 20–25 years						Age 46–55 years					
L_{1-2}	7	1.71	11.43	±1.28	4	0	17	3.41	39.50	±0.81	6	0
L_{2-3}	9	1,89	24.89	±1.36	4	0	17	3.88	51.86	±0.30	5	0
L_{3-4}	9	2.00	32.00	±1.54	4	0	17	4.24	25.10	±0.65	6	2
L_{4-5}	9	2.22	27.5	±1.43	4	0	17	4.29	61.50	±1.09	8	0
L_5-S_1	8	2.00	24.00	±1.55	4	0	16	4.13	59.5	±1.06	8	1
	Age 26–35 years						Age 56–65 years					
L_{1-2}	13	2.23	11.00	±1.92	6	0	13	2.62	27.10	±0.91	4	0
L_{2-3}	15	1.35	53.20	±1.60	4	0	13	3.46	29.20	±0.94	6	0
L_{3-4}	15	2.80	44.40	±0.97	5	0	13	3.92	40.90	±1.16	8	0
L_{4-5}	14	3.14	12.32	±0.58	4	2	11	4.18	19.60	±0.94	8	2
L_5-S_1	14	2.71	36.85	±0.97	4	0	11	3.82	33.60	±1.23	6	1
	Age 36–45 years						Age > 65 years					
L_{1-2}	14	2.71	36.85	±0.97	4	0	9	4.78	59.6	±2.11	8	0
L_{2-3}	14	3.21	28.36	±0.85	6	0	7	5.71	19.40	±1.44	8	4
L_{3-4}	12	2.83	27.61	±1.07	4	0	9	5.89	20.90	±1.25	8	4
L_{4-5}	15	2.73	36.90	±0.91	4	0	8	5.56	14.00	±1.19	6	4
L_5-S_1	14	2.86	29.70	±0.87	4	0	9	5.33	40.00	±1.72	8	2

Maximum segmental score = 8 (cf. p. 30)

Table 20. (Cont.)

A:b. Intercellular substance

Segments	N	M	$\sum (X-\bar{X})^2 \pm t \cdot S_{\bar{X}}$		Max.	Min.	N	M	$\sum (X-\bar{X})^2 \pm t \cdot S_{\bar{X}}$		Max.	Min.
	Age 20–25 years						Age 46–55 years					
L_{1-2}	7	2.00	18.00	±1.60	4	0	17	3.88	13.76	±0.48	6	2
L_{2-3}	9	2.11	21.9	±1.27	4	0	17	4.41	18.10	±0.55	8	4
L_{3-4}	9	2.56	45.6	±1.84	4	0	17	4.65	41.90	±0.83	8	4
L_{4-5}	9	2.89	16.90	±1.12	4	0	17	4.12	35.60	±0.78	8	2
L_5-S_1	8	3.25	57.50	±2.40	4	0	16	4.06	64.90	±1.11	8	1
	Age 26–35 years						Age 56–65 years					
L_{1-2}	13	3.92	30.90	±0.97	6	2	13	3.69	22.77	±0.83	6	2
L_{2-3}	15	3.47	21.7	±0.69	5	0	13	4.31	22.77	±0.83	6	2
L_{3-4}	15	3.20	30.6	±0.82	5	0	13	4,54	41.20	±1.12	8	2
L_{4-5}	14	3.43	19.4	±0.71	4	0	11	5.27	42.20	±1.38	8	2
L_5-S_1	14	3.57	11.43	±0.55	5	2	11	4.18	57.60	±1.61	8	1
	Age 36–45 years						Age > 65 years					
L_{1-2}	14	2.57	37.43	±0.98	4	0	9	4.56	33.9	±1.58	8	2
L_{2-3}	14	3.50	25.50	±0.81	5	1	7	5.43	15.70	±1.50	8	4
L_{3-4}	12	3.25	18.25	±0.82	4	0	9	6.56	22.2	±1.28	8	4
L_{4-5}	15	3.53	9.75	±0.46	4	2	8	7.00	10.00	±1.00	8	5
L_5-S_1	14	3.43	11.40	±0.54	4	2	9	5.56	38.20	±1.60	8	2

B. Calcified layer

Segments	N	M	$\sum (X-\bar{X})^2 \pm t \cdot S_{\bar{X}}$		Max.	Min.	N	M	$\sum (X-\bar{X})^2 \pm t \cdot S_{\bar{X}}$		Max.	Min.
	Age 20–25 years						Age 46–55 years					
L_{1-2}	7	0	0		0	0	17	2.24	53.10	±0.94	4	0
L_{2-3}	9	0	0		0	0	17	2.88	89.80	±1.22	8	0
L_{3-4}	9	0	0		0	0	17	2.35	35.90	±0.77	6	0
L_{4-5}	9	0.22	0.99	±0.27	2	0	17	1.82	34.50	±0.76	4	0
L_5-S_1	8	0.80	14.00	±1.19	4	0	16	2.50	58.00	±1.05	6	0
	Age 26–35 years						Age 56–65 years					
L_{1-2}	13	0.85	11.70	±0.60	2	0	13	2.77	60.30	±1.36	8	0
L_{2-3}	15	0.80	30.80	±0.82	4	0	13	3.23	52.30	±1.26	8	0
L_{3-4}	15	1.00	53.00	±1.08	6	0	13	3.54	17.30	±0.73	4	0
L_{4-5}	14	0.79	11.36	±0.54	3	0	11	3.45	16.73	±0.87	4	0
L_5-S_1	14	2.00	38.00	±0.99	4	0	11	3.09	24.90	±1.06	4	0
	Age 36–45 years						Age > 65 years					
L_{1-2}	15	1.27	44.90	±0.99	4	0	9	3.22	45.20	±1.06	6	1
L_{2-3}	15	1.27	36.90	±0.90	4	0	7	4.00	56.00	±2.83	8	0
L_{3-4}	13	1.85	32.70	±1.00	4	0	9	4.00	40.00	±1.72	8	0
L_{4-5}	16	1.69	33.40	±0.79	4	0	8	4.50	22.00	±1.49	8	2
L_5-S_1	15	1.33	45.30	±1.00	4	0	9	3.56	45.90	±1.85	8	0

Table 20. (Cont.)

C. Subchondral bone

Segments	N	M	$\sum (X-\overline{X})^2 \pm t \cdot s_{\overline{X}}$		Max.	Min.	N	M	$\sum (X-\overline{X})^2 \pm t \cdot S_{\overline{X}}$		Max.	Min.
			Age 20–25 years						Age 46–55 years			
L_{1-2}	7	0	0		0	0	17	2.18	67.42	±1.05	5	0
L_{2-3}	9	0.22	0.996	±0.27	0	0	17	2.24	47.05	±0.88	4	0
L_{3-4}	9	0	0		0	0	17	2.53	34.24	±0.75	4	0
L_{4-5}	9	0	0		0	0	17	2.76	31.06	±0.72	4	0
L_5-S_1	8	0	0		0	0	16	2.81	36.44	±0.83	4	0
			Age 26–35 years						Age 56–65 years			
L_{1-2}	13	0.77	20.31	±0.78	4	0	13	1.77	29.86	±0.95	5	0
L_{2-3}	15	0.67	16.35	±0.60	4	0	13	2.46	41.23	±1.12	4	0
L_{3-4}	15	0.33	7.33	±0.40	4	0	13	2.77	36.31	±1.06	4	0
L_{4-5}	14	1.14	31.71	±0.90	4	0	11	4.09	16.91	±0.87	6	2
L_5-S_1	14	1.14	31.71	±0.90	4	0	11	3.55	16.73	±0.87	5	1
			Age 36–45 years						Age > 65 years			
L_{1-2}	14	0.44	8.32	±0.46	2	0	10	2.40	28.02	±1.00	4	0
L_{2-3}	14	1.79	36.37	±0.97	4	0	8	3.31	23.32	±1.53	4	1
L_{3-4}	12	1.92	28.92	±1.03	4	0	10	4.50	40.50	±1.52	8	2
L_{4-5}	15	1.13	29.63	±0.81	4	0	9	5.11	18.89	±1.18	8	4
L_5-S_1	14	1.43	27.43	±0.84	4	0	10	4.00	32.00	±1.36	8	2

D. Capsular attachment

Segments	N	M	$\sum (X-\overline{X})^2 \pm t \cdot S_{\overline{X}}$		Max.	Min.	N	M	$\sum (X-\overline{X})^2 \pm t \cdot S_{\overline{X}}$		Max.	Min.
			Age 20–25 years						Age 46–55 years			
L_{1-2}	8	0			0	0	17	0.24	3.06	±0.23	1	0
L_{2-3}	9	0			0	0	17	0.76	29.06	±0.69	3	0
L_{3-4}	9	0			0	0	17	1.12	47.76	±0.89	6	0
L_{4-4}	9	0			0	0	17	1.88	33.76	±0.75	4	0
L_5-S_1	8	0			0	0	16	1.13	23.75	±0.67	4	0
			Age 26–35 years						Age 56–65 years			
L_{1-2}	13	0			0	0	13	1.00	60.00	±1.35	8	0
L_{2-3}	15	0.27	8.93	±0.44	1	0	13	1.15	19.70	±0.78	4	0
L_{3-4}	15	1.07	4.93	±0.33	2	0	13	1.62	55.08	±1.30	6	0
L_{4-5}	14	1.00	38.00	±0.99	5	0	11	2.45	46.73	±1.45	6	0
L_5-S_1	14	0.29	4.86	±0.35	2	0	11	1.18	19.63	±0.94	4	0
			Age 36–45 years						Age > 65 years			
L_{1-2}	14	0	0		0	0	9	1.56	19.51	±1.21	4	0
L_{2-3}	14	0.50	9.50	±0.49	2	0	7	2.14	28.84	±2.03	6	0
L_{3-4}	12	0.92	26.92	±0.99	4	0	9	3.44	22.22	±1.28	6	0
L_{4-5}	15	0.73	26.93	±0.77	4	0	8	4.50	30.10	±1.74	6	0
L_5-S_1	14	0.21	4.36	±0.27	2	0	8	1.88	40.88	±2.02	6	0

TABLE 21

Frequency of joint facets with osteoarthritic changes of grades 0, 1 or 2 (cf. p. 27) in separate lumbar spine segments.

A:a. Cell pattern.

Age	20–25			26–35			36–45			46–55			56–65			> 65 years		
Grade	0	1	2	0	1	2	0	1	2	0	1	2	0	1	2	0	1	2
Segments																		
L_{1-2}	14	12	0	21	25	2	12	42	0	9	52	3	10	34	0	3	14	14
L_{2-3}	14	14	0	32	34	0	11	49	2	8	54	7	6	35	5	0	12	14
L_{3-4}	12	20	0	12	40	1	11	36	0	1	59	9	3	39	3	1	13	20
L_{4-5}	14	20	0	6	42	0	20	45	0	2	47	13	2	38	4	0	20	12
$L_{5}-S_{1}$	12	16	0	11	38	0	12	44	0	2	38	13	0	30	6	0	16	16

A:b. Intercellular substance.

Age	20–25			26–35			36–45			46–55			56–65			> 65 years		
Grade	0	1	2	0	1	2	0	1	2	0	1	2	0	1	2	0	1	2
Segments																		
L_{1-2}	12	14	0	3	38	4	12	39	0	0	61	3	0	40	4	0	23	11
L_{2-3}	11	19	0	5	50	1	9	44	3	0	56	8	0	37	9	0	14	12
L_{3-4}	7	23	0	8	44	1	6	37	0	0	48	17	0	37	11	0	9	25
L_{4-5}	6	26	0	2	50	0	3	53	0	0	54	8	0	29	15	0	8	24
$L_{5}-S_{1}$	4	26	0	0	49	1	0	52	0	0	46	12	0	26	10	0	10	18

B. Calcified layer.

Age	20–25			26–35			36–45			46–55			56–65			> 65 years		
Grade	0	1	2	0	1	2	0	1	2	0	1	2	0	1	2	0	1	2
Segments																		
L_{1-2}	26	0	0	37	9	0	34	29	0	28	34	2	17	55	6	5	25	2
L_{2-3}	30	0	0	44	12	0	41	19	0	24	39	6	14	40	14	6	12	8
L_{3-4}	30	0	0	40	13	0	23	24	0	27	33	3	8	66	8	3	20	8
L_{4-5}	32	2	0	39	11	0	34	28	0	31	31	0	8	54	8	2	24	8
$L_{5}-S_{1}$	24	4	0	22	27	0	38	22	0	21	37	6	12	44	10	8	16	8

TABLE 21 (cont.)

C. Subchondral bone.

Age	20–25			26–35			36–45			46–55			56–65			> 65 years		
Grade	0	1	2	0	1	2	0	1	2	0	1	2	0	1	2	0	1	2
Segments																		
L_{1-2}	26	0	0	40	10	0	46	8	0	30	32	3	22	21	1	13	18	1
L_{2-3}	29	2	0	44	10	0	29	29	0	30	38	0	16	28	2	3	23	0
L_{3-4}	32	0	0	45	5	0	24	23	0	23	39	2	12	36	0	0	27	7
L_{4-5}	36	0	0	32	16	0	43	19	0	18	41	3	4	35	5	0	22	10
L_5-S_1	30	0	0	32	14	1	32	24	0	14	37	4	0	31	3	2	24	6

D. Capsular attachment.

Age	20–25			26–35			36–45			46–55			56–65			> 65 years		
Grade	0	1	2	0	1	2	0	1	2	0	1	2	0	1	2	0	1	2
Segments																		
L_{1-2}	26	0	0	41	0	0	51	1	0	56	4	0	34	4	5	19	12	1
L_{2-3}	30	0	0	48	3	1	49	9	0	51	9	2	30	15	0	13	15	2
L_{3-4}	30	0	0	46	3	0	36	11	0	50	10	4	30	16	3	8	19	5
L_{4-5}	32	0	0	34	13	1	48	14	0	30	24	3	24	13	7	5	16	10
L_5-S_1	26	0	0	42	4	0	51	3	0	39	11	3	26	9	2	15	11	2

TABLE 22.

Differences of segmental scores (cf. p. 30) for osteoarthritic changes between age groups. t-values in paranthesis ware not significant at a 5 per cent level. (For number of examined spines see Table 20.)

Age groups compared	26–35/20–25			36–45/20–25			36–45/26–35			46–55/20–25			46–55/26–35		
	Diff.	S.D.	t	Diff.	S.D.	t	Diff.	S.D.	t	Diff.	S.D.	t	Diff.	S.D.	t
							A:a. Cell pattern								
L_{1-2}	0.52	1.12	(0.95)	1.00	1.59	(1.36)	0.48	1.38	(0.84)	1.70	1.52	2.15	0.70	1.62	(1.2)
L_{2-3}	−0.29	1.88	(0.37)	1.32	1.59	(1.94)	1.61	1.74	2.49	2.28	2.14	3.01	0.67	1.66	(1.2)
L_{3-4}	0.80	1.78	(1.07)	0.83	1.77	(1.06)	0.03	1.70	(0.05)	2.24	1.54	3.28	1.44	1.52	2.68
L_{4-5}	0.92	1.32	(1.64)	0.51	1.70	(0.71)	−0.41	1.35	(0.80)	2.07	1.15	4.36	1.15	1.60	(1.99)
L_5-S_1	0.71	1.74	(0.92)	0.86	1.64	(1.18)	0.15	1.60	(0.26)	2.13	1.13	4.35	1.42	1.85	2.09
							A:b. Intercellular substance								
L_{1-2}	1.92	1.64	2.49	0.57	1.71	(0.72)	−1.35	1.66	(2.11)	1.88	1.20	2.66	−0.04	1.26	(0.86)
L_{2-3}	1.36	1.41	4.01	0.94	1.81	(1.19)	0.03	1.11	(0.08)	2.30	1.29	4.32	0.94	1.15	2.30
L_{3-4}	0.64	1.86	(0.81)	1.39	1.50	2.17	0.05	1.40	(0.09)	2.09	1.91	2.65	1.45	1.55	2.64
L_{4-5}	0.18	1.32	(0.37)	0.64	1.11	(1.50)	0.10	1.03	(0.27)	1.23	1.48	(2.01)	0.69	1.38	(1.39)
L_5-S_1	0.32	1.86	(0.38)	0.18	1.87	(0.22)	−0.14	0.94	(0.13)	0.81	2.45	(0.76)	0.49	1.65	(0.83)
							B. Calcified layer								
L_{1-2}	0.85	0.80	2.25	1.27	1.50	(1.85)	0.42	1.47	(0.75)	2.24	1.56	3.14	1.39	1.51	2.49
L_{2-3}	0.80	1.18	(1.60)	1.27	1.30	2.31	0.47	1.56	(0.80)	2.88	1.93	3.63	2.08	2.00	2.86
L_{3-4}	1.00	1.55	(1.53)	1.85	1.28	3.29	0.85	1.82	(1.23)	2.35	1.22	4.60	1.35	1.82	2.10
L_{4-5}	0.57	0.76	(1.75)	1.69	1.20	3.37	0.90	1.26	(1.95)	1.60	1.21	3.20	1.03	1.26	2.27
L_5-S_1	1.50	1.61	(2.10)	0.83	1.65	(1.15)	−0.67	1.76	(1.03)	2.00	1.81	2.55	0.50	1.85	(0.74)

Note: Table 3 and 4 show this information in a simplefied form (cf. p. 63).

Age groups compared	46–55/36–45			56–65/20–25			56–65/26–35			56–65/36–45			56–65/46–55		
	Diff.	S.D.	t	Diff.	S.D.	t	Diff.	S.D.	t	Diff.	S.D.	t	Diff.	S.D.	t
A:a. Cell pattern															
L_{1-2}	0.70	1.62	(1.20)	0.91	1.46	(1.45)	0.39	1.26	(0.79)	−0.09	1.60	(0.15)	−0.79	1.55	(1.36)
L_{2-3}	0.57	1.66	(0.95)	1.57	1.64	(1.32)	1.86	1.78	2.76	0.25	1.66	(0.40)	−0.42	1.70	(0.70)
L_{3-4}	1.41	1.39	2.74	1.92	1.91	2.30	1.12	2.07	(1.19)	1.09	1.73	(1.56)	−0.32	1.55	(0.54)
L_{4-5}	1.56	1.81	2.43	1.96	1.62	2.74	1.04	1.18	2.19	1.32	1.53	2.14	−0.11	1.77	(0.16)
L_5-S_1	1.27	1.79	(1.94)	1.82	1.84	2.13	1.11	1.75	(1.58)	0.96	1.66	(1.43)	−0.31	1.00	(0.77)
A:b. Intercellular substance															
L_{1-2}	1.31	1.33	2.74	1.69	1.49	2.43	−0.23	1.49	(0.33)	1.12	1.55	(1.98)	−0.19	1.14	(0.45)
L_{2-3}	0.91	1.23	2.06	2.20	1.50	3.39	0.84	1.31	(1.70)	0.81	1.39	(1.60)	−0.10	1.20	(0.23)
L_{3-4}	1.40	1.49	2.49	1.98	2.08	2.28	1.34	1.66	2.13	1.29	1.61	2.11	−0.11	1.73	(0.19)
L_{4-5}	0.59	1.23	(1.35)	2.48	1.81	3.03	1.84	1.66	(2.04)	1.74	1.47	2.99	1.15	1.73	(1.71)
L_5-S_1	0.63	1.93	(0.89)	0.93	2.60	(0.78)	0.61	1.42	(0.84)	0.75	1.73	(1.07)	0.12	2.21	(0.14)
B. Calcified layer															
L_{1-2}	0.97	1.81	(1.51)	2.77	1.83	3.14	1.92	1.73	2.83	1.50	2.01	(1.97)	0.53	2.01	(0.68)
L_{2-3}	1.61	2.05	2.20	3.23	1.62	4.62	2.43	1.79	3.60	1.96	1.85	2.79	0.35	2.25	(0.43)
L_{3-4}	0.50	1.57	(0.86)	3.54	0.93	8.78	2.54	1.64	3.99	1.69	1.44	3.09	1.19	1.38	2.34
L_{4-5}	0.13	1.48	(0.81)	3.23	0.99	7.36	2.66	1.63	4.04	1.76	1.43	3.13	1.63	1.40	3.00
L_5-S_1	1.17	1.87	(1.74)	2.59	1.51	3.73	1.09	1.65	(1.64)	1.76	1.29	3.42	0.59	1.82	(0.81)

Age groups compared	> 65/20–25			> 65/26–35			> 65/36–45			> 65/46–55			> 65/56–65		
	Diff.	S.D.	t	Diff.	S.D.	t	Diff.	S.D.	t	Diff.	S.D.	t	Diff.	S.D.	t
A:a. Cell pattern															
L_{1-2}	3.09	2.25	2.73	2.55	1.88	3.14	2.07	2.14	2.24	1.37	2.02	(1.96)	2.16	2.08	2.40
L_{2-3}	3.82	1.78	4.20	4.11	1.91	4.73	2.50	1.58	3.25	1.83	1.80	2.26	2.25	1.64	2.92
L_{3-4}	3.89	1.82	4.50	3.09	1.70	4.36	3.06	1.60	6.50	1.65	1.39	2.89	1.97	1.76	2.59
L_{4-5}	3.34	1.66	4.01	2.42	1.35	4.11	3.03	1.56	3.94	1.27	1.81	(1.64)	1.38	1.41	(2.11)
L_5-S_1	3.33	2.07	3.33	2.62	1.91	3.20	2.47	1.82	3.30	1.20	2.03	(1.44)	1.51	2.02	(1.66)
A:b. Intercellular substance															
L_{1-2}	2.56	1.75	2.64	0.64	1.80	(0.82)	1.99	1.84	2.53	0.68	1.41	(1.16)	0.87	1.68	(1.19)
L_{2-3}	3.32	1.44	4.08	1.96	1.37	3.12	1.93	1.47	2.84	1.02	1.24	(1.83)	1.12	1.46	(1.63)
L_{3-4}	4.00	2.07	4.16	3.36	1.55	5.14	3.31	1.46	5.23	1.91	1.63	2.85	2.02	1.78	2.62
L_{4-5}	4.11	1.34	6.29	3.57	1.21	6.64	3.47	0.97	8.19	2.88	1.41	4.44	1.73	1.94	(1.91)
L_5-S_1	2.31	2.53	(1.89)	1.99	1.54	3.03	2.13	1.54	3.24	1.50	2.04	(1.76)	1.38	2.37	(1.33)
B. Calcified layer															
L_{1-2}	3.22	1.80	3.55	2.37	1.69	3.25	1.95	2.02	2.28	0.98	2.02	(1.18)	0.65	2.30	(0.65)
L_{2-3}	4.00	2.00	3.87	3.20	2.08	3.35	2.73	2.15	2.78	1.12	2.57	(0.99)	0.77	2.45	(0.67)
L_{3-4}	4.00	1.58	5.36	3.00	2.06	3.42	2.15	1.91	2.60	1.65	1.78	2.26	0.46	1.69	(0.65)
L_{4-5}	4.28	1.24	7.07	3.71	1.29	6.48	2.81	1.59	2.77	2.68	1.57	4.02	1.15	1.51	(1.62)
L_5-S_1	3.66	2.00	3.15	1.56	2.00	(1.83)	2.23	2.04	2.59	1.06	2.13	(1.18)	0.47	1.97	(0.54)

Age groups compared	46–55/36–45			56–65/20–25			56–65/26–35			56–65/36–45			56–65/46–55		
	Diff.	S.D.	t	Diff.	S.D.	t	Diff.	S.D.	t	Diff.	S.D.	t	Diff.	S.D.	t
A:a. Cell pattern															
L_{1-2}	0.70	1.62	(1.20)	0.91	1.46	(1.45)	0.39	1.26	(0.79)	−0.09	1.60	(0.15)	−0.79	1.55	(1.36)
L_{2-3}	0.57	1.66	(0.95)	1.57	1.64	(1.32)	1.86	1.78	2.76	0.25	1.66	(0.40)	−0.42	1.70	(0.70)
L_{3-4}	1.41	1.39	2.74	1.92	1.91	2.30	1.12	2.07	(1.19)	1.09	1.73	(1.56)	−0.32	1.55	(0.54)
L_{4-5}	1.56	1.81	2.43	1.96	1.62	2.74	1.04	1.18	2.19	1.32	1.53	2.14	−0.11	1.77	(0.16)
$L_{5}-S_{1}$	1.27	1.79	(1.94)	1.82	1.84	2.13	1.11	1.75	(1.58)	0.96	1.66	(1.43)	−0.31	1.00	(0.77)
A:b. Intercellular substance															
L_{1-2}	1.31	1.33	2.74	1.69	1.49	2.43	−0.23	1.49	(0.33)	1.12	1.55	(1.98)	−0.19	1.14	(0.45)
L_{2-3}	0.91	1.23	2.06	2.20	1.50	3.39	0.84	1.31	(1.70)	0.81	1.39	(1.60)	−0.10	1.20	(0.23)
L_{3-4}	1.40	1.49	2.49	1.98	2.08	2.28	1.34	1.66	2.13	1.29	1.61	2.11	−0.11	1.73	(0.19)
L_{4-5}	0.59	1.23	(1.35)	2.48	1.81	3.03	1.84	1.66	(2.04)	1.74	1.47	2.99	1.15	1.73	(1.71)
$L_{5}-S_{1}$	0.63	1.93	(0.89)	0.93	2.60	(0.78)	0.61	1.42	(0.84)	0.75	1.73	(1.07)	0.12	2.21	(0.14)
B. Calcified layer															
L_{1-2}	0.97	1.81	(1.51)	2.77	1.83	3.14	1.92	1.73	2.83	1.50	2.01	(1.97)	0.53	2.01	(0.68)
L_{2-3}	1.61	2.05	2.20	3.23	1.62	4.62	2.43	1.79	3.60	1.96	1.85	2.79	0.35	2.25	(0.43)
L_{3-4}	0.50	1.57	(0.86)	3.54	0.93	8.78	2.54	1.64	3.99	1.69	1.44	3.09	1.19	1.38	2.34
L_{4-5}	0.13	1.48	(0.81)	3.23	0.99	7.36	2.66	1.63	4.04	1.76	1.43	3.13	1.63	1.40	3.00
$L_{5}-S_{1}$	1.17	1.87	(1.74)	2.59	1.51	3.73	1.09	1.65	(1.64)	1.76	1.29	3.42	0.59	1.82	(0.81)

Age groups compared	> 65/20–25			> 65/26–35			> 65/36–45			> 65/46–55			> 65/56–65		
	Diff.	S.D.	t	Diff.	S.D.	t	Diff.	S.D.	t	Diff.	S.D.	t	Diff.	S.D.	t
A:a. Cell pattern															
L_{1-2}	3.09	2.25	2.73	2.55	1.88	3.14	2.07	2.14	2.24	1.37	2.02	(1.96)	2.16	2.08	2.40
L_{2-3}	3.82	1.78	4.20	4.11	1.91	4.73	2.50	1.58	3.25	1.83	1.80	2.26	2.25	1.64	2.92
L_{3-4}	3.89	1.82	4.50	3.09	1.70	4.36	3.06	1.60	6.50	1.65	1.39	2.89	1.97	1.76	2.59
L_{4-5}	3.34	1.66	4.01	2.42	1.35	4.11	3.03	1.56	3.94	1.27	1.81	(1.64)	1.38	1.41	(2.11)
$L_{5}-S_{1}$	3.33	2.07	3.33	2.62	1.91	3.20	2.47	1.82	3.30	1.20	2.03	(1.44)	1.51	2.02	(1.66)
A:b. Intercellular substance															
L_{1-2}	2.56	1.75	2.64	0.64	1.80	(0.82)	1.99	1.84	2.53	0.68	1.41	(1.16)	0.87	1.68	(1.19)
L_{2-3}	3.32	1.44	4.08	1.96	1.37	3.12	1.93	1.47	2.84	1.02	1.24	(1.83)	1.12	1.46	(1.63)
L_{3-4}	4.00	2.07	4.16	3.36	1.55	5.14	3.31	1.46	5.23	1.91	1.63	2.85	2.02	1.78	2.62
L_{4-5}	4.11	1.34	6.29	3.57	1.21	6.64	3.47	0.97	8.19	2.88	1.41	4.44	1.73	1.94	(1.91)
$L_{5}-S_{1}$	2.31	2.53	(1.89)	1.99	1.54	3.03	2.13	1.54	3.24	1.50	2.04	(1.76)	1.38	2.37	(1.33)
B. Calcified layer															
L_{1-2}	3.22	1.80	3.55	2.37	1.69	3.25	1.95	2.02	2.28	0.98	2.02	(1.18)	0.65	2.30	(0.65)
L_{2-3}	4.00	2.00	3.87	3.20	2.08	3.35	2.73	2.15	2.78	1.12	2.57	(0.99)	0.77	2.45	(0.67)
L_{3-4}	4.00	1.58	5.36	3.00	2.06	3.42	2.15	1.91	2.60	1.65	1.78	2.26	0.46	1.69	(0.65)
L_{4-5}	4.28	1.24	7.07	3.71	1.29	6.48	2.81	1.59	2.77	2.68	1.57	4.02	1.15	1.51	(1.62)
$L_{5}-S_{1}$	3.66	2.00	3.15	1.56	2.00	(1.83)	2.23	2.04	2.59	1.06	2.13	(1.18)	0.47	1.97	(0.54)

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