Hunterian Lecture

[ABRIDGED]

ON

OSTEO-ARTHRITIS:

PATHOLOGY, ÆTIOLOGY, AND PRINCIPLES OF SURGICAL TREATMENT.*

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INTRODUCTORY.

THERE can be no doubt that the condition called by English writers "osteo-arthritis" has afflicted not only mankind, but the lower animals (Figs. 1 and 2), from remote periods in the earth's history. We find its stigmata in the skeletons of prehistoric animals and in human remains of considerable antiquity, for among the bones of ancient Egyptians at the Royal College of Surgeons of England are several exhibiting these changes (Fig. 3). Moreover, we find no race or clime exempt from the disease. The pathological changes are of very great interest and importance from their extraordinary diversity; in one joint we may see the phenomena of repair, inflammation and new growth merging indistinguishably into one another. Moreover, accompanying or following the cellular proliferations are unequivocal signs of degenerations. A striking feature which distinguishes the disease from the more acute and probably infective group of conditions known as "rheumatoid arthritis" is the almost invariable absence of small cell infiltration. There can be little doubt that in osteo-arthritis we are faced

In this paper a section is devoted to some largely experimental observations upon joint physiology, because it was felt that our knowledge concerning the basal principles of the physiology of the joints leaves much to be desired, and it was thought that a study of this might throw some light upon the peculiar pathological features of osteo-arthritis. The grosser anatomical features of the disease have been so carefully described by Adams and others that a description

FIG. 3.

Lower end of femur from an Egyptian of the Seventeenth Dynasty exhibiting osteo-arthritis changes. (Spec. 1186 D., Museum of Royal College of Surgeons of England.)

of these is purposely omitted. The morbid histology of the earlier stages, which appears to have not hitherto received the attention it deserves, has been investigated more fully in order to ascertain what light these earlier changes might throw upon ætiological problems. Symptomatology and treatment

FIG. 1.

Early osteo-arthritis changes in elbow-joint of a rhinoceros.

FIG. 2.

Shoulder-joint of horse (from the Royal Veterinary College) showing marked osteo-arthritis changes.

with a borderland between a frankly inflammatory condition and a neoplasm of the joint structures. The ætiology of osteo-arthritis is up to the present unknown. Research into this subject is urgently needed, not only for scientific treatment of this extremely common, universal, and crippling disease, but that such a line of research may also eventually throw some light upon the pathogenesis of neoplasms.

are given in a summarised form from considerations of space, and will receive more detailed consideration elsewhere. The ætiological observations are of a preliminary nature, as research is being continued into this aspect of the problem.

NOMENCLATURE.

Much of the existing confusion concerning osteo-arthritis can be traced to the fact that many writers have invented descriptive terms for the disease, in which an attempt is made to embody what appears to them to be its principal pathological characteristics. We have already noted how manifold and diverse

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these changes may be. This explains the fact that certain American workers have christened the disease by names which indicate diametrically opposite conditions. Goldthwait, for example, classifies chronic arthritis into (a) infectious arthritis, (b) atrophic arthritis, (c) hypertrophic arthritis. Nichols and Richardson have introduced the terms "proliferative" and "degenerative" arthritis corresponding respectively to the "atrophic" and "hypertrophic" arthritis of Goldthwait or to the "rheumatoid arthritis" and "osteo-arthritis" of English authors.

EXPERIMENTAL AND OTHER OBSERVATIONS UPON THE APPLIED ANATOMY AND PHYSIOLOGY OF ARTICULAR CARTILAGE.

It is a healthy sign that modern physiologists are devoting much attention to the structure and physiology of the individual cells—a movement that must lead to significant revelations. Only by study of the individual cells under abnormal conditions can we hope for a clearer comprehension of disease. The complicated problems connected with the ætiology and pathology of osteo-arthritis are so intimately bound up with the structure and physiology of the articular cartilage that it is essential to have a clear idea of its structure and physiology. My researches into the latter furnish, I venture to believe, the clue to many of the pathological phenomena of osteo-arthritis.

Costal Cartilage.—The periphery is formed by a connective-tissue perichondrium. As these connective-tissue cells are traced towards the deeper parts, the cells become larger, although still of connective-tissue type and not surrounded by any matrix. If traced still further these cells indistinguishably merge with the proper cartilage cells. The latter in the central portion of the cartilage are seen to be large somewhat angular cells occurring in groups of two, three, or four cells.

Repair in Costal Cartilage.—It appears that the fully-formed cartilage cells in the centre have little power of undergoing proliferation and that repair takes place by means of the perichondrium. In a Hunterian Lecture upon loose bodies in joints I demonstrated that in those loose bodies of the traumatic or "classical" type which contained both cartilage and bone, and which have been for some time quite free in the joint cavity, the cartilage cells retain their vitality, whereas the majority of the bone cells die. The marked vitality of the cartilage cell when compared with the bone cell requires emphasis in order to explain many of the phenomena of osteo-arthritis.

Articular Cartilage.—It will, perhaps, avoid confusion if we discuss the structure of articular cartilage under two headings—viz., the central and lateral articular areas.

(a) Central articular area. The superficial stratum is seen to consist of flattened cells arranged in groups which lie parallel to the surface. If the immediate surface is carefully examined it is found to be constituted by a well-defined regular curvilinear margin devoid of any actual cell covering, and evidently formed of matrix. Henle has described a delicate layer of cells (perichondrium) upon the actual free surface, but investigation convinces me that this must be very rare in the normal adult, although it unquestionably exists at an earlier stage of development. A point of importance is that the horizontal group of cells of the superficial stratum show no sign of degeneracy or diminished vitality, but even in the case of the most superficial the nuclei stain well, and there is no indication that they are other than normal and healthy cells. In the intermediate zone the groups of cells are more irregularly disposed, and in the deeper zone the cell groups are arranged vertically. Ogston's main conclusions were that articular cartilage is continually renewing itself from the focus of central growth and grows in two directions; and that it develops in the direction of the joint an effete layer that is worn away by the joint movements. However, examination of normal articular cartilage reveals no

justification for the assumption that it develops towards the joint this effete layer, or that this contributes in any way to the synovial fluid. It seems clear that these superficial cells, far from being degenerate, are the source from which the deeper cells are derived, and that from developmental and other reasons they are analogous to the superficial cells of the lateral portion of the articular cartilage, or to the perichondrial cells of costal cartilage.

(b) Lateral articular area. The lateral portion somewhat closely resembles those varieties of hyaline cartilage which are furnished with a perichondrium, for the surface of the cartilage is covered laterally by a delicate extension of the synovial membrane. When traced centralwards, the connective tissue is reduced to a single layer of close-set endothelial cells; these subsequently produce hyaline matrix, in which they become buried, so that the more central parts of the investing cartilage consist at the free surface of matrix—i.e., cartilaginous. At the edge the articular cartilage becomes markedly fibrillated and merges into the fibrous tissue beyond, which is furnished with capillaries, derived from the circulus, without any marked increase of cellularity accompanying the transition. In the thin synovial layer over the lateral articulating area lie capillaries derived from the circulus articuli vasculosus of William Hunter. This lateral part is, therefore, far better nourished than the central. This fact is of fundamental importance and in my opinion is the key to many of the phenomena of osteo-arthritis; for my theory, as will be seen later, is that the central part of the articular cartilage responds to the cause of osteo-arthritis by degeneration, whereas the lateral part proliferates, owing to its richer nutrient supply.

Development of Articular Cartilage.—This difference in structure of the central and lateral portions of the articular cartilage is capable of an explanation on developmental grounds. Towards the termination of the second month of intra-uterine life, the joint cavities have appeared—a split occurring in the mesenchymatous tissue, which usually commences laterally. At the fourth month, the surface of the joint cartilage is still covered by this layer of connective tissue. This is the stage normally found throughout life in certain birds—notably the ostrich. With the increasing movements of the child before birth the perichondrial layer *gradually recedes* from the more central parts of the articular surface, but at birth it still strays for a little way over its edge. Microscopically, however, the connective-tissue layer can be traced beyond the naked-eye delimitation. Shortly after the child begins to walk the extension of the synovial membrane over the lateral margin of the articular cartilage makes a further slight regression but soon assumes its permanent relationship. No perichondrium is present over the more central part, yet there can be no doubt from a study of their structure, staining reactions, and of their development and comparative anatomy that these cells have the same function as the perichondrial cells of the lateral part of the articular cartilage and are the parent cells of the more fully developed cartilage cells in the deeper parts.

Nutrition of Articular Cartilage.

Concerning this question of fundamental importance there has been hitherto a grave lack in our knowledge. In a paper entitled "Of the Structure and Diseases of Articular Cartilages" (Phil. Soc. Trans., Vol. XLII., 742–43), William Hunter first described the circulus articuli vasculus lying near the margin of the articular cartilage, and in younger subjects sending off shoots on to the articular surface as follows:—

"The distribution of the blood-vessels to the articulating cartilages is very peculiar, and seems calculated for obviating great inconvenience. Had they run on the outer surface, the pressure and motion of the two cartilages must infallibly have occasioned frequent obstructions, inflammations, &c., which would soon have rendered out motions painful, and at last entirely deprived us of them. But by creeping round the cartilaginous brim, where there is little friction, or under the cartilage, where there is none, they are perfectly well defended from such accidents."

The outstanding fact remains that Hunter believed that the circulus plays an important part in the nutrition of articular cartilage. From the developmental point of view and from that of comparative anatomy, the extent to which the minute branches of the circulus penetrate over the articular cartilage depends upon the degree of extension of the synovial membrane over its surface.

Fig. 4 shows the circulus articuli vasculosus in the knee-joint of an ostrich and was probably injected by William Hunter himself nearly 200 years ago. The minute injected vessels stray for a short distance at

FIG. 4.

Showing the injected circulus articuli vasculosus in the knee-joint of an ostrich (Hunterian). (Specimen B 171, Museum Royal College of Surgeons of England.)

certain spots over the surface of the articular cartilage. Toynbee came to the conclusion that the principle source of nutrition of adult articular cartilage consisted in the lymph exuded from the large and convoluted vessels lying beneath it in the cancellous spaces. There has recently been an attempt to attribute an important part in the nourishment of articular cartilage to the synovial fluid. An argument in favour of this view is the continued growth while free in the joint of loose bodies of the "classical" type. However, a loose body usually acts as an irritant and causes a greater or lesser degree of synovitis with an outpouring of fluid rich in albumin, which cannot in any sense of the word be designated "normal" synovial fluid. My analyses reveal such a low protein content in the normal fluid that it can hardly play more than a small part in nourishing the articular cartilage.

My own conclusions are that the deeper stratum of the articular cartilage is largely nourished in the manner described by Toynbee, that the superficial stratum of the central articular area is nourished by the synovial fluid, and that the remainder of the articular cartilage receives its nutrient supply from the circulus articuli vasculosus. It will be seen that in the infective and toxic types this arterial circle is an important medium by which toxins attack the joint.

The sub-articular bony lamella cannot be said to form an impenetrable barrier, since after an injection of carmine and gelatin the colour readily permeates

this zone. Neither can the calcified zone of the articular cartilage be said to form a serious barrier. The question next arises, how does the nutrient fluid gain access to the cartilage cells? No definite lymphatics with an endothelial lining have ever been demonstrated in articular cartilage. Prof. Shattock has recently discovered that if cartilage is stained by carbol-thionin which stains mucin pink, the zone of

FIG. 5.

Osteo-arthritis of knee-joint. Earlier changes in articular cartilage and synovial membrane.

matrix immediately surrounding the cell groups is stained pink, and is evidently the most recently formed and more mucinous part. In a well-stained section it will be seen that the pink zones branch and intercommunicate. In the superficial part of the articular cartilage the meshwork is horizontal; in the middle zone more irregular; and in the deeper zone the meshes lie vertically.

My theory, which I believe is now put forward for the first time, is that the articular cartilage receives its nourishment from plasma that percolates along the meshwork formed by this more mucinous part of the cartilage matrix which surrounds the cell groups, and the pathological changes seen in the infective and toxic group including the "senile," strongly suggest that the toxic substances percolate along these same nutrient paths.

Repair in Articular Cartilage.

The phenomena of repair in articular cartilage throw considerable light upon osteo-arthritis, especially the traumatic type. Redfern, who performed a large number of experiments upon animals to investigate the mode of repair in articular cartilage, concluded that incisions experimentally made remained open for *long periods*, and that when repair took place eventually the bond of union was formed of connective tissue derived from the cartilage cells at the margin of the incision. There was no actual formation of new cartilage cells. He also found that incisions in the lateral portions of the

articular cartilage healed sooner than those in the central parts. I have repeated certain of Redfern's experiments, and also performed others which appear not only to confirm the views concerning the nutrition of articular cartilage enunciated above, but also to afford some explanation of the osteophytic developments which are such a marked feature of osteo-arthritis.

EXPERIMENT 1.—Right knee-joint of rabbit opened from inner side. Small portion of articular cartilage, with a portion of the subjacent bone chiselled off—the portion involving the inner lip of the trochlear surface of femur and portion of the internal femoral condyle. The subsequent changes in this traumatic loose body I have described elsewhere. The animal was killed 22 weeks later, and the articular surface of the femur whence the small fragment had been detached was seen to be smoothly healed over and covered by a white and glistening substance. Microscopical examination revealed the following: The reparative tissue consists of well-formed cartilage covered superficially by a clearly-defined layer of connective tissue. Some of this cartilage is probably of the nature of cartilaginous callus, and appears to be derived from the connective-tissue cells of the cancellous spaces exposed by the trauma. The more superficial cartilage cells are formed from the connective tissue on the surface, but it is quite clear that much of the cartilage is derived from the deeper layer of the articular cartilage, which can be seen actively proliferating.

This experiment demonstrates that *the lateral part of the articular cartilage is capable of a certain amount of repair by formation of new cartilage* and this phenomenon can be explained on anatomical and physiological grounds, for we have already shown how the lateral part of the articular cartilage receives far better nourishment in the central parts, and, moreover, is furnished with a perichondrium.

EXPERIMENT 7.—Right knee-joint of a rabbit opened and the articular cartilage of the trochlear surface of femur longitudinally divided (a) in the centre, (b) near lateral edge. One month later the rabbit was killed and the portion of the trochlear surface examined microscopically. There is little, if any, proliferation at the sides of the central incision, but on either side of the lateral incision is a well-marked proliferation of cartilage cells. This experiment again demonstrates the greater vitality of the lateral portions of articular cartilage.

EXPERIMENT 5. Experimental production of traumatic osteo-arthritis.—Right knee-joint of rabbit. The central part of the articular cartilage covering the trochlear surface of the femur and patellar articular surface was pared away down to the calcified zone and the joint closed. After a few days the animal exhibited no limp or any sign of disability. Six weeks later it was killed. Microscopical examination of a transverse section of the trochlear surface is of considerable interest. There is no sign of repair of the pared surface—indeed, it has undergone necrosis. The contrast between the necrotic central parts and the lateral portion which extends for some distance over the central portion is very marked. The most interesting feature is that the cartilage of the lateral part *is in process of active proliferation*. The explanation of this occurrence undoubtedly is that the central part, owing to its poorer nutrition, is incapable of repair, and that proliferation of the lateral part must be regarded as compensatory.

EXPERIMENT 19. Traumatic osteo-arthritis experimentally produced by the action of radium. Rabbit K.—Tube containing 0.150 mgm. radium kindly lent to me by Prof. Lazarus-Barlow, was fixed against the inner border of the internal condyle near its junction with the trochlea. Four weeks later the articular cartilage at this spot is seen to have undergone well-marked proliferation, and below and internal to this zone is an area of degeneration. This experiment shows, moreover, the important influence that the vascularity of the tissues bears upon the action of radium.

The Effects of Lack of Cartilaginous Apposition and of Prolonged Cartilaginous Apposition upon Articular Cartilage.

EXPERIMENT 13.—The knee of a rabbit was fully flexed and immobilised by a staple driven on either side into the lower end of femur and upper end of tibia—the joint not being opened. A plaster bandage was applied to complete immobilisation. Rabbit killed six weeks later and post-mortem performed. The staples had become loose and there was a considerable amount of new periosteal bone formed in the vicinity of holes in femur and tibia. No intra-articular adhesions between the cartilaginous surfaces were present, and the latter were everywhere normal, save over the trochlear surface of the femur, which, owing to full

flexion of the joint, had not been in contact with a cartilaginous surface. Here the cartilage had disappeared. Full extension was prevented by scarring of the joint capsule.

EXPERIMENT 11.—The patella was completely dislocated to outer side of joint. After death 10 weeks later the articular cartilage of the patella and trochlear surface had almost entirely disappeared evidently owing to lack of cartilaginous apposition. Articular cartilage elsewhere normal. No compensatory formations had as yet occurred at the margin.

These and similar experiments have an important bearing upon the pathology of osteo-arthritis, as they show that although, in all probability, mere immobility of a joint, provided it be healthy and that cartilaginous surfaces be in apposition, causes no degenerative changes in the latter, yet lack of cartilaginous apposition usually causes the articular cartilage to undergo transformation into a connective tissue. Redfern found that the articular cartilage also underwent this change after experimental amputations through joints. It is clear that this change may occur in the human subject after amputation.

Physiological Effects of Trauma upon Articular Cartilages.

Experiments were performed, of which the following is an example, to ascertain whether an isolated series of traumata was in itself sufficient to produce changes in the articular cartilages.

EXPERIMENT 12.—Rabbit was anaesthetised, the knee flexed to bring the patella in contact with the trochlear surface of the femur, and the joint covered with a cloth; a series of rapid blows were applied to the patella with a hammer so that both it and the femur were subjected to repeated percussion for about two minutes. Five weeks later the rabbit was killed and the articular surfaces were found to be perfectly normal and free from fibrillation.

This experiment should be compared with experiment 16, described later, where a suspension of *Streptococcus salivarius*, isolated from a case of pyorrhoea, was injected after percussion of a joint.

PATHOLOGY.

A. Changes in the Articular Cartilage.

(a) *Central Part of the Articulating Area.*—Although not quite the earliest observable change, the most striking early departure from the normal consists in the well-known "fibrillation" (see Fig. 5) of the central area of the articular cartilage. The poorer nutrition of the central area already referred to appears to be at least as important a factor in its earlier involvement as the greater pressure to which it is normally subjected. In the knee-joint the articular surface of the patella and trochlear surface of the femur are, in my experience, almost invariably first affected. The term "fibrillation" is somewhat misleading, as I am unable to agree that the change consists in the formation of true connective tissue fibres, but find that in the cases examined by me there is a splitting of the matrix without fibrous metaplasia. Careful examination in early cases will often reveal that the first fibrils formed lie horizontally, and in their length occasionally far exceed the normal thickness of articular cartilage. The staining by mucicarmine of normal cartilage reveals the reason for this disposition, since the more collagenous portions of the matrix lie superficially in horizontal strata, but are vertically disposed in the deeper portion. When vertically fractured articular cartilage shows the same vertical striæ, and my theory is that the fibrillation in osteo-arthritis is due to the persistence of the strata of more collagenous matrix. In certain cases I have observed cystic degeneration of the articular cartilage.

Epi-articular Ecchondroses.—Not infrequently the surface of the articular cartilage is rendered irregular by smooth rounded elevations due to the invasion of the deeper layers of the cartilage by vascular inroads of osteoblasts actively forming new bone, the cartilage cells simultaneously proliferating. Prof. Shattock named these nodular formations "epi-articular ecchondroses" to distinguish them from the "peri-articular

ecchondroses" at the articular edges. As the changes progress, the cartilage gradually disappears from the central articular area revealing the subjacent bone—the changes in which will be shortly described below.

(b) *Lateral Part of the Articulating Area.*—The important differences not only in structure but in mode of nutrition between the lateral and central portions to which we have already referred, explain the marked difference in the reaction of these parts

FIG. 6.

Advanced osteo-arthritic changes in knee-joint.

to the cause of osteo-arthritis. The well-known "lipping" of the articular margins, in my experience, always succeeds the degenerative changes in the central areas. It is clear that the newly formed cartilage is largely formed by the synovial perichondrium, since, when traced from the surface towards the deeper parts, all the gradations from the connective tissue cells of this perichondrium to fully formed cartilage cells may be seen. The theory of Cornil and Ranvier, which figures so largely in textbooks, that the perichondrium merely prevents the proliferating cartilage cells from escaping into the joint, is not confirmed by my observations.

CASE 24.—Some of the principal microscopic features of a chondro-osteophyte are exemplified by the following description of these formations at two different spots from the knee-joint of Case 24 (personal series).

(a) Section (not figured) through a portion of the posterior aspect of the internal femoral condyle, including a small recurved osteophyte. The bone is of open texture containing fatty marrow covered with cartilage, in the deeper part of which there is an irregular violet zone of calcification. Near this zone there are a certain number of protrusions of cellular connective tissue, some of which also occur into the cartilage of the osteophyte itself, and others towards the articulating area of the cartilage (early epi-articular formations.) The osteogenetic processes of connective tissue are

richly provided with cells, and in the case of one its continuity with the bone-marrow through a constricted neck was readily traceable; the marrow immediately beyond the neck on the side of the shaft is well-formed adipose tissue, and in the neck itself the connective tissue is being converted into fat. The general articular cartilage shows a certain amount of horizontal fibrillation at the free surface and a little proliferation of cartilage cells.

(b) Another portion of articular surface, including the lipped margin, reveals the same general appearances as in the last described. However, at one spot near the base of the osteophyte there is on the deep side of the articular cartilage a triangular focus of vascular connective tissue. The tissue is lax in character, well furnished with nuclei, and merges at its base into the super-adjacent cartilage, from which it is clearly derived by a process of metaplasia. Sections of synovial membrane from immediate vicinity of articular edge show perfectly normal structure, with no sclerosis or thrombosis of capillaries or arterioles. The villi are abnormally voluminous, the investing cells intact and devoid of any small-celled infiltration, either polymorphonuclear or lymphocytic. The vessels in the sub-synovial fat are quite normal in structure and patulous.

Although the above is the usual mode of formation of a chondro-osteophyte, occasionally a development of cartilage in a synovial fold may become superimposed upon the lateral portion of the articular cartilage with which it fuses. In rare cases the articular cartilage may be buried beneath a layer of newly formed bone formed in this manner. Although at first formed of cartilage only, the chondrophyte is invaded by osteoblasts, so that the cartilage is reduced to a thin layer on the surface. This eventually undergoes similar degenerative changes and may disappear, and the subjacent bone become eburnated, showing that the formations actually in many cases extend the articular surface, and are to a certain extent compensatory formations. In some cases the under surface of an osteophyte presents supporting buttresses resembling those in the roof of a Gothic cathedral. The part played by these buttresses is clear when we remember that the cancellous spaces of an osteophyte are of extremely open and rarefied texture, and the contents largely adipose tissue. Beyond the articulating surface of a chondro-osteophyte the new formation is usually recurved, so that at first the movements of the joint remain comparatively unimpaired. Impairment of movement by osteophytes is often due to the fact that the joint has not been regularly put through its full range of movement.

Purposive Chondro-osteophytic Formations.—In very many cases, although the production of osteophytes is excessive, and may interfere with movement, or cause pain by pressure upon adjacent structures, we are often able to see evidence of definite purpose underlying these formations. The response of the central area of the articular cartilage to the cause of osteo-arthritis is by degeneration, whereas the better nourished lateral part proliferates. The latter may be regarded as Nature's effort to make good the loss of the central portions. An excellent example of this is seen in the changes that the femoral head undergoes. The successive changes are exemplified by three different specimens from Guy's Hospital Pathological Museum. The first shows the head of the femur surrounded to an equal extent on all sides by an osteophytic outgrowth; the second shows the upper part of the head flattened from pressure atrophy, the lower part of the osteophytic ring having undergone compensatory enlargement; and in the third specimen the lower part of the osteophytic development now forms a smooth articulating surface continuous with the remnant of the femoral head. The actual angle formed by the neck with the shaft remains unaltered.

Chondro-osteophytes in Rheumatoid Arthritis.—Although we occasionally see cases presenting anomalous features and association of the two conditions, yet typical cases of osteo-arthritis and rheumatoid arthritis present definite clinical and pathological features. The typical case of rheumatoid arthritis presents the picture of a subacute, non-suppurative arthritis similar to certain forms of arthritis of known infective origin, such as gonorrhoeal. The first and most marked inflammatory changes occur in the

synovial membrane and capsular structures, giving rise to the typical "spindle-shaped" swelling of the joint. A very important distinguishing factor lies in the fact that rheumatoid arthritis is associated with a far greater amount of protective muscular spasm; this leads to limitation of joint movement, and as a result there is nothing to prevent the pannus of granulative tissue from the synovial membrane extending over the surface of the articular cartilage, and often leading to the disappearance of the latter. The ultimate result is therefore in most cases ankylosis between joint surfaces which may be partial, complete, fibrous, cartilaginous, or bony. In certain cases where ankylosis has been prevented I have observed the formation of true compensatory chondro-osteophytes at those situations where the lateral portion of the articular cartilage has not been destroyed by the synovial pannus. These may exactly resemble those occurring in osteo-arthritis, and, indeed, it may be said that osteo-arthritis has supervened upon rheumatoid arthritis.

Changes in the Original Bone in Osteo-arthritis (Fig. 6).—If vertical sections be made through the articular end at different stages, I have observed that before the subarticular lamella of bone is actually exposed it has already begun to undergo sclerosis; the increased thickness of this bony layer beneath a patch of degenerate cartilage may be very striking. This remarkable change is evidently compensatory, since the bone is deprived of its normal protection. The invasion of the peri- and epi-articular ecchondroses by outgrowths from the bone has been referred to above. The eburnation that occurs in the late stages is well shown in the figure.

CASE 27.—A section through the patella shows the most peripheral part of the cartilage still of normal thickness, and the artificial "flaking" due to the detachment of the flat-celled layer at the surface—the cells being still living. More centrally there is a second vertical splitting in the cartilage; the cell nuclei retain their stain and there is no obvious formation of fibre. Still more centrally the cartilage becomes thinner, the cells remaining healthy, till it disappears after breaking up into irregular fragments. The exposed articulating area here consists of very dense bone obviously due to sclerosis of the normal cancellous tissue. For a short way the osseous trabeculae continued from the sclerotic layer are thickened. At one spot immediately below the sclerotic zone there is a microscopic island of hyaline cartilage, having in its centre a small pseudo-cyst resulting from liquefaction—the matrix containing here no cell nuclei. Where the cartilage is wanting, or its remnants quite detached, the sclerotic bone beneath presents a certain number of areas extending from the calcified zone, and distinguished from the proper osseous substance by their staining of a faint violet colour and being quite homogeneous in structure—the proper bone being stained red with the eosin. This homogeneous material in certain spots is intimately mixed with the laminated structure of the bone, suggesting that it has arisen by a process of degeneration occurring in the latter. The cells in the degenerate areas are unstained or stained very faintly. Here and there the more superficial parts of the degenerate tissue contains groups of cells apparently cartilaginous. Slightly below one of the extensions of degenerate tissue is the small nodule of cartilage already described.

If this small cartilaginous focus be examined under a higher power the degenerate and more faintly staining osseous tissue may be seen above and to the right, and it is clear that the cartilage cells have arisen by a process of metaplasia from the bone corpuscles, and that in a similar manner the cartilaginous matrix has arisen from the bony matrix. The cause of the degeneration still continuing to act, the cartilage itself is undergoing degeneration in the centre. The presence of cysts in the articular cartilage has already been noted; the synovial chondromata may also undergo cystic degeneration. We thus see that there are at least three topographical varieties of cyst in osteo-arthritis. There is no evidence at present that cysts of the semilunar cartilages may own the same pathogenesis.

Changes in the Synovial Membrane.

In a very large proportion of cases the first naked-eye appearance of the disease occurs in the central area of the articular cartilage, and the synovial membrane very rarely shows any obvious changes until the first sign of "lipping" appears, when thickening of the membrane at these spots and

enlargement of existing—with formation of new—villous processes will be found. These changes may be quite localised in the early stages. When examined during life at operation the affected portion of the synovial membrane appears unduly vascular. Microscopical examination of the membrane in all save the very advanced cases shows general hyperplasia affecting all its elements, the membrane and the newly formed villi being well supplied with blood-vessels, and the arterioles and capillaries perfectly patent, with no signs of arterio-sclerosis. Specimens injected with carmine and gelatin demonstrate well that the membrane is not in a state of diminished vascularity.

In certain cases, as is well known, the enlarged villi become the seats of a formation of adipose tissue (lipoma arborescens of Müller). A further remarkable change is the formation of nodules of cartilage in the synovial villi. I have discussed these interesting tumours elsewhere, and have named them "synovial chondromata." In the later stages of osteo-arthritis the hypertrophied synovial villi undergo secondary changes and the membrane becomes comparatively smooth and atrophic. In this late stage arterio-sclerotic changes may sometimes be observed in the vessels of the capsule and membrane. These have been noted in one case by Hoffa and Wollenberg and more recently by Strangeways.† Since, however, these vascular changes, if they occur at all, occur late in the disease, it is difficult to see how they can, as these observers state, constitute an ætiological factor.

In a later stage a section from near the edge of the trochlear surface shows fibrotic elongation of the fringes, the tissue almost as far as the endothelium being dense and somewhat homogeneous. Most of the capillaries are patent in the fibrotic areas, although the fibre immediately around them is arranged somewhat conformably with the lumen. In other fringes the concentric arrangement of fibres around the capillaries obtains without any surrounding fibrosis. Professor Shattock suggests that this striking development of fibres round the capillaries might well be termed "peri-capillaritis diffusa." None of the fringes contains any fat. In a few spots the capillary is blocked by an associated proliferation of endothelium. The gross changes in the capsule and intra-articular structures are too well known to require separate consideration.

Suppuration, as was originally pointed out by Sir Benjamin Brodie, is a very rare complication of osteo-arthritis. A probable explanation of this fact will be adduced in the final portion of the Report.

(To be concluded.)

† Observations on the Nutrition of Articular Cartilage, Brit. Med. Jour., 1920, May 15th.

SOCIETY FOR THE STUDY OF INEBRIETY.—The next meeting of this society will be held in the rooms of the Medical Society of London, 11, Chandos-street, Cavendish-square, London, W., on July 11th, at 4 P.M. Mr. Charles J. Bond, the President of the society, will deliver an address on the Influence of Hospitals on Temperance Reform.

DONATIONS AND BEQUESTS.—The late Miss Alice Charlotte de Rothschild, of Waddesdon Manor, Buckinghamshire, left, among other bequests, £2500 to the Buckinghamshire County Hospital, Aylesbury.—By the will of the late Rev. George Edward Aspinall, of Halls Ings, Southwam, Yorks, the Royal Halifax Infirmary will receive £1000.—The late Mr. Henry H. Wills, of Bristol, who left estate valued provisionally at £2,750,000, established by will a trust fund for the benefit of Mrs. Wills for life, which is charged at her death with certain charitable and other bequests. The residue of this fund and all the testator's residuary estate will be divided into 200 shares, according to which the West of England Sanatorium, Dr. Barnardo's Homes, and the Church of England Waifs and Strays Society will each receive £5000; the National Society for Prevention of Cruelty to Children, £3000; the Society for Prevention of Cruelty to Animals, £1500; and the School for Deaf and Dumb Children, Margate, and the Edith Cavell Homes of Rest for Nurses, £1000.—The Chelsea Hospital for Women has received from an anonymous donor ("In Loving Memory") £50, and £50 for the Convalescent Home. The £36 final instalment of the bequest of the late Mrs. Stephenson has also been received.