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OSTEOARTHROSIS IN PATIENTS AND POPULATIONS*

BY

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The history of osteoarthrosis is long, for degenerative joint changes can be seen in fossil skeletons of prehistoric animals and in the joints of ancient Egyptian mummies. Despite this long history our knowledge of the disease is incomplete, perhaps because it is one of those dull commonplace disorders that are hard to study with enthusiasm, but new knowledge of osteoarthrosis must be gained if the later years of our lengthening lives are not to be plagued by increasing pain and disability.

Osteoarthrosis can be defined as an expression of a joint's inadequacy to meet the mechanical stress placed upon it, and in certain patients and in certain joints, notably the hip, abnormal mechanical factors do obviously play a dominant part in both causation and treatment. But are such joints representative of the total problem of degenerative joint disease? May there not be important constitutional factors which predispose to premature degeneration of multiple joints submitted to no more than average mechanical stress? Detailed laboratory studies of individual patients have been unrewarding in this respect, except in such rare conditions as alkaptonuria, where congenital absence of the single enzyme homogentisic acid oxidase (La Du, Zannoni, Laster, and Seegmiller, 1958) is associated with premature degeneration of all the intervertebral disks and articular cartilages. This lack of positive laboratory findings, however, may only reflect the inadequacy of our methods, and while we are waiting for the biochemists to devise new methods it may be interesting to review some of the information obtained in recent years from the study of osteoarthrosis in population groups by field-survey techniques.

OSTEOARTHROSIS IN POPULATIONS

The epidemiological approach requires both definition and quantitation of the abnormality under study.

Osteoarthrosis is best defined in terms of anatomical abnormalities in the joints. The earliest changes, such as softening, fibrillation, or disintegration of the articular cartilage, can be recognized with certainty only by direct inspection of the joint surface—a procedure applicable only to post-mortem surveys (Heine, 1926; Bennett, Waine, and Bauer 1942). The later changes of subchondral bone sclerosis and marginal osteophytic outgrowths are, however, easily demonstrated radiologically, and radiographs give a good index of these later and more severe changes. Furthermore, radiographs provide evidence that can be studied in such a manner that inter- and intra-observer error can be reduced to a minimum and standard gradings for the degree of radiological change can be elaborated (Kellgren and Lawrence, 1957), so providing for quantitation. Although radiographs provide the best objective evidence of the advanced degrees of osteoarthrosis they give no information about pain and disability, so that a clinical examination of the articular system and questionaries about rheumatic complaints are also needed.

The early surveys which were carried out in Lancashire (Lawrence and Aitken-Swan, 1952; Kellgren, Lawrence, and Aitken-Swan, 1953) were planned jointly with the Manchester University Department of Occupational Health and were done for the National Coal Board because it has been suggested that miners suffered from some special form of rheumatism.

In the first of these studies information about rheumatic complaints of all kinds was collected from various population samples totalling nearly 7,000, composed of miners and men from other occupational groups, and women from both mining and non-mining families, living in the town of Leigh, in Lancashire.

The complaints were classified by site, duration, and degree of resulting disability, and only secondarily by diagnostic categories, since diagnostic definition in the rheumatic diseases is at best difficult and rarely precise enough for use in field work. Nevertheless, it became clear that osteoarthrosis in women and disk disorders in

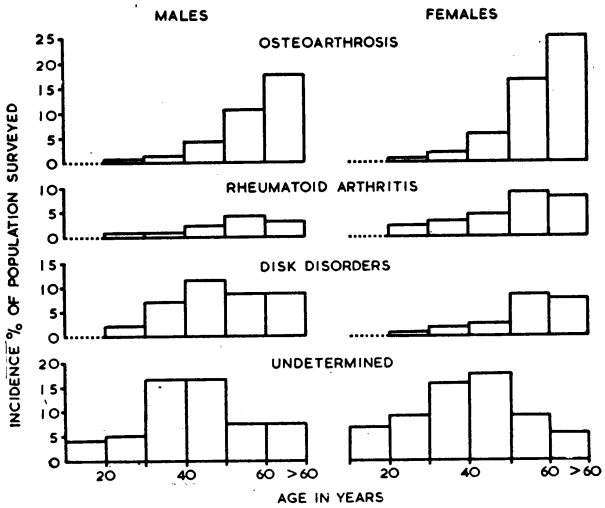

FIG. 1.—Rheumatic complaints by age and sex occurring at some time during a five-year period in a random sample of 1,619 men and 1,896 women from the town of Leigh, Lancs.

*Based on a Honyman Gillespie Lecture delivered in Edinburgh on November 3, 1960. The terms of the lecture preclude the mentioning of experiments on animals.

men were the most frequent and important causes of pain and disability and that rheumatoid arthritis, though less frequent, often caused prolonged disability, especially in middle-aged women. In the younger age-groups there were many undiagnosable episodes of pain and stiffness, some of which may well represent early stages of these other more serious conditions (Fig. 1).

Survey in Miners

When miners were compared with the surrounding population it was found that the total complaint rate for pains in the limbs and spine in miners differed little from that in other men, but the miners lost more working-time and their pains were situated mainly in the knees and back-sciatic distribution. Such rough diagnostic classification as could be made suggested that miners suffered more from disk disorders and osteoarthrosis than non-miners, but rheumatoid arthritis was equally distributed and possibly even less frequent among miners in the older age-groups.

Since the problem in miners appeared to be one of osteoarthrosis and disk degeneration, a sample of miners, manual workers, and office workers in the 40–49 age-group were studied radiologically as well as clinically to see whether the excess of back and knee pain in miners was associated with anatomical changes in the joints (Kellgren and Lawrence, 1952). Severe radiological signs of disk degeneration in the lumbar spine were found in 43% of miners but in only 7% of office workers. Conversely, only 8% of miners had radiologically normal spines compared with 67% of office workers (Fig. 2). The findings in the manual workers, who were engineers, were intermediate but nearer to the office workers than the miners. A similar excess of radiological osteoarthrosis was noted in the knees of the miners, but radiological evidence of disk degeneration in the cervical spine was found equally in the three occupational groups. A fairly close association was found between these *x*-ray changes in the knees and the lumbar spine and pain in the knees and back-sciatic distribution respectively, but not all men with severe *x*-ray changes had symptoms.

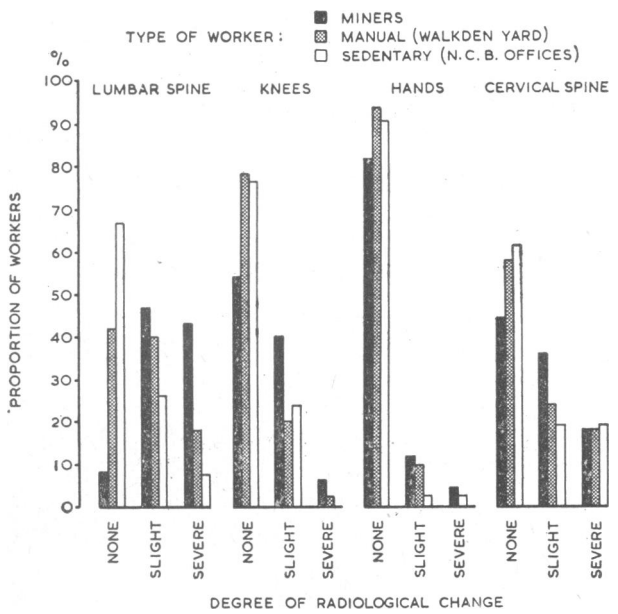

FIG. 2.—Incidence of osteoarthrosis and disk degeneration in 84 miners, 45 manual workers, and 42 office workers aged 40–49 years.

A similar study of groups of men working under different conditions (Lawrence, 1955) showed that radiological signs of disk degeneration in the lumbar spine were especially related to heavy lifting and trauma to the back, whereas working in a stooping position, stature, stem height, and exposure to wet aggravated symptoms and disability but had no influence on the radiological changes. Similarly, radiological osteoarthrosis in the knees was related to injury and body weight but not to kneeling, whereas deformity of the knees aggravated symptoms and disability but had no influence on the radiological changes.

These results in miners were entirely in keeping with the predominant role of mechanical factors in the production of osteoarthrosis in men, but there were also some unexpected findings.

Although the miners had much more frequent and severe anatomical changes in the joints, their complaint rate differed little from men in other occupations, while the women from mining families had fewer complaints than other women in Lancashire, and the male non-mining members of the mining families had only half as many rheumatic complaints as men from non-mining families. These differences were noted at all sites of pain and in all diagnostic categories except rheumatoid arthritis, and it seemed difficult to explain this by any other means than a group difference in complaint threshold. This question of complaint threshold may in fact be one of the most important parameters to assess in patients with rheumatic diseases, and the existence of such group differences of complaint rate precludes the use of complaints alone as an index of articular disease.

The second unexpected finding was the high prevalence in the women of Leigh of what appeared to be osteoarthrosis of multiple joints, affecting particularly the hands. Though this involvement of the hands might to some extent be explained in terms of the mechanical stresses peculiar to household chores, the widespread involvement of many joints suggested a constitutional factor.

At the same time it was noted that many of the female patients attending the rheumatism clinic at the Manchester Royal Infirmary appeared to be suffering from multiple osteoarthrosis affecting the diarthrodial joints in a symmetrical and characteristic manner. This polyarticular osteoarthrosis was usually associated with Heberden's nodes, and it was suggested that osteoarthrosis in women might often be a generalized condition which, like Heberden's nodes, could result from some inherited constitutional disorder (Kellgren and Moore, 1952).

To investigate this possibility further surveys were made in which routine radiographs were taken of many joints and in which a blood sample was also obtained from each respondent. The concentration of the rheumatoid serum factor has been determined in these surveys by Dr. J. Ball, using his modification of the sensitized sheep-cell agglutination test (Ball, 1950; Kellgren and Ball, 1959), and the serum uric acid and serum cholesterol have been estimated by Miss V. Hewitt, whose work has been supported by the Nuffield Foundation.

Multiple Osteoarthrosis in an Urban Population

In the first of these studies, which was carried out in co-operation with the Medical Research Council's

Pneumoconiosis Research Unit, a random sample of the inhabitants of Leigh aged 55–64 years was surveyed and *x*-ray films were obtained from 173 men and 206 women ; Figs. 3–6 are based on this sample (Kellgren and Lawrence, 1958).

The first point to emerge from this survey was the striking pattern of joint involvement (Fig. 3), which differed somewhat in the two sexes. In females the distal interphalangeal joints of the fingers were most affected, together with the proximal interphalangeal, first carpometacarpal joints, the knees, the first metatarsophalangeal joints, and the apophysial joints of the spine. Whereas other joints, such as the wrists, sacro-iliacs, hips, and lateral metatarsophalangeals, were usually spared. In a proportion of individuals there was a history of previous trauma or radiological evidence of past injury, and the prevalence of post-traumatic osteoarthrosis defined in these terms is shown in Fig. 4, from which it will be seen that such trauma accounts for only a small proportion of osteoarthrosis, though in men this proportion is not insignificant, especially in the knee-joints. On the other hand, the presence of clinically recognizable Heberden's nodes appeared to be a major factor determining the presence or absence of osteoarthrosis in other joints (Fig. 5). Since Stecher (1955) has shown that the digital nodes described by Heberden (1802) may be inherited as a single autosomal gene dominant in females and possibly recessive in males it would seem that such an inherited predisposition might be the most important factor in the causation of osteoarthrosis of multiple joints, especially in females.

A relationship between obesity and osteoarthrosis has long been recognized, and the mechanical effect of excess body weight upon joints of the lower limbs is self-evident. A comparison of the prevalence of osteoarthrosis in obese and non-obese individuals in the random sample at Leigh (Fig. 6) confirmed the expected association between obesity and osteoarthrosis of the weight-bearing joints, there being nearly twice as much osteoarthrosis of the knees in obese individuals. An

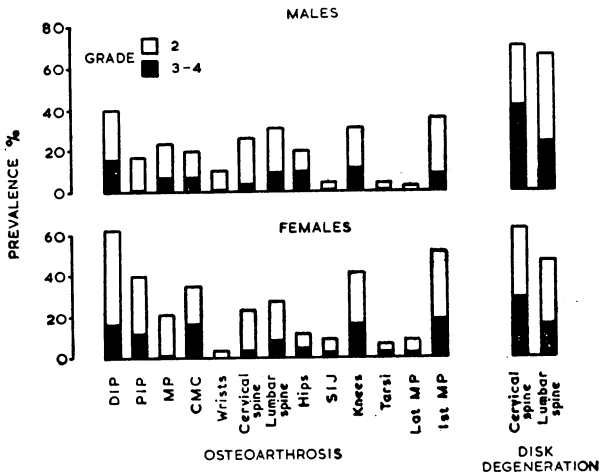

FIG. 3.—Pattern of osteoarthrosis and disk degeneration in males and females. Each column represents the proportion of groups of joints *x*-rayed which showed radiological signs of osteoarthrosis or disk degeneration. The grade recorded is that of the most severely affected joint in each group.

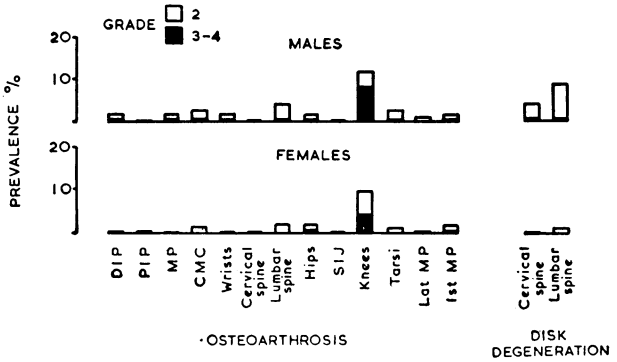

FIG. 4.—Pattern of osteoarthrosis and disk degeneration recorded as being related to injury in males and females.

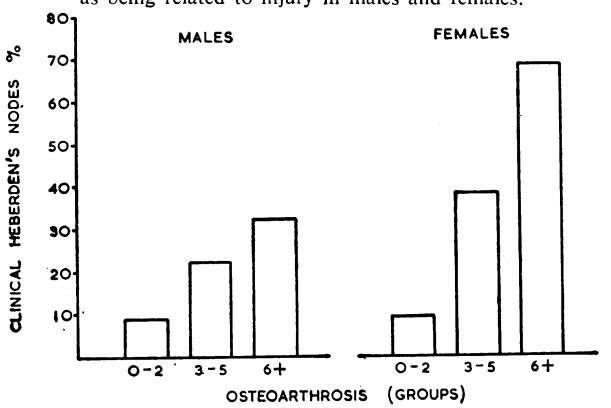

FIG. 5.—Relationship between definite Heberden's nodes, as recorded at the clinical examination, and the number of groups of joints showing definite radiological signs of osteoarthrosis in males and females.

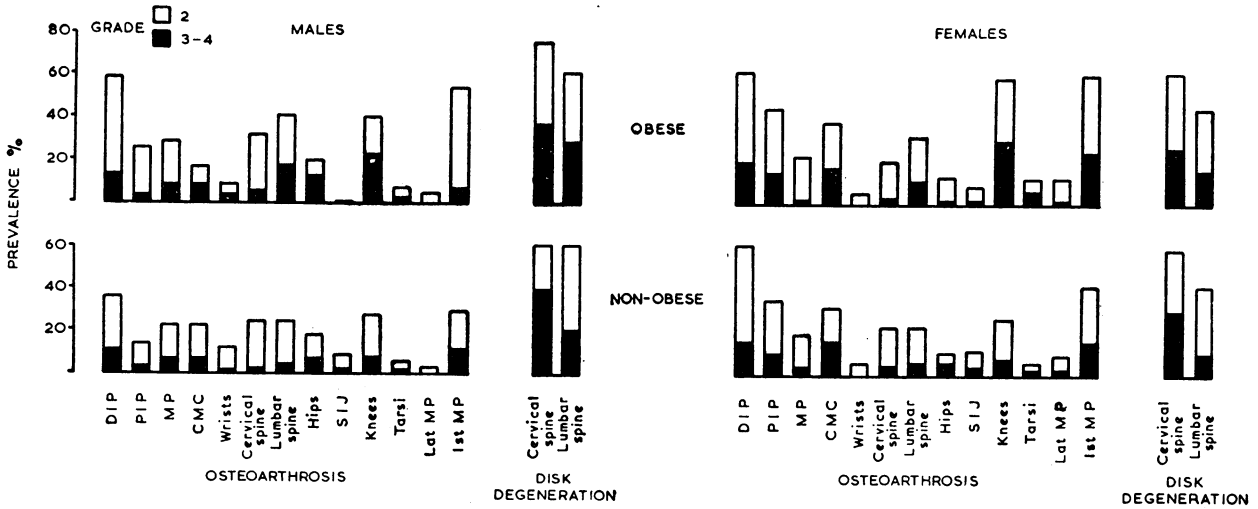

FIG. 6.—Pattern of osteoarthrosis and disk degeneration in obese and non-obese males and females.

unexpected finding, however, was an excess of generalized osteoarthrosis in obese males ; indeed, obese males had nearly twice as much osteoarthrosis of the distal interphalangeal joints, and the pattern of osteoarthrosis in obese males resembled that of females.

Later such comprehensive surveys were extended by Dr. J. S. Lawrence, as Director of the Empire Rheumatism Council's Field Unit, to include all ages over 15 years at Leigh. A mobile examination centre provided by the Wellcome Trust was used in these later surveys. Evidence about the possible relation of lipid metabolism to osteoarthrosis was obtained by comparing serum cholesterol levels with the degree of osteoarthrosis found in the hands in 438 males and 466 females over 35 years of age from the random sample at Leigh. A significant association was found between osteoarthrosis of the hands and above-average serum cholesterol levels (Fig. 7), especially in women, but this was less apparent in the few individuals with serum cholesterol of over 360 mg./100 ml.

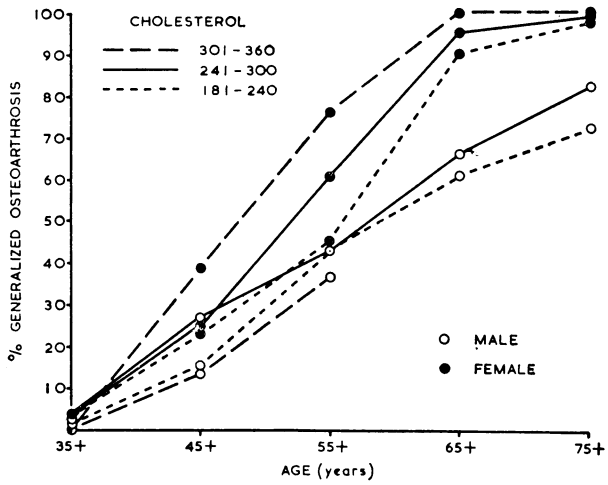

FIG. 7.—Radiological osteoarthrosis of the hands at three cholesterol levels in males and females.

Inflammatory Joint Diseases as a Causative Factor

Inflammatory joint diseases such as rheumatoid arthritis are often mentioned as a causative factor in osteoarthrosis, and in the random sample at Leigh (Kellgren and Lawrence, 1958) a clinical diagnosis of present or past inflammatory polyarthritis was associated with an excess of osteoarthrosis, especially in certain joints such as the metacarpophalangeals, the wrists, the lumbar spine, and the knees. However, there was no correlation between the rheumatoid serum factor and multiple osteoarthrosis, nor was there any correlation between radiological signs of erosive joint disease and osteoarthrosis. Indeed, in another survey in which only individuals with a history of pain and swelling of the hand joints were examined, a slight negative correlation was observed between the radiological signs of rheumatoid arthritis and osteoarthrosis in hand films (Miall, Ball, and Kellgren, 1958). This is perhaps not surprising, since rheumatoid arthritis, especially when defined in terms of the rheumatoid serum factor, is essentially a destructive atrophic process, which might be expected to inhibit the proliferative osteophytic outgrowths of osteoarthrosis, and it seems likely that osteoarthrosis only follows the milder forms of inflammatory polyarthritis in which prolonged remissions are frequent.

Gout is another disease which in its milder forms may predispose to osteoarthrosis, but we have not yet analysed our survey data to see whether there is any correlation between hyperuricaemia and osteoarthrosis.

Involvement of the Hip-joint

The hip-joint is not commonly affected by osteoarthrosis. Fig. 8, based on the same sample as Fig. 7, shows that some 80% of individuals retain radiologically

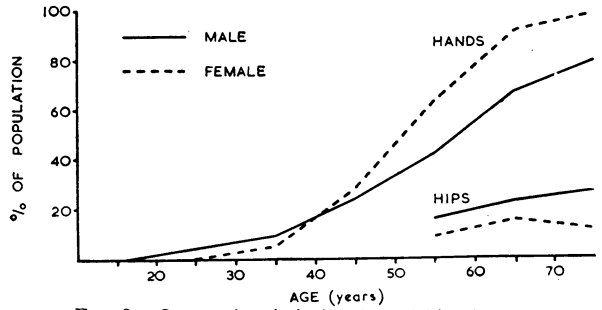

FIG. 8.—Osteoarthrosis in hands and hips by sex.

normal hips throughout life, but when this joint is affected the resulting disability is often severe, so that osteoarthrosis of the hip is a relatively common reason for consultation, especially in orthopaedic clinics. The hip is also peculiar in that it is rarely affected by the generalized form of osteoarthrosis associated with Heberden's nodes. On the contrary, osteoarthrosis of the hip is usually secondary to local mechanical defects such as dysplasia of the acetabulum and femoral head, previous Perthes's disease, slipped epiphysis, or previous inflammatory arthritis. Thus the hip presents a very special case, and it is probably unwise to extrapolate from studies of the hip-joint to the problem of osteoarthrosis in general.

There is, however, one form of osteoarthrosis of the hip which is associated with multiple disk degeneration and sometimes with osteoarthrosis in all the joints, and that is the group of the rare familial diseases classified under the general terms of chondrodystrophy and epiphysial dysplasia. These conditions will almost certainly be found to have a metabolic basis when adequate methods of investigation are available, and minor degrees of these conditions may turn out to be another significant cause of multiple osteoarthrosis in the population when we know how to recognize them.

Conclusions from Surveys

These various considerations suggest that osteoarthrosis may often be the articular expression of a generalized constitutional condition resulting from inherited metabolic abnormalities and/or dietary and other environmental factors. The future prospects for prevention and medical treatment may therefore not be as barren as they at present appear to be, but the eradication of osteoarthrosis is still an ideal goal for the remote future. In the meantime there are millions of patients requiring diagnosis and treatment.

OSTEOARTHROSIS IN PATIENTS

Although the anatomical changes of osteoarthrosis become almost universal in the later decades of life, most of these pathological changes are not associated with significant pain or disability, but in some joints in some patients the symptoms may be severe and disabling.

The question of osteoarthrosis in patients is therefore best considered in terms of the type of osteoarthrosis and the particular joint or joints affected.

The Worn Joint

In osteoarthrosis secondary to mechanical factors the process is a simple wearing-out of the joint, a process which is not necessarily painful; but the worn joint is mechanically defective and therefore more easily sprained than the normal joint. In the upper limb where the stresses are slight this is of little importance, and secondary osteoarthrosis of this type in joints such as the wrist and elbow produces nothing more serious than some painless restriction of the range of motion, but in large weight-bearing joints, such as the hip and knee, recurrent ligamentous sprains or traumatic effusions are common and persist for longer than similar sprains of a normal joint (Kellgren, 1940).

The individual episode of pain and stiffness, which is worse after rest and in the morning, can be rapidly and effectively relieved by infiltrating the affected ligament with hydrocortisone suspension, but this procedure is technically more difficult than it would appear, because the site at which pain is felt is a very poor guide to its source (Kellgren, 1939, 1949), and in treatment by local injection precise anatomical localization of the source of pain is essential to success. It is therefore useful to combine some local anaesthetic with the hydrocortisone suspension, as otherwise it is impossible to know whether the injection has been correctly placed. The risk of introducing bacterial infection during such injection therapy is great and the most scrupulous aseptic technique must be used. In the knee, quadriceps exercises are also essential, since the quadriceps is the guardian of the knee-joint, but in the hip and other joints it is doubtful whether exercise or other methods of physical treatment are of the same value. A worn-out inefficient joint can, of course, be protected from sprains if the patient is prepared to live within the exercise tolerance of the affected joint with the help of simple analgesics of the aspirin type and any orthopaedic appliances that may be indicated, and this is often the best method of dealing with the situation.

As the wearing process progresses some joints will become so disorganized that every attempt at weight-bearing produces a sprain. The bone ends may also become crumbled and riddled with cysts causing incongruity of the joint surface and total disorganization of the joint which is often accompanied by severe pain and disability. At this stage relief can be obtained only by surgical reconstruction, which in suitable cases should not be too long delayed.

Primary Generalized Osteoarthrosis

In this form of osteoarthrosis the problem is quite different because in this condition there is a peculiar pain mechanism which is seen most clearly in the acute Heberden's node. In such acute nodes the affected joint is swollen and hot and tender; but the centre of the swelling is not an inflammatory exudate but a collection of highly polymerized hyaluronic acid unconjugated with protein (Jackson and Kellgren, 1957). The pain is continuous, often worse at night. If the collection of hyaluronic acid is evacuated the painful state disappears in a few days, but hyaluronic acid produces no pain when injected. The pain is aggravated by use of the joint and relieved by rest and immobilization, it is not associated with pronounced stiffness after rest or sleep, and it is little influenced by drugs such as salicylates, phenylbutazone, or corticosteroids. Thus in many ways this pain differs from the pain of trauma or inflammatory conditions such as rheumatoid arthritis, and is presumably produced by some chemical mechanisms which we do not yet understand.

Fortunately this painful phase subsides once the ligaments and cartilages of the joint are largely replaced by new bone, so that the final result is a bony enlarged joint with a limited range of motion but which causes no pain provided it is not subjected to mechanical stresses that are beyond its capacity.

In the hands this process is easily seen and recognized because of the characteristic symptoms and pattern of joint involvement, and the only condition with which it is likely to be confused is psoriatic arthropathy.

When the spine is affected the diagnosis is more difficult; but backache without stiffness in a middle-aged woman whose back shows exaggerated curves and only slight limitation of motion suggests this possibility, and the presence of Heberden's nodes on the fingers serves to remind us that similar nodes may be forming on the apophysial joints of the spine. In the knee the acute phase presents as an aching warm knee containing a slight excess of highly viscous fluid but without synovial thickening and with little limitation of motion. Evidence of generalized osteoarthrosis in other joints will help to establish the diagnosis. This is important, since the pain is rapidly relieved by rest and immobilization, but it is unaffected by most drugs, including local injections of hydrocortisone, and aggravated by all forms of physiotherapy.

When the hip is affected there is the same pain after use with little stiffness. Although the range of motion may become grossly reduced by osteophytic outgrowths, the femoral head and acetabulum retain their normal shape, and adduction and flexion deformities do not develop. Excess pain can be relieved by a period off weight-bearing, and surgical treatment is rarely needed.

Only in the more florid and rapidly developing forms of osteoarthrosis do the joints pass through this acutely painful phase. In most individuals bony enlargement of the joints develops slowly and painlessly and with only such minor aching after use as can be disregarded under favourable conditions. If, however, such an individual's complaint threshold is lower than average or becomes lowered temporarily by some intercurrent disease, psycho-social difficulties, or the onset of a depressive state, previously tolerable discomfort becomes intolerable pain and a cause for medical consultation. A true assessment of this situation is vital because in such cases it is the lowered complaint threshold and not the joint that requires treatment.

Inflammatory Conditions

The presence of generalized osteoarthrosis provides no protection against inflammatory conditions such as rheumatoid arthritis, and the onset of such another more painful disease is a common reason for medical consultation. This situation should be suspected when symptoms become prominent some years after the onset of bony enlargement of the joints; especially when there is generalized morning stiffness of more than a few minutes' duration and the joint symptoms are accompanied by malaise and loss of weight. Certain joints, such as the wrist, ankle, and tarsus, are spared

in generalized osteoarthrosis, and if these are abnormal some other form of arthritis is present. A great excess of low-viscosity joint fluid, synovial thickening, and lesions in the bursae, tendon sheaths, and tendons are further indications of inflammatory polyarthritis.

Although some subjects with a very high erythrocyte sedimentation rate were included in our original study of patients with generalized osteoarthrosis (Kellgren and Moore, 1952), subsequent experience has suggested that in uncomplicated generalized osteoarthrosis the E.S.R. is not greatly elevated, and a value of over 30 mm./hour (Westergren) is now regarded as evidence of the existence of some other disease, as is the presence of anaemia. A positive sheep-cell agglutination test is also strong evidence for the presence of concomitant rheumatoid arthritis. Rheumatoid arthritis in elderly males may present as increasing pain and stiffness in a single large joint, such as the hip, which may lead to an erroneous diagnosis of osteoarthrosis; but this can be avoided by routine examination of all joints, because such patients usually have definite signs of rheumatoid arthritis in other more accessible sites, especially in the feet and hands, and it should be remembered that gross erosive changes in these joints in old men are often painless. It is obviously essential to aim at a correct diagnosis in all patients with osteoarthrosis in whom some other diseases, such as rheumatoid arthritis, are present, since it is the latter conditions that determine prognosis and treatment.

Finally, pain and stiffness in the limbs and back in a patient with obvious osteoarthrosis may not be due to the joint disease but to some concomitant non-articular disorder, especially disease of the nervous and cardio-vascular systems. For instance, patients with a stiff hip may get leg pain from a prolapsed disk, and stiffness of the legs in patients with obvious osteoarthrosis of the hips may be due to a concurrent spastic paraplegia or Parkinsonism, and it is surprising to what an extent a radiograph showing gross osteoarthrosis of the hip concentrates our attention on the hip-joint.

SUMMARY AND CONCLUSIONS

Osteoarthrosis has been studied in population groups as well as in patients, and such studies have led to the conclusion that osteoarthrosis in women is predominantly a polyarticular condition resulting from inherited constitutional factors which may also be influenced by diet and other environmental conditions. In men the same causative factors may operate; but trauma, occupational stress, and mechanical factors in the joints probably play a predominant part. Osteoarthrosis as a sequel to inflammatory joint disease also contributes to the sum of osteoarthrosis in both sexes. The future prospects for prevention and medical treatment of osteoarthrosis may therefore be good, and further research along both epidemiological and experimental lines is urgently needed.

In the meantime a proper differential diagnosis of the type of osteoarthrosis present and the true reasons for seeking medical consultation can lead to more successful palliative treatment.

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METHICILLIN

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Methicillin ("celbenin") is of proved value in the treatment of staphylococcal infections that are resistant to benzylpenicillin (penicillin G) (Douthwaite and Trafford, 1960; Stewart, Nixon, and Coles, 1960). Investigation into the problems arising from its use have continued to be made. In particular, the question of the occurrence of resistance *in vivo* of staphylococci has been studied. A method of achieving satisfactory blood levels of methicillin in combination with probenecid in a low dose regime is here described.

Clinical Material and Methods

The series consists of 46 patients, all of whom had benzylpenicillin-resistant staphylococcal infections of varying types. The types of cases treated were:

	Cases		Cases
Pneumonia	9	Bacterial endocarditis	4
Empyema	1	Lung abscess	2
Septicaemia	4	Cervical abscess	1
Osteomyelitis	2	Neonatal pemphigus	2
Meningitis	1	Multiple boils and abscesses	4
Cerebral abscess	1	Urinary tract infection	4
Bronchiectasis with acute exacerbations	5	Wound infections	6

Levels of methicillin in the blood and cerebrospinal fluid were measured whenever practicable and routine haematological, radiological, and bacteriological investigations were carried out.

The dosage of methicillin was altered according to the blood levels (see below). The maximum dose was