ANKYLOSING SPONDYLITIS:

ITS AETIOLOGY AND PATHOLOGY

BY

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One of the most striking features in the incidence of rheumatic diseases in the recent war has been the number of cases of spondylitis which have been met with in all branches of the Forces. At the time of the Great War of 1914-18 spondylitis was a rare disease, though the conditions to which it has often been attributed by its victims—fatigue, exhaustion, and exposure to cold and damp—were certainly no less common. The history of minor degrees of trauma within a few months prior to the onset of symptoms has been noted, and it is likely that jarring of the spine in travel in lorries over rough country, in parachute descents, or airplane crashes may be worth investigating as a contributory factor, but in a large proportion of cases no definite history of anything of the kind can be obtained. The incidence in the male sex, not less than 90%, and the tendency to attack robust and virile types rather than the weakly has been well marked. It is easy to overlook this last feature, since by the time the disease has become established the constant pain and disability may have reduced the patient's strength and vigour considerably.

Gilbert Scott advocated the name "adolescent spondylitis," as the most severe and typical cases begin within a few years after puberty; the importance of this age period will be discussed later. The cases met with in the Services usually dated the onset in the early twenties or before and it must be noted that the first symptoms may be slight and intermittent and thus overlooked. There are cases which never develop beyond a very early stage, the evidences being discovered years later under examination for other conditions. The pains in the back and limbs may be slight at first with intervals of complete freedom before the nature of the disease becomes manifest. Scott's advice that all cases of indefinite rheumatic pains appearing soon after puberty should be submitted to x-ray examination of the sacro-iliac region is sound. The diagnosis of ankylosing spondylitis may, however, be made on the basis of such an examination and prove erroneous in the light of the clinical features and the progress of the patient, therefore the x-ray examination should always be accompanied by estimation of the sedimentation rate.

Problem of Aetiology

The constitutional characters, the frequent occurrence of low-grade fever, and the sedimentation

rate, raised in the great majority of cases often to a considerable degree, point to an infective origin arising from a focus, but more often than not it is impossible to identify it and removal of teeth, tonsils, and the like has rarely been found to make any impression on the disease. Oppenheimer of Beyrout (1938) has described three different types of what he terms atrophic arthritis of the spine: an acute form localized in the cervical region and due to infected tonsils; a chronic form, also chiefly affecting the upper part of the spine, of which he reports four cases—two of them had chronic amoebiasis and in one, treatment of this condition resulted in cure; and a third form which he terms ankylopoietic spondylarthritis, which is identical apparently with ankylosing spondylitis. Eleven cases of this third form are reported and in every case the patient stated that the pain in the region of the spine had followed some acute infection. Such a definite relation to infection has not been reported in Britain or America and it may be that spondylitis in the Near East differs in some respects from the forms met with in western countries; it should also be noted that amoebiasis is common in this part of the world, from 12 to 28% of the population being infected.

Boland and Present (1945) have investigated a series of 100 cases admitted to an army general hospital in the United States. They found spondylitis of the ankylosing type in 18% of patients with chronic back complaints; in 80% of the series no possible immediate cause could be found, though in 12 cases there was a history of injury to the back but not clearly related to the spondylitis. In 5 cases acute gonorrhoeal urethritis was related to the onset of back symptoms, and in 8 others an unrelated past history of gonorrhoea was elicited. In one instance a non-specific urinary infection immediately preceded the first back symptoms, which is of interest in view of the spread of the disease from a pelvic centre, which will be discussed later. Forestier (1939) suggested that the primary focus was in the genito-urinary system and recently the possibility that the prostate gland might be responsible has been mentioned (Buckley, 1943), in view of the sex incidence and the centrifugal course of the disease starting in the pelvic region. The view originally held that it was gonococcal in origin has been abandoned, since the closest investigation has failed to reveal any evidence of gonorrhoea in at

least 90% of cases, but it is well known that streptococci, staphylococci, and *Bact. coli*, among others, may invade the prostate gland, and virus infection is also a possibility. If focal infection is responsible it may act directly on the bones and joints, or by modifying the internal secretion of the prostate, or in the female by similar influence on other pelvic organs.

Robinson (1940) investigated the tuberculin-sensitivity of 45 cases of ankylosing spondylitis and found it 30% higher than that of 90 cases of other rheumatic diseases. He concluded that these results reflect either a non-specific irritant in the tuberculin used or a subclinical tuberculous state in the patient due possibly to an immunizing infection. In a previous investigation an intradermal tuberculin test was carried out and gave positive reactions in 15 out of 18 cases (Buckley, 1935). It is difficult to determine the significance of this finding in the aetiology of spondylitis.

Clinical Pathology

The clinical features and pathology are best studied in cases beginning before the union of the epiphyses in the vertebral and pelvic regions. Centres for epiphyses for the tips of the transverse processes and the spinous processes, and for the upper and lower surfaces of the vertebral bodies, appear about the sixteenth year, and those for the lateral surfaces of the sacrum about two years later, all uniting about the twenty-fifth year or later, at the same time as the epiphyses of the scapular and pelvic girdles. The epiphyses of the bones of the limbs all unite about the twentieth year, with the exception of that for the upper extremity of the tibia. In view of the association of the pathological process with actively growing bone these dates are important.

The centrifugal spread of the disease from the region of the pelvis to the vertebral column, the costo-vertebral joints, the hips, and later to the shoulders, sterno-clavicular joints, and knees but rarely beyond, is one of the most characteristic features and is invariable, though the x-ray appearances may not be uniform. In cases beginning after the union of the epiphyses, the apophyseal joints in the dorso-lumbar region and the costo-vertebral joints may show more advanced changes than those in the lower lumbar area, and the cervical spine may be extensively affected before the lumbar spine becomes ankylosed. This appears to depend on the degree of mobility; the dorso-lumbar and cervical are the regions of greatest mobility in the spinal column and movement in the costo-vertebral joints is constant, whereas the lower lumbar region may be kept at rest by muscle spasm. This point has a bearing on the question of rest or movement in treatment.

The explanation of the centrifugal progress is unknown, but recent experiments conducted by Batson (1940) to elucidate the spread of metastases from carcinoma of the prostate have thrown light upon the problem. He observed that the only

anatomical system that fitted in with the distribution of the secondary deposits was the plexiform system of veins investing the prostate, the sacrum, and the iliac bones, communicating with the veins of the vertebral column. He therefore injected the dorsal vein of the penis in a cadaver with a radio-opaque pigment and observed that it spread through the venous plexus of the prostate to the common iliac, the inferior vena cava, the lateral sacral veins, and the alae of the ilium. He repeated the experiment using a thinner pigment and found that it reached the lower lumbar vertebrae and that none entered the vena cava. He then injected a monkey in the same way under anaesthesia and verified these results, but observed also that increased intra-abdominal pressure, obtained by bandaging the abdomen, prevented the dye from entering the vena cava; he concluded that straining efforts with a closed glottis would produce the same effect. With a higher pressure the injection reached the intercostal veins and as high as the base of the skull.

These veins are without valves and the flow is very slow, tending to stagnation; they appear to be storage lakes as well as pathways of drainage. Batson suggests that there are frequent reversals of flow, which might be caused by spinal movements, and proposes that in addition to the caval, portal, and pulmonary venous systems we should add a fourth—the vertebral, including the veins of the spinal column and girdles, the neck, skull and brain. Cunningham (1923) describes a thin-walled plexus of veins between the periosteum and the spinal canal. If the blood in these veins contained a morbid agent from the prostate inflammation of the dura would be likely. This may explain the features of the spondylitis described by von Bechterew in which the meninges were implicated, but since in the usual type of ankylosing spondylitis only the bones and ligamentous structures are affected there is evidently a specific affinity for these structures. Nathan (1916) observed, "whether or not these parts are involved is merely an accident of location of a generalized process and such accidental distribution provides the forms commonly associated with the names of von Bechterew, Strumpell, Marie, etc. These conditions are not essentially different, they may be chronic, transient, or progressive with or without permanent changes in the tissues involved." The importance of this observation has generally escaped notice.

Osteoporosis

In an earlier paper (1931) the opinion was expressed by the writer that the earliest recognizable change in radiographs was osteoporosis. This occurs to the most marked extent in the growing parts of the bone, as may be seen in the sacro-iliac region though the appearance may be somewhat masked by calcification of the sacro-iliac ligaments overlying the joint giving rise to an appearance of uneven density or sclerosis of the bone margins. In the bodies of the vertebrae osteoporosis is often extreme, affecting the whole of the body which thus

becomes translucent, permitting the denser lines caused by the ossified spinous ligaments or the ligaments of the facet joints to stand out conspicuously. Hilton Fagge (1877) called attention to this decalcification in his account of the first necropsy of which there is any record, and remarked that the vertebrae were so soft that they could be cut with a knife. Osteoporosis is met with in many conditions but in very few is it associated with ossification of the ligaments and tissues in its vicinity. This is sometimes seen in tuberculosis of the spine, in which Knaggs (1926) described considerable deposits of new periosteal bone and ankylosis of the vertebrae by bars of bone, which are formed by ossification of the ligaments, fibre by fibre in a uniform manner, as described by Léri (1926) in his account of ankylosing spondylitis.

In rheumatoid arthritis a similar osteoporosis occurs but without the ossification of neighbouring tissues, and in this, as in other forms of osteoporosis, the calcium removed from the bone is excreted. In spondylitis the calcium appears to be redeposited immediately in the fibrous and fibro-cartilaginous tissues in the vicinity, the ligaments begin to ossify and the joint capsules become bone, as may be seen in the facet joints of the spine and in many cases more clearly in the hip-joints. Deposition also takes place in fibro-cartilaginous tissues, such as the rim of fibro-cartilage forming the edge of the acetabulum and that of the pubic symphysis (more frequently in women than in men), but not in the articular cartilages. The outer fibres of the annulus fibrosus of the intervertebral disks become calcified, particularly those which pass from the disk to merge into the anterior and lateral ligaments, giving rise to the characteristic bridging and ultimate conversion of the outer part of the disks into solid bone. Connor (1700) described this condition very vividly. He gives an account of a skeleton which he had examined and says, "the cartilaginous edge of the vertebrae themselves were turned to perfect bone, but when I had sawed two vertebrae asunder at the commisure I found that this uniting did not enter above two lines deep." The contrast between the decalcified and softened bone of the vertebral bodies, which yield under the weight of the body [and the turgor of the nucleus pulposus of the disks] to assume the typical bobbin shape, and the marginally ossified disk, which is expanded in its centre, is very striking and characteristic. Ehrhardt records one case in which the disks were completely replaced by spongiosa continuous with that of the bodies. Deposition of calcium also takes place in the periosteum and this may be seen in the form of fringing of the bones of the pelvis.

Biochemical Factors

Resorption and redeposition of calcium in the bone is normally a continuous process. In the stage of bone growth deposition of calcium takes place at a more rapid rate than resorption, while in osteoporosis the reverse is the case, and this may be due to excessive resorption or deficient rede-

position, varying in degree in different diseases. Willis (1939) in dealing with tuberculosis of bone said, "calcification of soft tissues and decalcification of bone are matters of local biochemical conditions, the former associated with anaemia and ischaemia, and the latter with active hyperaemia," but this is inadequate to explain all forms, such, for example, as senile osteoporosis. The osteoporosis of spondylitis must be considered in association with the characteristic deposition in the adjacent tissues.

The problem of calcification as an essential stage in bone growth has been the subject of research for many years, but for the most part as a normal physiological process and so far as the writer is aware the process as it occurs in ankylosing spondylitis has not received attention. Robison and Soames (1924) put forward a hypothesis based on experiment which has been the foundation of much of the subsequent work. They noted that the osteoblasts, the hypertrophic cartilage cells, and certain cells of the inner portion of the periosteum in a growing bone contain, or can secrete, a very active enzyme, which by hydrolysing the salts of phosphoric esters brought to the ossifying zone by the blood stream caused a local increase in the concentration of phosphate ions. The solubility product for calcium phosphate, which is probably nearly reached in circulating plasma at normal pH, is thus exceeded locally and a deposition of calcium phosphate takes place in the neighbourhood of the cells which secrete the enzyme. This enzyme is a phosphoric esterase or phosphatase and there are several varieties, those of bone, kidney, and intestinal mucosa are "alkaline" phosphatases while that secreted by the prostate and some other organs is the "acid" phosphatase; by these terms is meant that the optimum substrate pH is over 7 for the alkaline and under 7 for the acid form. In carcinoma of the prostate with metastases in bone the acid phosphatase is greatly increased, and this observation led to speculation as to the possibility that it might also have a bearing on the aetiology of ankylosing spondylitis. Different methods are in use for measuring the amount of phosphatase in the plasma. Race (1945) in a series of 13 cases of spondylitis found the average level of acid phosphatase was 2.2 by a method in which the normal maximum is taken as 4 units; the highest figure obtained was 3.8 and the lowest 0.9. While the number of cases is insufficient to justify any sweeping conclusion it indicates fairly clearly that "acid" phosphatase has probably no bearing on ankylosing spondylitis.

The alkaline phosphatase on the other hand showed a slight increase in plasma in a series of cases reported by the writer (1935), the average being 0.34 (Kay units) compared with a normal maximum by this method of 0.20; a few additional cases examined since have been within the same range. The presence of phosphatase in the plasma is for the most part due to its passage from the tissues, and Kay (1932) suggested that it might arise from leakage from the bones and that such leakage might be the cause of irregular deposition of bone outside the usual sites. The types of phosphatase from the bone, kidney, and intestinal mucosa are identical in their power of hydrolysing phosphoric esters *in vitro*, but experiments *in vitro* may not adequately account for what happens in the living body, and it has been suggested that the cells in bone develop their enzyme for the specific object of calcification, those of the intestinal mucosa to effect the breakdown of phosphoric esters in the food (Kay, 1932), and those of the kidney to convert phosphoric esters to the inorganic phosphates which are excreted in the urine (Eichholz, Brull, and Robison, 1925). The kidney, however, may calcify if the blood supply is interfered with (Remesow, 1925).

In rickets calcification does not take place in the bone in spite of the fact that there is a high level of phos-

phatase in the zone of hypertrophic cartilage. This appears to be due to the low inorganic phosphate content of the circulating blood (Kay, 1932). The deficient calcification in the cartilage zone in rickets may throw some light on the rarefaction of bone in spondylitis. It is essential for the calcifying process that in addition to the presence of the enzyme there should be an adequate supply of phosphoric esters for it to act upon. In the absence of this, calcification does not take place, but it is not clear whether such a deficiency could exist in the bone and not in its vicinity where calcification does occur in spondylitis. Leriche and Policard (1928) point out that precipitation of bone salts depends less on the blood than on the lymph, and such material might be abundant in lymph but much less abundant in the blood.

The pH *in vitro* has an important bearing on the process of hydrolysis. The activity of bone phosphatase is at its maximum with the esters which are believed to form the most probable substrate between 8.4 and 9.4, increasing with the increase in alkalinity; this may also influence the process *in vivo* since the pH of the blood is 7.4, at which level the activity would probably be very low. Page (1930) states that the mobilization of calcium and phosphorus from the bone is a process in which diminution of the activity of bone phosphatase is the first step. The toxic material which is responsible for the pathology of spondylitis may possibly act by lowering the pH of the bone cells and thus diminishing the phosphatase activity, acting as an inhibitor. Another factor may call for consideration—namely, the presence or absence of activators. It has been shown (Jenner and Kay, 1931) that magnesium has an activating effect on bone phosphatase, and they put forward the suggestion that this may be important in the therapy of some bone diseases. The value of aluminium acetate in osteitis deformans may be due to an action of this nature, furnishing a parallel.

While hydrolysis of phosphoric esters is the usual function of phosphatase, there is some evidence that reverse action may take place—synthesis of the ester from inorganic phosphate of calcium. This has been demonstrated *in vitro* and Kay (1932) says, "it may be that the enzyme plays an active part also in bone resorption and demineralization under both normal and pathological conditions by synthesizing, from some of the insoluble calcium phosphate of the bone, soluble phosphoric esters of calcium. It is not impossible, though perhaps unlikely, that the synthetic as well as the hydrolytic activity of the enzyme plays a part in normal bone formation, that the effect of the enzyme is diphasic, producing synthesis of phosphoric esters in one part of the ossifying zone and hydrolysis with deposition of calcium phosphate in another." If this suggestion should be confirmed it would throw light on the process in ankylosing spondylitis and also in rickets.

It appears reasonable in the light of these biochemical findings and the anatomical path of the disease to conclude that ankylosing spondylitis is due to the action of a toxin, which may be bacterial or may be due to the high metabolic activity of the prostate at the age at which the disease is most virulent. The greater activity of phosphatase in the region of the epiphyses before their union also accounts in part for the greater severity of ankylosing spondylitis in the young. It is obvious that after the epiphyses have joined up the effects will be modified, but it must be remembered that resorption and redeposition of calcium is a continuous process even in adult bone, though at a slower rate. Both osteoporosis and new bone formation are much less pronounced in cases beginning after the age of 25 or thereabouts and this has an important bearing on prognosis, which is then much more favourable;

in fact, such cases sometimes become arrested without any specific line of treatment.

It will be useful to compare rheumatoid arthritis, rickets, and spondylitis as three diseases presenting osteoporosis, in view especially of the common confusion between arthritis and spondylitis. In arthritis, osteoporosis, may be extreme but is not directly associated with the epiphyseal area nor with the period of active growth. In arthritis the plasma phosphatase is not increased, in spondylitis a moderate increase is usual, and in rickets the increase is generally considerable. In arthritis, ankylosis only occurs as a terminal event after the breakdown of the articular surfaces; in spondylitis and in rickets there is no tendency to breakdown of the bone structure but softening may lead to deformity, owing to the effects of weight and posture; there is new bone formation in the ligaments and joint capsules in spondylitis leading to early ankylosis, and sub-periosteally in both. In arthritis the joints are the chief seats of damage, beginning with synovial inflammation, but in spondylitis the damage in the joints is probably due to extension from the bone through the articular cartilage which does not contain phosphatase until it becomes vascularized (Goodwin and Robison, 1924), and to the spread of calcification from the ligaments and capsules.

Influence of Sex Hormones

The evidence as to the source from which the disease appears to start leads to consideration of the possible influence of the sex glands on its development. It is noteworthy that it so often attacks youths of robust and virile type soon after puberty, and there has been evidence in some of my cases of high activity of sexual functions. There is some evidence that the sex glands have an influence on bone formation. Paterson (1929) states that hyperactivity of the sex glands accelerates fusion of the epiphyses, and castration delays ossification. It is uncertain whether this is a direct action or through the medium of other glands, the thyroid or pituitary. Gardner and Pfeiffer (1938) concluded from experiments that testosterone propionate inhibits skeletal changes which occur when oestrogens are injected over a long period. Silberberg (1939) described complex changes in ossification under the influence of oestrogen administration, with ossification of intercartilaginous ground substance in the epiphyseal disks, ribs, and vertebrae. From the clinical aspect the condition formerly described as senile osteoporosis but which is now known not to be limited to ages which may be regarded as senile, and to which the name post-menopausal spondylitis has also been applied, has some bearing on the problem. It is more common in women, developing soon after the menopause in many cases, but Burrows and Graham (1945) in an exhaustive study of spinal osteoporosis appear to attach importance not to the sex glands but rather to dietetic deficiency, especially to the possible effect of vitamin C. The

same factors appear to apply to puerperal osteomalacia.

Albright and his colleagues (1940) showed that after the menopause women are prone to develop osteoporosis of the pelvis and spine, which can be corrected by oestrogen therapy; the long bones are rarely affected, which differentiates it from hyperparathyroidism. In Cushing's syndrome osteoporosis is a symptom and oestrogen formation is decreased and urinary androgens are increased. From these scanty data it is impossible to assume with certainty that the sex glands have any influence in spondylitis. Freiberg (1942) found no benefit from the administration of oestrogens in spondylitis but other observers are still studying this possible line of treatment.

Sequence of Changes in Spondylitis

It is now desirable to consider the sequence of the changes in spondylitis and their association with the pathological and biochemical changes. The first definite objective evidence in x-ray films is osteoporosis beginning in the region of the epiphyses of the sacro-iliac joints, in the bodies of the lower lumbar vertebrae, and in their articular processes. It may be due to toxic substances conveyed in the blood from the region of the prostate. Marie and Léri (1908) described spondylitis as primarily an infectious or toxic rarefying osteopathy, a definition with which the present writer agrees, holding that it is definitely not a form of rheumatoid arthritis. The osteoporosis may be due to excessive resorption of the inorganic calcium phosphate, or alternatively to failure in the normal process of redeposition. This may be due to diminished production of phosphatase, but it is to be noted that in rickets where the level of phosphatase is raised osteoporosis occurs; or to lack of adequate substrate; or to a pH unfavourable to its action; or possibly to a reversal of the normal action of the enzyme which has already been mentioned. Leakage of phosphatase from the bone to the adjacent subperiosteal region and the ligaments takes place, and deposition of calcium phosphate follows. This may be derived from the mobilized calcium phosphate from the bone which has there been converted into phosphoric esters and may be conveyed in the lymph channels, or to the calcium phosphate of the plasma, which is, however, small in amount. The deposit is at first calcium phosphate or a more complex salt of calcium which becomes converted into true bone, but if intermission in the disease occurs the calcium salt may be reabsorbed. This explains the fact that radiographs under such conditions often show a degree of improvement in the bony changes that might be thought impossible. Hilton Fagge in the report of the necropsy already referred to, noted that, "an opaque, white, mortar-like substance filled the cancellous spaces at the head of the ribs, the femur, and the innominate bone, and a similar material was deposited here and there about the outer surface of the arches." This was evidently

the calcified material which was about to undergo transformation into bone.

There is an obstacle to the full acceptance of the theory of the spread of the disease through the prostatic plexus and vertebral veins—namely, that the knees are occasionally affected in severe cases and it is not possible to assume a backflow in the veins which would go as far as the knees. It may be that they are attacked through the toxic material entering the vena cava in small amounts. In such a case, however, it might be argued that the small joints of the limbs would be equally open to attack, which in my experience occurs so rarely in true ankylosing spondylitis as to be of importance in differential diagnosis. The latter part of this statement may be disputed but in a study of over 200 cases the writer has never seen a case in which the small joints of the hands and feet were affected in true ankylosing spondylitis. In 3 cases which showed arthritis in the hands and feet the condition was evidently a gonorrhoeal arthritis; in 2 others the feet and hands were affected long before the spine and the condition was rheumatoid arthritis spreading to the vertebral joints.

The true joints of the vertebral column, those between the articular processes, are naturally liable to be attacked by the same diseases as those of the rest of the body, and this occurs in rheumatoid and gonorrhoeal arthritis, in tuberculosis, undulant fever, dysentery, and other conditions, but a critical examination of the history and the radiographic appearances will generally serve to differentiate these forms of arthritis from ankylosing spondylitis. Centrifugal progression from a pelvic focus, marked osteoporosis and deposition of calcium around the joints, and bony ankylosis without bone destruction are cardinal features. The radiographic appearances of an ankylosed hip-joint in spondylitis, in which the head of the femur appears practically intact and the bony trabeculae extend from the pelvis to the shaft of the femur along the lines of stress, is in marked contrast to the appearances of an ankylosed joint in rheumatoid arthritis. The ossification of ligaments may be seen in other diseases in accordance with the so-called law of Wolf and Holzknecht; "every tissue which is submitted to an excessive pressure or strain reacts by such type of formation as is best adapted to withstand it." The new bone formation in spinal tuberculosis has already been referred to, but in this and other diseases the relentless centrifugal progress is lacking.

Some Characteristic Symptoms

Pain is generally the first sign of the onset of the disease and may be indefinite in distribution without objective evidence, but three general types may be recognized.

Referred pains from the region of the sacro-iliac joints will be felt in the area of distribution of the lower lumbar and upper sacral nerve roots, and from the hip-joint will be felt along the inner aspect of the thigh and knee, and these sciatic pains are among the earliest signs.

Girdle pains occur in the active phase in the lumbar and dorsal regions, but it rarely happens that the foramina are actually obstructed by calcareous deposit; the pain is due to local congestion and swelling in the region of the foramina and to the affection of the costo-vertebral joints; any movement of the affected parts of the spinal column will be painful.

In the later stages pain will be due to stiffness or ankylosis and difficulties of posture, such as may be experienced when the joints have become ankylosed in a bad position.

The facies and gait are often characteristic even in an early stage. Muscle wasting is not conspicuous until the disease is well advanced and is due to disuse, contrasting with the trophic wasting of acute rheumatoid arthritis. Iritis is noted in about 10% of cases and was first reported about twenty years ago at a meeting of the Brussels Ophthalmological Congress. This was marked in one of my cases, a woman in whom the disease appeared to be related to a form of colitis or dysentery from which she suffered recurrent attacks. This is of interest in view of the cases associated with amoebiasis already referred to; in this case there had been no search for amoebic infection so far as the writer is aware. The occurrence of iritis has been cited as evidence that spondylitis is a form of rheumatoid arthritis but can carry no weight as an argument; it is probably due to rubbing the eyes with infected fingers.

Boland and Present (1945) have discussed fully the symptoms and radiographic appearances in a study of 100 cases, and set forth the evidence for and against the view that ankylosing spondylitis is a form of rheumatoid arthritis. They accept their identity—a view commonly held in America—but the arguments as stated by them against such a conclusion appear to be very strong. Oppenheimer (1938) is also of this opinion but the problem calls for further investigation; the evidence submitted in this paper points in the opposite direction.

Although this paper is not concerned with treatment reference to a report on the use of gold may be made as it has a bearing on the nature of the disease. Sherwood (1940) in discussing gold treatment in arthritis stated that haematuria only occurred in cases of ankylosing spondylitis and he had met with it frequently in that disease. It was his experience, which is generally shared, that gold was rarely of service in spondylitis; the writer would go further and suggest that if benefit followed

the use of gold in a case of spinal arthritis it was probably rheumatoid arthritis of the spine and not true ankylosing spondylitis.

Summary

The aetiology and pathology of ankylosing spondylitis are discussed in the light of Batson's work on the venous circulation from the prostatic plexus.

The influence of phosphatase on bone resorption and redeposition is described, and the possibility of a toxin from the prostate influencing this process is considered.

The bone changes in rheumatoid arthritis, spondylitis, and rickets are compared, and the conclusion is drawn that ankylosing spondylitis is not a form of arthritis but a toxic osteopathy.

The possible influence of sex hormones is discussed and found to be "not proven" but calling for further investigation. The importance of the dates of union of the epiphyses and the bearing of this on the disease is mentioned; the effect of the age at onset on the prognosis in the light of the pathology is pointed out.

Further investigation is urgently required in view of the great increase in the incidence of the disease, particularly in those cases which do not conform strictly to the classical pattern, since their inclusion in lists of cases used for drawing statistical and other conclusions is responsible for confusion.

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