Ankylosing Spondylitis*

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Within the last few years, the study of ankylosing spondylitis has produced some of the more remarkable new developments in the field of the rheumatic diseases. In modern days the disease has been described in Germany by Strümpell and in France by Marie. As a result, in Germany it is known as Strümpell's disease and in France as Marie's disease. Physicians in the United States and England, to be fair, call it Marie-Strümpell disease. It should be emphasized at this point that ankylosing spondylitis is not a variant of rheumatoid arthritis as it had been considered for a number of years. The term rheumatoid spondylitis is still occasionally used but should be completely abandoned.

The initial diagnosis of ankylosing spondylitis is often a difficult one to make. The best criteria we have are quite simple. They are 1) limitation of motion of the lumbar spine; 2) pain in the low back; and 3) limitation of chest expansion. As you can see, no laboratory tests except the x-ray film are used and in the early stages, x-ray film examination may not be helpful.

Examination of the lumbar spine in some studies shows that limitation of extension may actually be a better way of separating normal from abnormal spines (1), although limitation of flexion (flattening of the lumbar curve) is usually what we look for in the back examination. Moll and Wright (2) have shown that lateral spinal flexion is the best way to distinguish between spondylitis and lumbar disc disease. Spondylitis will also cause limitation in this direction.

The erythrocyte sedimentation rate can be normal in patients with ankylosing spondylitis. Even patients with rather marked degrees of pain can have normal sedimentation rates while patients who may just show changes in the sacroiliac, hips, or back without pain can have a significantly elevated sedimentation rate. Of course, rheumatoid factor is not found in these patients and can be of diagnostic help only by its absence.

The patient with ankylosing spondylitis is usually a young white male who gives a fairly typical story. Back pain usually wakes him up in the small hours of the morning. It is rare that he will complain of being unable to go to sleep because of pain. He will usually awake because of discomfort in the lower back and get out of bed. He may get relief (and go back to sleep) lying on the floor or sitting up in a hard back chair or sitting on the floor with his back against the wall. The pain frequently, as with sciatica, goes down the back of the legs. Alternation of the radiating pain from one side to the other is a typical feature which helps to distinguish the symptoms from those produced by a lumbar disc protrusion.

Examination of the x-ray films may initially show erosions in the sacroiliac joints and finally fusion, and of course, the "bamboo" spine of late disease is well known. The development of the changes in the spine can be shown diagrammatically so one can differentiate the syndesmophyte of ankylosing spondylitis from the osteophyte of degenerative joint disease (Fig. 1). This is taken from a recent article of Riley, Ansell, and Bywaters (3). On the left in the figure is seen the progression of osteophytosis and on the right, the progression of syndesmophytosis. The osteophyte is associated with disc narrowing. The bony plate is marginal and most importantly is horizontal as seen in stages three and four. It is built up at the base with subperiosteal bone. The base appears to lie against protruded disc substance. In ankylosing spondylitis, there is no

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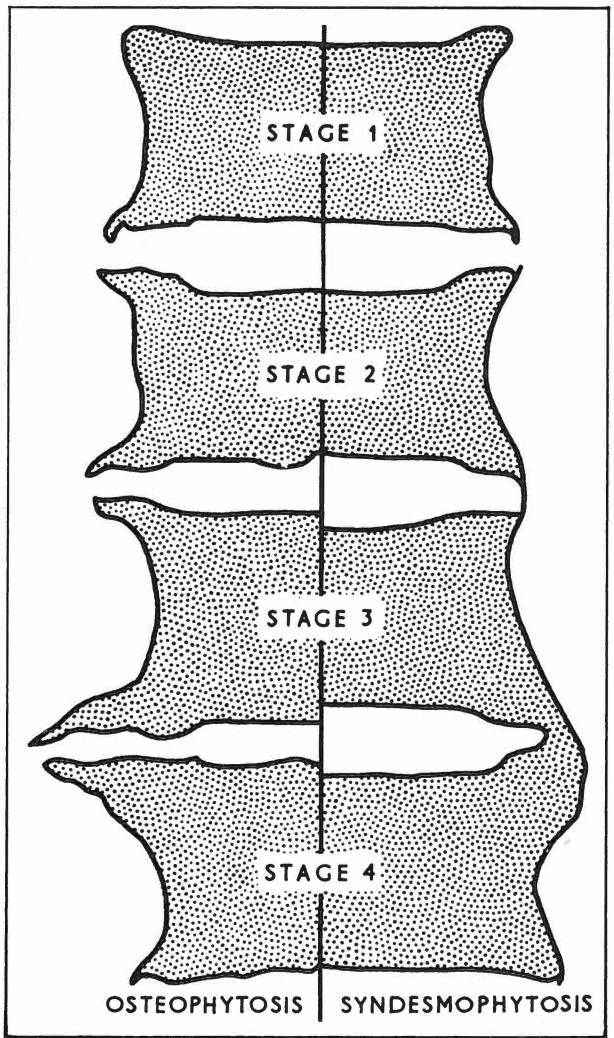

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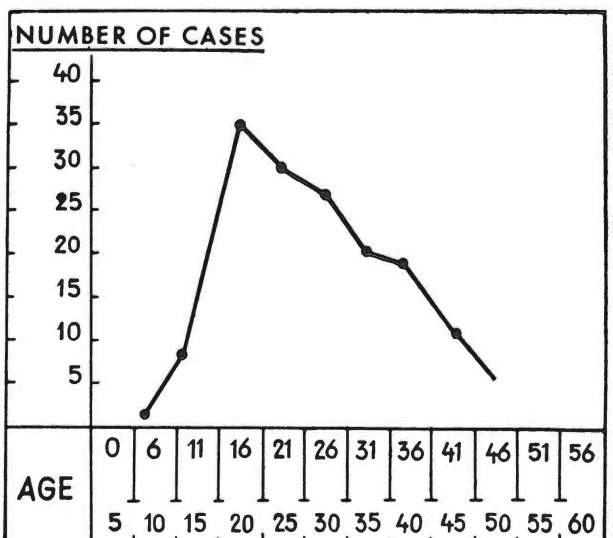
Fig 1.

disc narrowing or protrusion. A vertical plate is built up in the outer layer of the annulus fibrosis. These syndesmophytes will ultimately bridge in stage IV of the disease.

Ankylosing spondylitis is a disease of young males, seen in Figure 2 where the peak in a large series is found to occur in the late teens and early 20's (4, pg. 10). There is, however, a group of ankylosing spondylitics who start at an earlier age. Barbara Ansell and Eric Bywaters in Taplow, England followed up 139 patients with juvenile rheumatoid arthritis (JRA), 55 males and 84 females, for at least 15 years into adult life. What was striking about the 55 males was that 9% of them, as they went on to adulthood, developed typical ankylosing spondylitis.

Joint involvement in ankylosing spondylitis is, of course, different from that seen in patients with rheumatoid arthritis. Forestier (4) showed (Table 1) the high frequency of hip involvement in this disease when compared to patients with rheumatoid arthritis. In the rheumatoid, there is much more peripheral joint involvement.

There are a number of complications which are more specific and more frequent in ankylosing spondylitis than in many of the other forms of arthritis. Most of the complications that have been noted are listed in Table 2. Iritis is said to occur in up to 20% of patients. Aortic insufficiency is usually seen quite late in the disease. Heart block is rarely seen but also probably represents the same type of inflammatory action in the myocardium as is seen in the aorta. Amyloidosis, again, is not seen frequently but is a recognized cause of death in ankylosing spondylitis—certainly more so than with rheumatoid arthritis. Atlantoaxial subluxation is a constant threat to these people with spine fusion and can sometimes be fatal after only moderate degrees of trauma. Cauda equina involvement is rarely seen but, again, is a well-recognized problem. Pulmonary fibrosis of the upper lobe is of interest because this fibrosis, which may be typical of spondylitics, has been mistaken for tumor, tuberculosis, and the like.



From Forestier, J. et al., (4). Courtesy of Charles C Thomas, Publisher, Springfield, Illinois.
Fig. 2.

TABLE 1

PERIPHERAL JOINT INVOLVEMENT AT ONSET*

Joint	Ankylosing Spondylitis (200 patients) %	Rheumatoid Arthritis (100 patients) %
Hips	42	10
Knees	29	62
Ankles	7	58
Feet	12	28
Shoulders	30	64
Elbows	3	46
Wrists	5	82
Hands	7	94
Temperomandibular	6	8
Sternoclavicular	11	7

* After Forestier (4)

It probably accounts for some of the earlier statements made about the higher frequency of tuberculosis in these patients. It is remarkable how good pulmonary function is in these men with limited chest expansion. A recent study indicates that impairment of lung function is minimal in most of the patients with this disease (5).

The variants of ankylosing spondylitis are shown in Table 3. All of these conditions can show sacroiliitis and indeed in some cases, go on to more extensive spinal involvement quite similar to those seen in ankylosing spondylitis. I will mention some of these again later because of an interesting relationship.

For many years, it has been felt that there were strong genetic features connected with ankylosing spondylitis. Several years ago, when I was still in Dallas, Morris Ziff and I, seeing our patients at the Veterans Administration Hospital, were struck by the relative rarity of ankylosing spondylitis among our black patients. (One of the earliest clinicians to note this rarity was Elam Toone in 1949.) He found, in a group of patients that he was studying in the McGuire Veterans Administration Hospital in Richmond, 26 white and only three black patients with ankylosing spondylitis (6). Table 4 shows what we found in Dallas at the Veterans Hospital when we looked at the frequency of ankylosing spondylitis in relation to a number of other disease admissions rates and the male population of Dallas (7). As you can see, although the admission rate to the Veterans Hospital clearly reflected the racial distribution of the population, there was a marked discrepancy in the relative ratio of patients

TABLE 2

COMPLICATIONS OF ANKYLOSING SPONDYLITIS

Iritis
Aortic Insufficiency (Aortitis)
Heart Block (Myocarditis)
Amyloidosis
Atlantoaxial Subluxation
Cauda Equina Involvement
Upper Lobe Fibrosis

with ankylosing spondylitis. We were not satisfied with this view, thinking perhaps we might have an unusual situation. When data were pooled from a number of VA hospitals, we found a fourfold difference in the frequency of ankylosing spondylitis between whites and blacks. A search of the African literature showed that there are virtually no patients with ankylosing spondylitis in Africa among the black native population. A review of genetic studies in the United States indicated that the black population of the United States has a 20-25% admixture of white genes. This admixture of white genes would very nicely account for the fact that ankylosing spondylitis was only found in about 20-25% of the expected frequency, if it had the same distribution in the blacks as it did in whites.

This information was subsequently utilized by Schlosstein, Terasaki, Bluestone, and Pearson (8) at the Wadsworth VA Hospital in Los Angeles. The transplantation antigen known as W-27 was found in 8% of a caucasian population but was found in 88% of a group of patients with ankylosing spondylitis. It was also interesting to note that W-27 is not found in Black Africans and is present in an approximate frequency of 4% in Black Americans. To further support the relationship of this antigen to ankylosing spondylitis, W-27 was found in eight of ten Black Americans with ankylosing spondylitis.

Another and perhaps more striking correlary of

TABLE 3

VARIANTS OF ANKYLOSING SPONDYLITIS

Psoriatic Arthritis
Ulcerative Colitis
Crohn's Disease
Whipple's Disease
Behcet's Disease
Reiter's Disease

TABLE 4

RACIAL DISTRIBUTION OF ADMISSIONS AND OF ANKYLOSING SPONDYLITIS, RHEUMATOID ARTHRITIS, AND REITER'S SYNDROME AT DALLAS VETERANS ADMINISTRATION HOSPITAL

	Number White	Number Black	% White	% Black	White-Black Ratio
Males—Dallas, Texas (1960 census)	263,354	61,911	81	19	4.2
Male Admissions (10 months, 1966)	5,182	1,227	81	19	4.2
Ankylosing Spondylitis (1959–1966)	41	3	93	7	13.7
Rheumatoid Arthritis (1959–1966)	90	16	85	15	5.6
Reiter's Syndrome (1959–1966)	7	4			1.8

this data was recently presented by Rodney Bluestone of this group at the XIIIth International Congress of Rheumatology in Kyoto, Japan (9). In Table 5 are seen their most recent data. As you can see, W-27 is found in 14 of 156 patients with psoriasis alone. This is just about the frequency found in the normal population; however, in those patients with psoriasis who develop spondylitis it has been found in four of six individuals. In patients with colitis who developed spondylitis, this high frequency was again found. Perhaps even more remarkable are 15 out of 16 juvenile rheumatoid arthritics with W-27 who had spondylitis. Chronic Reiter's syndrome had the W-27 antigen in every case. Perhaps more astonishing were the studies they subsequently did looking at patients with acute Reiter's syndrome. Even those who do not have spondylitis showed W-27 in a remarkably high frequency.

We now seem to have a new tool for the diagnosis of some forms of arthritis. For example, in male children who develop what appears to be juvenile rheumatoid arthritis, looking for W-27 might give us a strong clue as to the future course of their disease. A similar use could be in suspected Reiter's syndrome. This has certainly opened the door to a most fascinating series of studies and conjectures about the relationship of the W-27 antigen and spondylitis.

In the treatment of ankylosing spondylitis, radiation therapy was at an early date, found to be effective for relief of pain; it's use was given up because of a reported high frequency of blood dyscrasias following its application. There are still some authors who feel that its limited use in patients who are having pain in spite of other therapy is of distinct benefit and of low risk (10). Indomethacin and phenylbutazone are the most frequently used drugs in the treatment of this disease. An observation was made recently that a patient with severe ankylosing spondylitis who did not respond to the above mentioned drugs responded quite well to penicillamine therapy (11). Steroids are of little use in this group of patients. Teaching the patients exercises in an attempt to increase diaphragmatic breathing is of benefit and exercises may sometimes help to maintain the spine in better position.

It is worth noting that what we have learned about this disease in recent years has provided us with better methods of establishing the diagnosis and prognosis of ankylosing spondylitis.

TABLE 5

	Frequency of W-27
Psoriasis with Spondylitis	4/6
Psoriasis Alone	14/156
Colitis with Spondylitis	4/6
JRA with Spondylitis	15/16
Chronic Reiter's with Spondylitis	8/8
Acute and Chronic Reiter's	22/23

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