DEFINITION

1. **Ankylosing spondylitis** is a chronic systemic inflammatory disorder principally affecting the axial skeleton, that is to say the sacro-iliac joints and the spine; the presence of sacroiliitis is its hallmark.

CLINICAL MANIFESTATIONS

Skeletal

2. Symptoms usually begin in late adolescence or early adulthood, the average age of onset being 25 years. The disease is three times more common in men than women. It is rare for the onset to be later than age 45.

3. The initial symptoms are low backache together with stiffness and discomfort in the thighs or buttocks. These symptoms are usually worse in the early morning, and are relieved by moving about. In some patients, the onset is in a peripheral joint, bilateral hip joint involvement being the most common. Occasionally the onset is acute and may be associated with generalised aching and fever.

4. Rheumatic disorders such as ankylosing spondylitis have a specific tendency to cause inflammation at the junction of tendons and bones (enthesitis), especially in the heels or feet; this process gives rise to localised pain, tenderness and sometimes swelling. Enthesitis may precede the development of the characteristic spinal changes, even by some years.

5. Physical signs may be minimal in the early stages but usually there will be limitation of movement of the lower spine and pain on forced movements of the sacro-iliac joints. There is likely to be tenderness at various bony sites affected by enthesitis. X-ray examination may show characteristic changes in the sacro-iliac joints and vertebral column.

6. Progress is extremely variable. In the more severe cases the lumbar spine becomes flattened, neck movements are restricted and peripheral joints may become involved. Eventually kyphosis may occur with the typical "poker back". At any point in its progress, the disease may subside temporarily or permanently.

Extraskeletal

7. Some patients with ankylosing spondylitis develop a progressive fibrosis at the lung apices. Cavities may develop in the lungs and become colonised by Aspergillus organisms.

8. As ankylosing spondylitis advances, there may be increasing fixation of the rib cage. The patient compensates by diaphragmatic breathing and there is little impairment of lung function until the degree of chest fixation is severe

9. Other extraskeletal manifestations of ankylosing spondylltis which may occur are -

   9.1. acute anterior uveitis. This is unilateral and has a tendency to recur. Recurrence may target the other eye.

   9.2. aortitis and aortic incompetence.

   9.3. cardiac conduction abnormalities.

   9.4. amyloid disease.

AETIOLOGY

10. The prevalence of ankylosing spondylitis differs in various ethnic groupings. It has a prevalence of 0.25%-1% in Europe and North America. The pattern of occurrence is changing as a result of changing environment. The disease tends to present at a later age in advanced countries than in underdeveloped ones. This may be due to modification of, or later exposure to, an environmental trigger.

Genetic factors

11. Ankylosing spondylitis is one of a group of conditions believed to have an **autoimmune** pathogenesis, but the exact cause remains unknown.

12. The body's immune system provides an essential barrier to a large range of pathogenic organisms. **Autoimmune disease** occurs if the immune network response becomes directed at the body itself rather than at foreign antigens, and thereby causes damage to the body's tissues.

13. Most work on autoimmune disease and its mechanisms has been done in animals. Despite recent advances in the molecular biology of the immune response, the precise aetiology of autoimmune disease remains unknown. In humans genetic factors are thought to play a part. This is supported by studies of familial aggregation of the conditions, and high concordance in monozgotic twins. However concordance is not complete and therefore genetic factors alone are insufficient for disease to develop.

14. Environmental factors which have been postulated as producing disease in predisposed individuals include infection (viral and bacterial), drugs and toxins. However positive identification of specific factors in the individual conditions and cases is very rare.

15. Individuals with one autoimmune disease appear to be at increased risk of other autoimmune conditions. These further conditions do not arise as a consequence of the first, rather the common factor is the genetic predisposition.

16. Heredity plays a role in susceptibility to ankylosing spondylitis; the concordance rate for monozygotic twins is 50% and the disease is 30 times more prevalent among relatives than non-relatives.

17. Several important genetic markers relating to inflammatory rheumatic diseases have been identified. These are inherited antigens on the surface of cells throughout the body which, because they were first identified on leucocytes, are known as **human leucocyte antigens** or **HLA**.

18. About 90% of white recipients with ankylosing spondylitis carry the antigen **HLA B27** compared with about 8% of the normal population. The prevalence of ankylosing spondylitis follows the distribution of HLA B27 in populations, and the highest prevalence of both has been observed in the Haida Indians living in British Columbia. The strength of the association between HLA B27 and ankylosing spondylitis differs appreciably among various ethnic and racial groups.

External factors

19. Ankylosing spondylitis occurs in Western Europe in about 2% of those who carry HLA B27. It is generally agreed that an environmental event is needed to initiate the disease process, though no specific agent has been identified. The likeliest candidate is bacterial infection.

20. The enteric bacterium Klebsiella pneumoniae has been suggested as an aetiological agent in ankylosing spondylitis. Extensive studies have been inconclusive, though they have served to emphasise the role of intestinal bacteria in the pathogenesis; elevated serum litres of antibodies to enteric bacteria such as K pneumoniae are common in patients with ankylosing spondylitis. It appears that infection with these or other organisms can act as a triggering factor in individuals rendered genetically susceptible by the HLA B27 antigen.

21. An increased incidence of prostatitis has been noted in those suffering from ankylosing spondylitis and a relationship with Reiter's disease has been suggested. It is now agreed that the two diseases are separate entities. However, non-specific urethritis or bacillary dysentery may precipitate the onset of ankylosing spondylitis or may cause exacerbations in established cases of spondylitis.

22. While physical trauma and severe physical stress may lead to symptoms in an asymptomatic case or aggravate symptoms in an overt case, there is no published evidence that these factors cause the condition.

CONCLUSION

23. Ankylosing spondylitis is an inflammatory disease of the spine. It is one of a group of conditions thought to have an autoimmune pathogenesis. The disease occurs when an exogenous agent triggers an immune response in persons carrying the genetic marker HLA B27.

REFERENCES

Calin A. In: Eds. Maddison P J, lsenberg D A, Woo P, Glass D N. Oxford Textbook of Rheumatology. 2nd Ed. 1998. Oxford. Oxford University Press. 5.5.5.

Eds. Calin A and Taurog J D. The Spondylarthritides. 1998. Oxford University Press.

Eastmond C J. Seronegative spondarthropathles. in: Eds. Weatherall D J, Ledingham J G, Warrell D A. Oxford Textbook of Medicine. 3rd Ed. 1996. Oxford. Oxford University Press. 18.5.

June 1999