*Occasional Survey*

# Haematology and Biochemistry of Ankylosing Spondylitis

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## Summary

**Forty men with ankylosing spondylitis have been reviewed clinically, radiologically, haematologically, and biochemically, and the results of the last two compared with a male group of rheumatoid patients and a control group. In the patients with ankylosing spondylitis the haemoglobin levels were much higher and the E.S.R. significantly lower than in the rheumatoid group, and the E.S.R. in the patients with ankylosing spondylitis was unrelated to disease activity as evidenced by pain. The alkaline phosphatase level was raised in 19 cases and in most was derived from bone. Though 10 patients had abnormal globulin levels, the albumin levels were normal, as was renal function in all cases.**


## Introduction

Ankylosing spondylitis is an inflammatory arthropathy of unknown aetiology which affects the sacro-iliac joints, spreads to involve the whole spine, and may affect the peripheral joints. It differs from rheumatoid, the other common inflammatory arthritis of uncertain aetiology, in the pattern of joint involvement, the predominance of male patients, and the tendency to bony ankylosis—though the early changes in the joint may be similar in the two conditions.[1] It is now well recognized that rheumatoid disease is a systemic disorder which may involve the kidneys,[2] the liver,[3] the lungs, and many other organs;[4 5] it frequently causes anaemia[5] and many abnormalities in the serum biochemistry.[6] Less is known about the systemic effects of ankylosing spondylitis though iritis and aortitis are well-recognized complications and there is probably an increased incidence of pulmonary fibrosis,[7–11] pulmonary tuberculosis, amyloid and peptic ulceration.[12]

This paper is a study of the haematological and biochemical features of a group of patients with ankylosing spondylitis in which we have looked for other evidence of systemic disease and also compared the results with those in a group of men with rheumatoid disease.

## Patients and Methods

Forty men, mean age 48·75 years (range 24 to 72) were seen as outpatients as part of a routine follow-up procedure. Most (87·5%) had received radiotherapy in the past. In each case the diagnosis was made on clinical grounds and was confirmed by the classical appearances of the radiographs of the sacro-iliac joints and spine. The degree of pain was assessed on an arbitrary scale before any of the other data were available: 0 for no pain at all, 1 for occasional pain produced by physical stress, 2 for some pain most of the time, and 3 for distressing pain. All the patients were assessed fully and in no case was there any coexisting disease which might of itself produce changes in the blood.

Haematological assessment included haemoglobin estimation, absolute values, red cell, white cell, and platelet counts, and a Westergren E.S.R. Biochemical estimations included: sodium, potassium, urea, alkaline phosphatase, bilirubin, albumin, globulin, calcium, and serum aspartate aminotransferase (SGOT). Patients who had a high alkaline phosphatase on the initial visit were seen again, the tests were repeated, and 5-nucleotidase, uric acid, and serum protein electrophoresis were performed. In addition a serum gamma-glutamyl transpeptidase which is raised in liver cell disease[13] was estimated by the method of Sasz.[14] A further specimen of serum was also electrophoresed on polyacrylamide gel to determine whether the alkaline phosphatase was of bony or hepatic origin. All patients had their urine tested for protein and a Rose-Waaler test was carried out on the initial visit.

The results have been compared with the normal range for the haematology and biochemistry departments. In the latter, the results are based on males in a random group of 200 normal blood donors, and the possible effects of age have been taken into consideration by deriving values for an age-matched control group and then obtaining the mean. In addition, for comparison, haematological and biochemical results were obtained on 40 unselected men with rheumatoid disease, mean age 54·35 years (range 24 to 71), of whom 20 were classical and 20 were definite by the revised American Rheumatism Association criteria.[15]

## Results

The important haematological and biochemical results are summarized in tables I and II and are compared both with the normal range and with the corresponding values for the group of men with rheumatoid disease. The red cell indices, total white counts and differentials, and the platelet counts were all normal. Similarly, the values for urea and electrolytes, the bilirubin, SGOT, calcium, and uric acid were almost all normal, and the means were well within the normal range. None of the patients had proteinuria and all had a negative sheep cell agglutination test.

Altogether, 19 of the 40 patients had a raised alkaline phosphatase, and after an interval 18 of these were reviewed and had the estimation repeated (the nineteenth had died in the interim period). Twelve still had a raised or borderline result. The level of alkaline phosphatase was unrelated to the activity or duration of the disease, and changes in the level in no way reflected changes in the clinical picture. However, the disease

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TABLE I—*Comparison of Haemoglobin and E.S.R. Results in 40 Patients with Ankylosing Spondylitis and 40 with Rheumatoid Disease*

| | Normal Range | Ankylosing Spondylitis | | Rheumatoid Disease | | Significance of Difference |
|---|---|---|---|---|---|---|
| | | Mean (S.D.) | Abnormal Results | Mean (S.D.) | Abnormal Results | |
| Haemoglobin (g/100 ml) .. .. .. .. .. | 14–18 | 14·89 (1·38) | 6 Low | 12·73 (1·85) | 20 Low | Highly significant ($P < 0·001$) |
| E.S.R. (Westergren) (mm/hr) .. .. .. .. | 0–12 | 28·75 (23·63) | 27 High | 59·19 (31·27) | 33 High | Highly significant ($P < 0·001$) |

TABLE II—*Comparison of Serum Alkaline Phosphatase, Albumin, and Globulin Results in 40 Patients with Ankylosing Spondylitis and 40 with Rheumatoid Disease*

| | Normal Range | Mean Corrected for Age | Ankylosing Spondylitis | | Rheumatoid Disease | | Significance of Difference |
|---|---|---|---|---|---|---|---|
| | | | Mean (S.D.) | No. Abnormal | Mean (S.D.) | No. Abnormal | |
| Alkaline phosphatase (K.A. units/100 ml) .. .. .. .. | 4–13 | 8·94 | 13·33 (4·81) | 19 High | 11·71 (5·71) | 3 High | Not significant |
| Albumin (g/100 ml) .. .. .. | 3·7–4·8 | 4·106 | 4·48 (0·41) | 6 High, 2 Low | 3·66 (0·50) | 19 Low | Highly significant ($P < 0·001$) |
| Globulin (g/100 ml) .. .. | 2·5–3·9 | 2·665 | 3·56 (0·59) | 8 High | 3·54 (0·73) | 4 High, 2 Low | Not significant |

TABLE III—*Results of Repeat Alkaline Phosphatase Estimations, Liver Function Tests, and Polyacrilamide Gel Electrophoresis on the 18 Patients with Raised Alkaline Phosphatase on First Visit*

| | No. of Patients | Alkaline Phosphatase (K.A. units/100 ml) | 5-Nucleotidase (IU/l) | Gamma-glutamyl Transpetidase (mU/ml) | Electrophoretic Pattern | Conclusion |
|---|---|---|---|---|---|---|
| Group 1 .. .. .. | 5 | 10–12 | 6–11 | 11–33 | Liver | Normal |
| Group 2 .. .. .. | 9 | 13–21 | 9–13 | 5–24 | Bone | Bone disease |
| Group 3 .. .. .. | 2 | 11·5 | 8 | 14 | Bone | Abnormal bone pattern |
| | | 11·5 | 15 | 10 | Liver and bone | |
| Group 4 .. .. .. | 2 | 13 | 18 | 66 | Liver | Liver disease |
| | | 15 | 14 | 47 | Liver | |
| Normal ranges .. .. | 4 | 4–13 | 0–12 | 0–33 | | |

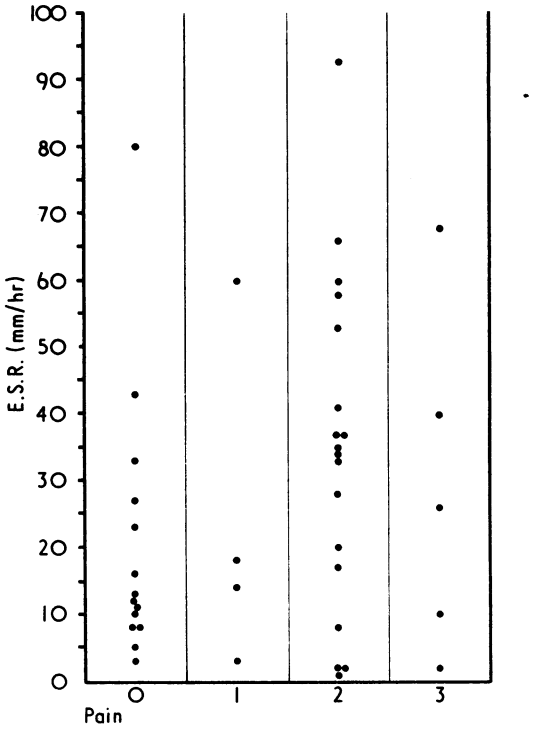
was more extensive in those with a raised alkaline phosphatase, 12 out of 18 having shoulder or hip involvement compared with only five with a normal phosphatase.

The source of the raised alkaline phosphatase initially found in these 18 patients was largely clarified by the estimations of the serum 5-nucleotidase, gamma-glutamyl transpeptidase, and the polyacrilamide gel electrophoresis carried out at their subsequent review, the results of which are shown in table III. No abnormality was found in five, a bony pattern was found in 11, and a liver pattern in two.

The E.S.R. was moderately raised in most patients but was poorly related to disease activity as judged by the amount of pain suffered (see chart). Eight of the patients had a raised globulin and all of these had a high alkaline phosphatase though there was no direct correlation between the actual figures. Those patients seen a second time all had an electrophoretic protein strip and 10 of the 18 showed abnormal patterns: raised alpha 2 in two, raised gamma in three, and both raised in five.

## Discussion

Ankylosing spondylitis has been regarded as a chronic inflammatory arthropathy with few systemic complications and few haematological or biochemical abnormalities. The most striking finding of this survey was the frequency of a moderately raised alkaline phosphatase (47·5%). This is known to occur in rheumatoid disease,[6] when it is a manifestation of liver dysfunction,[3] and similar results have been reported in cranial arteritis[16] and in polymyalgia rheumatica.[17] In ankylosing spondylitis, however, the abnormal alkaline phosphatase in most cases is derived from bone as shown by the bony type of electrophoretic pattern, the normal gamma-glutamyl transpeptidase, and the normal 5-nucleotidase. The significance of




Scattergram of E.S.R. results in patients with ankylosing spondylitis arranged according to amount of pain suffered. 0 = No pain. 1 = Occasional pain on physical stress. 2 = Some pain. 3 = Severe pain.

this observation remains uncertain but we presume it is the result of the process of bony ankylosis. It is of interest that it occurs in the more severely affected patients with a raised serum globulin and those with hip and shoulder involvement, but perhaps surprising that it was unrelated to the duration or the activity of the disease. In two cases the raised alkaline phosphatase was associated with high values for 5-nucleotidase and gamma-glutamyl transpeptidase and a liver pattern on electrophoresis, which is good evidence that they had liver disease.

The relatively high values for the haemoglobin and the serum albumin were unexpected. Most chronic inflammatory disorders are associated with a normochromic anaemia and many cause a low serum albumin. Altogether, 8 patients had haemoglobin levels over 16 g/100 ml with normal white cell and platelet counts. This raised the possibility of a mild secondary polycythaemia caused by the restriction of chest expansion which occurs in this condition.[18] The lungs, however, are usually normal in ankylosing spondylitis and an increased diaphragmatic contribution helps compensate for the rigidity of the chest wall.[19 20] Though the serum globulin is sometimes raised and there are abnormalities on the protein strip, the E.S.R. is of little value in this condition. It is unrelated to the amount of pain and appears to be a poor guide to disease activity, response to therapy, or to prognosis.

The negative findings are also of interest. Leucopenia or thrombocytopenia and renal disease are frequent complications of the "autoimmune disease" and related disorders. We found no evidence of these in this survey. Thus, though ankylosing spondylitis is known to be associated with extra-articular complications, such as iritis and aortitis, and we have shown that liver dysfunction can occur, the kidney and the bone marrow are not affected.

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# *Any Questions?*

*We publish below a selection of questions and answers of general interest*

### Gluten-free Diet in Multiple Sclerosis

*Is a gluten-free diet of any value in the treatment of multiple sclerosis?*

The use of a gluten-free diet in multiple sclerosis is based upon a chance observation of a well-known sufferer that after taking a diet of this nature his multiple sclerosis remitted to a remarkable degree. Marked spontaneous remissions are, of course, common in multiple sclerosis and, so far as is known, there is no valid scientific evidence to support the use of such a diet in the management of this disease. Nevertheless the diet though inconvenient can do no harm; for this reason many neurologists, aware that their patients have heard or have read of the publicity concerning this matter, are recommending their patients to try the diet. No controlled trials have yet been published and many patients under observation by the writer have found that the diet has been of no benefit to them personally.

### Risks of Simultaneous Use of Beta-adrenergic Blockers and Tricyclic Drugs

*Is there any clinical evidence of incompatibility between the beta-adrenergic blockers like propranolol and the tricyclic group of drugs—for example, amitriptyline, imipramine?*

Though I know of no documented clinical evidence for an incompatibility between beta-adrenergic blockers and the tricyclic antidepressants, the concurrent use of these drugs might be expected to potentiate their individual effects. Propranolol (but not practolol) and the tricyclic antidepressants undergo oxidation by microsomal enzymes in the liver. In vitro[1] studies have shown that the metabolism of propranolol is inhibited in the presence of tricyclic antidepressant drugs. Similarly, propranolol will delay the metabolism of antidepressants such as imipramine. Whereas findings obtained in vitro do not necessarily apply to the clinical situation, recent (unpublished) evidence obtained in dogs has confirmed that this interaction occurs in vivo. It would be wise, therefore, to exercise caution when using beta-adrenergic blockers and tricyclic antidepressant drugs together.

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### Topical Sensitivity to Chloramphenicol

*Have any cases been reported of sensitivity to chloramphenicol developing after its topical use?*

Delayed immune hypersensitivity to chloramphenicol is not uncommon after topical application. The clinical picture is of a contact dermatitis particularly around the eyes since the application is often used by ophthalmologists. The diagnosis is easily confirmed by a patch test.