

**Inhibitory Effect of Rheumatoid Sera on Cell Damage by Lymphocytes.** By I. G. BARNETT and I. C. M. MACLENNAN (*Radcliffe Infirmary, Oxford*)

If certain lymphocytes are cultured with target cells plus appropriate antibody against the target cells, the lymphocytes damage the target cells (Moller, 1965). In the rat, such cell damage can be inhibited by soluble antigen-antibody complexes (MacLennan, 1972).

In our experiments, normal human peripheral blood lymphocytes have been used to damage Chang liver cells grown in culture. Damage has been assayed by labelling these target cells with radioactive chromium before incubation and measuring the amount of radioactivity released into the supernatant fluid after exposure to antibody and lymphocytes (Holm and Perlmann, 1967).

We have found that sera from some patients with rheumatoid arthritis added to such cultures inhibit cell damage. Some apparently normal sera are also moderately inhibitory, but the inhibitory activity of rheumatoid sera is significantly greater than normal. Gel filtration chromatography on a Sepharose 4B column shows that the inhibitory activity lies between the IgG and IgM markers. (Similar work by Dr. Derek Jewell in our laboratory using serum from patients with inflammatory bowel disease has given similar results.)

These data are consistent with the hypothesis that the inhibitory activity in rheumatoid sera is due to physically altered IgG, very possibly in antigen-antibody complexes.

*Discussion*

PROF. E. G. L. BYWATERS (*Taplow*) I wonder whether sera from patients with infections such as malaria, for instance, will inhibit this type of cell damage?

DR. BARNETT We have not yet tested sera from patients suffering primarily from infectious diseases.

PROF. K. W. WALTON (*Birmingham*) I was also going to ask whether this is a non-specific method of detecting antigen-antibody complexes. Situations in which these are recognized to be present, such as systemic lupus erythematosus, might be ideal for investigating this possibility.

DR. BARNETT We certainly hope to be doing this.

DR. W. W. BUCHANAN (*Glasgow*) You suggested that this action may be caused by intermediate rheumatoid factor antigen-antibody complexes which are found in much higher titres in seropositive than in seronegative cases. Have you found any difference between seropositive and seronegative rheumatoid serum? Furthermore, if you suggest that the serum is protective in this way, how do you explain that the higher the rheumatoid titre, the worse the disease?

DR. BARNETT The complexes we are dealing with are much too small to contain 19S rheumatoid factor, and I suspect that when we have analysed the data fully we shall find that the titre of these complexes does not correlate with the titre of rheumatoid factor. Indeed, if rheumatoid factor were to combine with the intermediate complexes in the circulation, the resultant large complexes would be expected to be removed by the reticuloendothelial system more quickly than the intermediate complexes alone (Davis and Torrigiani, 1967).

DR. M. K. JASANI (*Horsham*) Although your data might suggest that synovial damage would be minimal in spite of continued lymphocytic infiltration in patients possessing the serum inhibitory factors—an inference which could incidentally explain the observations of Muirden and Mills (VII European Rheumatology Congress, 1971)—it remains possible that the joint inflammation persists in such patients because of vasculitis. In this respect our recent findings (unpublished), that skin homograft rejection in rabbits is mainly due to vasculitis, whereas the severity of lymphocytic infiltration depends largely upon the strain of the animal studied, may be of some interest.

DR. BARNETT Vasculitis is particularly associated with IgM-containing complexes which are much larger than the complexes that we are dealing with.

DR. A. G. MOWAT (*Oxford*) Is there a relationship between your material and the rheumatoid biologically active factor that Broder and his colleagues (1968, 1969) have been describing.

DR. MACLENNAN The physical properties of the activity we found would fit in very well with the findings of Baumel and Broder (1968).

**References**

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**Some Problems in the Development of a Total Shoulder Endo-Prosthesis.** By B. REEVES, B. JOBBINS, F. FLOWERS, D. DOWSON, and V. WRIGHT (*Orthopaedic Research Unit, St. James Hospital, Leeds, and the Department of Mechanical Engineering, University of Leeds*)

Replacement of the shoulder joint by previous prostheses involving substituting the humeral head have been unsatisfactory, because of faulty geometric design with failure to reproduce the wandering fulcrum normally seen in gleno-humeral movement, and to the frequent extensive damage to the rotator cuff when capsulectomy has been performed, so that stabilisation of the joint cannot occur to allow the prime movers to act.

To overcome this a total shoulder prosthesis has been designed with a wide range of movement as its own inherent stability. To attain the maximum use of the limited space in the shoulder joint after removal of the head and to retain the whole of the limited bone at the neck of the scapula for fixation of the glenoid component the head/socket relationship has been reversed, the ball being put on the glenoid component and the cup on the humerus.

A design problem has been the fixation of the glenoid component as methyl methacrylate has no bonding properties to metal. A series of experiments with various types of surface finish has shown increased adhesion under tensile loading with increasing roughness of the surface finish and extremely high loads were seen with grooved and knurled specimens. The scapular component designed with single and twin parallel spikes was tested and both these back plates showed failure in the region of 65–70 lb., which was the load failure for the cancellous

bone at the neck of the scapula into which the spikes had been inserted.

A small group of patients has been studied in whom the prosthesis was being inserted with complete relief from pain and the provision of a stable, mobile shoulder. One technical problem not yet fully overcome has been a loss of some potential movement due to tightness of the inferior capsule despite division of this at operation, within the limits imposed by its anatomical relationship.

#### Discussion

DR. D. BREWERTON (*London*) We have an alternative prosthesis at the Royal National Orthopaedic Hospital with a total follow-up of 2½ years. So far six of the patients have had rheumatoid arthritis. Since this prosthesis has been available it has been even more apparent how many patients there are in a rheumatoid clinic with excruciating shoulder pain for whom there is no other satisfactory answer. Apart from relief of pain, retaining internal rotation and flexion has great advantages over arthrodesis.

MR. REEVES I thoroughly agree that rotation is very important and that an arc of at least 90° is necessary, which must be associated with a total abduction of about 90° before these patients can make proper use of their upper limb.

#### Cardiac Involvement in Rheumatoid Arthritis—An Echocardiograph Study. By P. A. BACON and D. G. GIBSON (*St. Bartholomew's Hospital, London*)

Pericarditis in rheumatoid arthritis (RA) has been recognized for 90 years. It may easily escape notice but careful clinical investigation will show its existence in 10 per cent. of patients with chronic RA (Kirk and Cosh, 1969). The incidence in *post mortem* series is higher, averaging 30 per cent. Endocardial and myocardial involvement with granulomata similar to rheumatoid nodules have been described (Sinclair and Cruickshank, 1956) and may occasionally present as clinical valvular heart disease. The frequency of endocardial involvement has not previously been estimated. The development of echocardiography has made it possible to examine both the pericarditis and the mitral valve by a harmless non-invasive technique. We have used echocardiography to investigate a series of 22 patients with chronic nodular RA, 22 patients with classical or definite non-nodular RA, and 22 osteoarthritic controls matched for age and sex.

Pericardial effusion was found in eleven (50 per cent.) of the nodular and four (15 per cent.) of the non-nodular patients. It was found at all stages of the disease. An effusion was not detected in any of the controls. The incidence of pericardial involvement in severe RA is found to be higher by this technique than the usual clinical estimate and approximates to the *post mortem* incidence.

A slow rate of initial mitral valve movement was seen more frequently in the nodular than in the non-nodular RA patients. The mean rate of movement in both groups was less than that of the control group. A very slow rate of mitral valve opening, comparable to that seen in rheumatic mitral stenosis, was found in three nodular patients, but none of the others. It is suggested that this may represent granulomatous infiltration of the valve while the more general slowing may be related to myocardial disease.

#### Discussion

DR. J. A. COSH (*Bath*) May I congratulate Dr. Bacon on this very nice presentation, confirming what can be found by careful clinical assessment.

You spoke of a posterior pericardial effusion in one case; does this mean that it was loculated by effusions? Does your technique tell us when there is shaggy thickening of the pericardium as distinct from free fluid?

Regarding the changes in the mitral valve, Cruickshank (1958) found non-specific changes in the endocardium and sometimes in the valve which are not the same as granulomata. Is this what you have been finding?

DR. BACON With large pericardial effusions one expects to find them both anteriorly and posteriorly. In these cases most were posterior, suggesting that they may be loculated, although there is no direct evidence to this effect.

Regarding the mitral valve, it is, of course, possible that this is non-specific thickening but, in most cases of so-called non-specific thickening that have been histologically examined, one has been surprised to find granulomata.

PROF. E. G. L. BYWATERS (*Taplow*) Have you had an opportunity to look at valvular movement in other patients with prolonged locomotor disability, and have you studied any cases of systemic lupus erythematosus where mitral disease sometimes occurs?

DR. BACON Most of the control patients, particularly the older ones, were in-patients for hip replacement for severe osteoarthritis. We have looked at one or two cases of systemic lupus erythematosus. They had abnormal myocardia but we have not seen a mitral valve abnormality.

#### References

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#### Surgical Trends in Rheumatology. By H. HILL (*Stoke Mandeville*)

An eighteen-bed Rheumatology Unit was established in the Oxford Region in 1953. The first operation, excision of the head of the radius, was performed in 1956. Now two-thirds of the in-patients are admitted primarily for a surgical procedure, this procedure being regarded as an incident in the overall management of rheumatic conditions. Patients are admitted to the medical ward and return there after the operation to ensure continuity of medical and nursing care, and physio- and occupational therapy.

From 1956 to 1970 patients have made 1,835 visits to theatre, 827 for major surgery, 687 for minor surgery, and 321 for manipulation. Manipulations were common in the early years, but this procedure is now largely confined to the ankle and tarsus. From 1962 to 1970, the annual number of minor operations has fluctuated between sixty and eighty. The number of major operations has risen gradually, and since 1956 has exceeded minor operations, now averaging 100 per annum. Total replacement of the hip, synovectomy of the knee, and excision of the lower end of the ulna account for most of the increased turnover in major surgery.

The indications for some operations are clear and