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

- Baumel, R., and Broder, I. (1968) *Clin. exp. immunol.*, 3, 525
 Davis, J. S., and Torrigiani, G. (1967) *Proc. Soc. exp. Biol. (N.Y.)*, 125, 772
 Gordon, D. A., Bell, D. A., Baumel, R., and Broder, I. (1969) *Ibid.*, 5, 57
 Holm, G., and Perlmann, P. (1967) *Immunology*, 12, 525
 MacLennan, I. C. M. (1972) *Clin. exp. Immunol.*, 10, 275
 Moller, E. (1965) *Science*, 147, 873

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