Discussion

DR. J. BENRAAD (*Holland*) Did you measure the concentration of cortisol acetate before and after phenylbutazone?

DR. DOWNIE No.

DR. J. BENRAAD (*Holland*) I asked this question because it has been reported (Wise, Margraf, and Ballinger, 1971) that in rheumatoid arthritis there exists a very high concentration of cortisol acetate in blood as compared to the concentration in normal individuals.

DR. DOWNIE Much has been done on the metabolism of cortisol in rheumatoid arthritis, but one wonders just what the significance of this is.

DR. F. W. J. GRIBNAU (*Holland*) You have already mentioned the work of Stenlake, Davidson, Jasani, and Williams (1968) and you will know the work of the Copenhagen group (Hvidberg, Schou, and Jansen, 1971).

Brodie (1966), speaking on the pharmacological implications of drug transport, speculated about the role of displacement of corticosteroids from transcortine in rat plasma by various compounds and particularly related this to the anti-inflammatory activity of these compounds. Would you like to comment on this?

DR. DOWNIE There have been many suggestions that the anti-inflammatory drugs act by displacement on cortisol-binding sites. The problem with Stenlake's work, and I was associated with it, was that we used rather unphysiological levels. There may be some displacement but it is very difficult to be sure, as it requires measuring micro amounts of cortisol by a radioimmune assay technique and we do not have this available at the present time. One of the problems is that most people look at the plasma proteins and forget that, as far as cortisol is concerned, up to 25 per cent may be bound to the red cells, and it may well be that we split it from these rather than from the proteins.

References

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Mechanism of Action of Some Anti-Rheumatic Drugs in Allergic Blood Diseases. By H. O. NIEWEG, G. S. VAN DER SCHANS, F. BOS-VAN ZWOL, and P. J. STIJNEN (*Division of Haematology, University of Groningen, Holland*)

Some years ago we reported that in some individuals thrombocytopenic purpura may be related to the use of aspirin. This was confirmed by subsequent provocation tests with this drug. Since then we have tried to differentiate aspirin-induced thrombocytopenia from the idiopathic type by laboratory methods such as the platelet factor 3 activation (PF3A) test. The results with normal platelets, patients' serum, and aspirin suggested that 25 out of 34 thrombocytopenic patients were hypersensitive to this drug.

In allergic thrombocytopenia, drugs are generally believed to act as haptens, but this is unlikely in the case of aspirin, because IgG from patients does not bind with this drug. Moreover, the antibodies also injure normal platelets in PF3A tests in the presence of quinine, quinidine, chloroquine, 1,4-naphthoquinone, and especially of PCMBS, a selective inhibitor of membrane SH groups.

Antibodies active in the presence of PCMBS were detected in sera not only from patients with thrombocytopenia induced by various drugs but also from patients with other types of thrombocytopenia. We assume that the various primary factors—known or unknown—apparently induce an identical change of the platelet membrane which makes it antigenic. In drug-induced thrombocytopenia, a sublethal membrane change induced by the drug is made lethal by subsequent antibody action. For this two-step mechanism the term 'spoiled membrane allergy' is used.

A similar final common pathway of minor chemical damage amplified by immunological injury also seems probable in drug-induced aplastic anaemia and agranulocytosis.

Discussion

DR. L. E. GLYNN (*Taplow*) Do the complement components of serum play an important part in this reaction?

PROF. NIEWEG Not necessarily. We have performed complement-fixation experiments with platelets, serum, and PCMBS and about half are positive.

DR. L. E. GLYNN (*Taplow*) In the absence of complement, could you get a positive effect on the stypven time?

PROF. NIEWEG For the normal platelets, we used a platelet-rich plasma so that the complement was present.

DR. L. E. GLYNN (*Taplow*) But in the presence, for example, of cobra venom, would that inhibit the reaction?

PROF. NIEWEG I do not know; we have not tried that.

DR. W. H. D. DE HAAS (*Holland*) Did you study the influence of gold, which is one of our chief tools?

PROF. NIEWEG We have not studied gold *in vitro*. We had some patients with gold thrombocytopenia, but gold is rather difficult to handle *in vitro* as it is oily, whereas quinine and chloroquine are nicely soluble and can be easily handled.

DR. J. KAKAKI (*Holland*) Did you look for specific drug antibodies in other immunoglobulin classes besides IgG.?

PROF. NIEWEG No.

Mobility of the Metacarpophalangeal Joints in Normal Subjects and in Rheumatoid Patients. By W. Y. LOEBL (*Westminster Hospital and Institute of Orthopaedics, London*)

The function of the hand depends to a considerable extent on the function of the metacarpophalangeal (MCP) joints. Ulnar drift in rheumatoid arthritis cannot