two. Skull traction was applied for a few days to 10 weeks before operation. Neurological disturbances disappeared before operation in most cases. Owing to poor general health two patients were not operated upon. A stabilizing operation was performed in fourteen cases and a wire bone graft spondylosis was performed using the posterior approach. Postoperatively skull traction was continued for 2 to 5 months (average $2\frac{1}{2}$). The results are tabulated below.

Operation	Neurological symptoms directly after operation	Follow-up period (yrs)	Neurological complaints at follow-up
On C 1/2 7 RA 2 RA	None to few None to few	2-8 $1\frac{1}{2}$ * 4*	Unaltered Many
1 RA	Died 15 days post-operatively of pulmonary embolism		
1 AS 1 not known	None None	9 6	None None
Below C2 1 RA	None	1*	Many
Both on and below C1/2 1 RA	Few	1	Unaltered

The postoperative neurological symptoms were none or few in all cases. In three patients (marked *), a relapse of the neurological complaints occurred. In two cases this happened 1 and $1\frac{1}{2}$ years later due to an unstable graft; in the other case operated on for a slip C1/2, this was due to a new slip of the C7-T1 level 4 years after operation. Eight patients died 15 days to 8 years after operation. One was probably due to a cord lesion due to an unstable graft, and the others to miscellaneous causes.

Six patients are alive 2 to 9 years postoperatively, but one has a neurological relapse due to a slip of C7-T1.

At follow-up *x* ray we have found, in two RA cases, a progression of the destructive lesions and in two others ankylosis at lower levels. Except for the three patients with relapse, all were happy with the results of the operation. We think that the results of this type of treatment are gratifying and shall therefore continue with it.

Discussion

PROF. G. CHAPCHAL (*Holland*) I think it is most important to immobilize and reduce the condition. This is followed by fusion. We immobilize the head and neck in a 'halo' traction; this allows operation without any movement between the head and cervical spine and enables the patient to walk immediately after the operation.

DR. R. M. BENNETT (*London*) It has often occurred to me, in more flippant moments, that patients with erosions of the odontoid process may possess one peculiar advantage over the rest of us—namely, an immunity from judicial execution by hanging. The cause of death in hanging is usually attributed to a 'pithing' of the spinal cord by the odontoid peg.

DR. L. E. GLYNN (*Taplow*) I am probably the only person here who has ever done a *post mortem* on persons who have been hanged, and I did this on two who were executed in Pentonville Prison some years ago. Neither had dislocations of the odontoid process; their cervical spines were broken much lower down.

DR. R. L. F. NIENHUIS (*Holland*) In patients with rheumatoid arthritis undergoing operations there may be cervical lesions without neurological symptoms or signs. This is especially important when they are going to receive endotracheal anaesthesia. Preoperative *x* rays of the cervical spine must therefore be made.

DR. MEIJERS It is the custom in our unit to do that. We also ask the E.N.T. surgeons to examine these patients as there may be difficulties due to crico-arytenoid joint involvement. Regarding Prof. Chapchal's comment, our patients are so very disabled that a plaster jacket for them is a burden—so heavy that they are unable to stand it. This is why we have not used 'halo' traction.

DR. J. A. MATHEWS (*London*) I should like some practical advice. We try to protect the cervical spine of these patients by giving them restrictive collars of one sort or another. It seems to me that the more restrictive the collar, the more dangerous it may be to the upper cervical spine, as when we effectively immobilize the occiput and chin the only way the patient can open his mouth to eat is by flexion and extension of the upper cervical spine. There are some very complicated ways of overcoming this but I have no practical experience of success with these. Have you?

DR. MEIJERS Collars are a very difficult subject; the more complicated they are the more difficult they are to wear, and I think a simple cardboard collar is the best. Many patients patiently wear the collars in hospital but discard them at home. On one occasion we had a patient with a C3/4 subluxation who was immobilized in a collar and has worn this faithfully for 3 years. Now these vertebrae have fused.

Effects of Phenylbutazone on the Metabolism of ^{14}C -Cortisol. By W. W. DOWNIE, G. REID, and M. C. K. BROWNING (*Departments of Pharmacology and Therapeutics, and Clinical Chemistry, Dundee University*)

It is known that drugs such as phenobarbitone and diphenylhydantoin alter the metabolism of endogenous cortisol by their effects on steroid-metabolizing enzymes in the liver. Phenylbutazone has been shown in animals to induce such enzymes, and as this drug is frequently used for long periods in the treatment of rheumatic disorders, it was considered of value to investigate its effects on endogenous cortisol metabolism in man. A number of indices were studied before and after one month's ingestion of phenylbutazone at therapeutic dose levels in normal volunteer subjects. These indices included the disappearance rate of ^{14}C -cortisol from plasma, plasma 11-hydroxycorticosteroid levels, cortisol secretion rate, 6-hydroxycortisol, and the distribution of radioactivity in the urinary metabolites. A significant fall in the half-life of ^{14}C -cortisol in plasma was noted, although there was no significant rise in the cortisol secretion rate nor in the excretion of 6-hydroxycortisol. An increase in the percentage of radioactivity associated with the urinary polar compounds, cortol and cortolone, was found, suggesting that phenylbutazone had produced enhanced activity of the enzyme 20-hydrogenase.

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.

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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