unstintingly during the laparotomies upon the chimpanzees. I wish to thank Mr. Boife Freeman, senior technician, for the preparation of the histological sections.

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Medical Memoranda

Prevention of Peptic Ulceration During Corticosteroid Therapy

That the oral administration of cortisone and its analogues predisposes to peptic ulceration is no longer in dispute. In a study reported by Kammerer *et al.* (1958), 36 out of 117 rheumatoid arthritic patients receiving oral corticosteroid therapy were found to have radiological evidence of peptic ulceration. Treatment of the affected patients included cortisone, hydrocortisone, prednisone, "medrol" (6-methyl prednisolone), and triamcinolone. Of special interest was the finding that 31 of the 36 ulcers were gastric and the majority were on the greater curvature. This finding, also noted by others, suggested that oral cortisone-like steroids do not activate the factors that commonly lead to peptic ulceration, but have a separate contribution to make.

We have found the incidence of dyspepsia remarkably low in patients receiving controlled adrenal stimulation therapy (corticotrophin) for prolonged periods (West, 1957). This, coupled with the finding that there is not an increased incidence of peptic ulceration in patients with Cushing's syndrome (Kirsner and Palmer, 1952), suggests that orally administered cortisone-like steroids may affect the stomach wall *directly*. Such a local action might be avoided in the following ways:

1. By giving antacids with the steroid. This has been done routinely by many physicians ever since cortisone became available, and has not prevented the formation of ulcers.

2. By giving an anticholinergic drug that will reduce gastric secretory activity (Carbone and Liebowitz, 1958). This may be of value even though the consensus of opinion is that oral corticosteroid therapy does not raise the level of free hydrochloric acid and pepsin above the normal. A preliminary trial at this centre of prednisolone combined with an anticholinergic drug ("ultracortenol"+"antrenyl") in patients who already had dyspepsia on oral prednisolone has proved encouraging enough to justify a controlled trial.

3. By coating the prednisolone tablet so that it will not dissolve in the stomach. Experience with the use of such a tablet is reported below.

4. By giving the corticosteroid parenterally.

We have found that prednisolone given as "delta cortril suspension intramuscular" is suitable for long-term depot therapy and that it is of real value in the treatment of patients who have severe gastric symptoms (West, 1958).

Enteric-coated Prednisolone Tablets

The cortisone type side-chain, which is common to all the physiologically active cortisone-like steroids at present in use, is readily destroyed by certain intestinal bacteria. This can be shown *in vitro*, and is found to be the case *in vivo* if an enteric-coated prednisolone tablet does not dissolve rapidly after leaving the stomach. We found that if a patient was changed from plain prednisolone tablets to an enteric-coated tablet that had too thick a coating his symptoms relapsed. The failure to absorb all the prednisolone could be confirmed by changes in the urinary excretion of total 17-hydroxy-corticosteroids. Tablets very heavily coated may, of course, be passed unchanged.

After a number of failures we found that an enteric-coated prednisolone tablet was absorbed normally, so we proceeded to give it to a series of patients who were complaining of dyspepsia while receiving plain prednisolone tablets.

Fifteen patients were treated. Of these, three thought the tablets had less effect on their arthritis, so they reverted to plain tablets before the effect upon their gastric symptoms could be assessed. One patient found her gastric symptoms worse. She had at the same time symptoms arising from diverticulitis, so was not really a suitable patient for the trial. The remaining 11 patients all claimed a major relief of gastric symptoms and found the antirheumatic effect unchanged. Conventional antacid therapy was being given before the changeover. Subsequently most of these patients were able to dispense entirely with the antacids. All 11 patients were suffering from rheumatoid arthritis. Two were receiving a high dose of prednisolone for complicating polyarteritis and a third had recently had a haematemesis. The findings justified the change to enteric-coated tablets, but the case for their use would have been stronger had the trial been "controlled." As it was, preliminary studies of enteric-coated capsules and tablets had provided evidence of the value of such coating so that subsequently it was not regarded as ethical to withhold them from the patients with dyspepsia referred to above in order to have a control group.

Thanks are due to Pfizer Ltd., who prepared the enteric-coated prednisolone tablets for us and made available a generous supply, and to Dr. E. V. B. Morton, of Boots Pure Drug Co. Ltd., who supplied enteric-coated capsules and tablets for the preliminary studies.

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After several meetings between representatives of the medical profession from all parts of the country, the International Diabetes Federation, a predominantly lay organization, has decided to form a Medical Section. Membership will be open to any doctor who is interested, but non-medical members will be eligible for election only with the consent of the Section's executive committee. It is proposed to hold at least one medical meeting a year when special lectures and discussions will be arranged. (*News Bulletin*, July, 1959, International Diabetes Federation.)