HEBERDEN SOCIETY

Clinical Meeting.—At a meeting held at the West London Hospital on February 26, 1960, the president, Dr. F. Dudley Hart, was in the chair, and the following papers were presented:

Results of Long-term Treatment of Rheumatoid Arthritis with Corticotrophin. DR. P. S. DAVIS (West London Hospital): Daily subcutaneous injections of corticotrophin gel were given to forty patients, all of whom were suffering from severe, active rheumatoid arthritis and had not improved with rest in hospital, salicylates, and (in the majority of cases) gold or phenylbutazone, and they were followed up for a minimum of 2 years. Treatment had been discontinued in six patients because of side-effects and in seven because of acquired resistance, and complete remissions in a further six patients had allowed treatments to be stopped before the conclusion of the 2-year assessment. Dosage was adjusted according to the clinical response, and the total 17-hydroxycorticosteroid output was watched in order to avoid over-stimulation of the adrenals and to minimize side-effects.

The results of treatment on the strength of grip, erythrocyte sedimentation rate, and radiological appearances were at least as good as those obtained with prednisolone according to the published results of the Medical Research Council/Nuffield Foundation Prednisolone-Analgesic Trial (Ann. rheum. Dis., 1959, 18, 173). Preliminary results also indicated that corticotrophin gel caused a fall in the titre of the Rose-Waaler test in an appreciable number of patients, in contrast to the tendency of the titre to rise with prednisolone therapy. The relative ease of withdrawal of therapy when necessary was another factor in favour of corticotrophin gel.

Discussion.—The President asked whether there were any septic or allergic reactions.

Dr. Davis replied that they had had none since they went over to subcutaneous injections, and only two or three in patients receiving the original intra-muscular injections. One or two cases of allergy associated with resistance to corticotrophin subsequently responded to increased dosage.

Dr. G. R. Newnes (Sheffield) said that their experience in Sheffield corresponded very closely with that of Dr. Davis. They felt convinced that corticotrophin was the treatment of choice for the severe rheumatoid arthritic. It was more physiological than treatment with steroids and, provided the dosage was controlled carefully, and the patient very quickly learnt to help with the control of dosage, the complications and side-effects were very much less. They felt that there was evidence that corticotrophin could be given for prolonged periods. They had met the difficulty of acquired resistance to corticotrophin, and that was something to be overcome.

During the past 8 years, in many thousands of injections, they had had only one abscess, which was due to an intramuscular injection.

Dr. A. St. J. Dixon (London) said that these results were encouraging, but before accepting them entirely there were one or two points he would like to clear up. He wondered if the improvement in the sheep-cell titre could be due to improvement in the test? He asked if there were any deaths in the series, and whether they had compared their x rays with those of the M.R.C. series.

Dr. Davis replied that they could exclude improvement in the test because the patients transferred from corticotrophin to steroids then showed a rising titre, in the same year. They had not had an opportunity of seeing the x rays of the M.R.C. trial, but their own x rays were read without knowledge of what each patient was receiving. They had had one death from diffuse intestinal bleeding in a patient who was overstimulated with corticotrophin.

Dr. J. Sharp (Manchester) asked for further information about acquired resistance.

Dr. Davis replied that that was a very complex problem. They had found that in some patients the resistance was a temporary phenomenon. If the dosage were increased or injections given twice daily the adrenals might respond. In one striking case, a young woman, after an initial good response, became resistant and needed 80 units daily. Then, some months later she became responsive again and the dosage could be cut to 10 units daily. They had sometimes had to increase the dosage to 80 units twice daily to obtain a response.

The President asked whether this involved the same batch of ACTH gel.

Dr. Davis replied that the problem of batch variation was largely a thing of the past.

Dr. G. D. Kersley (Bath) asked whether anybody was working with a combination of ACTH and steroids. He had used them together in several difficult cases with benefit, but he wondered whether stimulation occurred once or twice a week in a patient on steroids would be beneficial if the patient had an accident or any sudden stress.

Dr. Davis said that it had been shown that stimulation with corticotrophin did not protect the patient on ordinary oral steroids, as it was pituitary suppression that resulted from corticosteroids. Why the patient did not have a withdrawal syndrome when corticotrophin was stopped was far from clear. He thought one important factor was the way in which the drug was given once daily. There was only intermittent adrenal stimulation for about 16 hours in the day.

Dr. W. A. Bourne (Hove) asked whether they had made any observations on the effects on the spine during treatment.

Dr. Davis said that osteoporosis was the same as with oral corticosteroids. In the entire series they had seen only about 4 per cent. in the 8 years.
Generalized Rheumatism in Temporal Arteritis. Dr. G. Parsons Smith (West London Hospital): A review of the clinical and pathological features of temporal arteritis, with representative cases shows that, although the lesions occur principally in the carotid and vertebral arteries, with especial threat to vision, the characteristic giant cell arteritis has been found in the larger arteries to the limbs and viscera. Among the presenting symptoms of the disease, diffuse muscle and joint pains are not uncommon, and severe, localized, muscular pain may occur during an acute episode. Corticotrophin therapy was of some value, especially when ocular symptoms called for urgent treatment to save vision.

Heberden (1816) mentioned, among cures for headache, the opening of a temporal artery, an operation which is now most effective in relieving the local pain. The rheumatic symptoms are immediately controlled with 5 mg. prednisolone thrice daily, but in those patients in whom vision fails intravenous corticotrophin should be given as soon as possible.

REFERENCES

Discussion.—Dr. M. S. Good (Aylesbury) asked whether heparin had been used in many cases. The pathology was in some doubt and it was difficult to know how much was due to thrombosis and how much to arteritis. He agreed with the speaker’s views on the use of steroids. He had had a personal communication from Dr. G. A. K. Missen who had examined seventeen cases which had come to post mortem; in this series the circle of Willis had not been affected, but mainly the vertebral and, to a lesser degree, the meningeal arteries.

Dr. Parsons Smith replied that he had used heparin, occasionally. The posterior cerebral artery could be involved as in the case described by Crompton.

The President said that on the reported findings early steroid therapy was justified in prevention of the ocular features. He had been disappointed in one or two cases, but he had probably started too late and given too little.

Dr. Parsons Smith replied that he would recommend the use of corticotrophin for every elderly person who suddenly lost the sight of an eye. It could do no harm and might be the means of saving sight. He gave ACTH for one month and apart from a few rheumatic pains there were no residua.

The President said that there was occasionally a residual raised erythrocyte sedimentation rate for some weeks or months, which suggested that the inflammation was not completely suppressed.

Dr. W. A. Bourne (Hove) said that he agreed with starting steroids at an early date. In one case in which the diagnosis had been made he had waited for 24 hours to obtain the result of a biopsy and the patient had lost his sight in that time. Another patient had lost his sight and developed a monoplegia.

Dr. G. D. Kersley (Bath) asked what dosage of corticotrophin had been given.

Dr. Parsons Smith said that he gave 20 units intramuscularly the first day and 20 units the second day; then 50 units intramuscularly for 2 days, and 20 units intramuscularly twice daily for a month.

Dr. M. S. Good (Aylesbury) said that, of the twenty personal cases he had seen, twelve had eye signs and symptoms, and in these corticosteroids were essential. The question whether one should start the treatment in patients who were merely suffering from headaches before biopsy confirmation of the disease was a more difficult one. He did not think that those patients should be given ACTH straightaway. It was only rarely that the eye symptoms were early and so dramatic as in the case demonstrated by Dr. Parsons Smith.

The President: "How rare?"

Dr. M. S. Good: "About 1 per cent."

The President: "I thought it was more than that."

Dr. Parsons Smith: "The world literature gives 25 per cent."

Dr. Good: "As presenting symptoms of blindness, only about 1 per cent."

The President: "You mean temporal arteritis with acute ocular involvement, do you not?"

CLINICAL PRESENTATIONS
Arthrodosis of the Wrist in Rheumatoid Arthritis. Mr. J. C. F. Hindench (West London Hospital) showed cases and described the indications, technique, and results of arthrodesis of the radiocarpal joints in rheumatoid arthritis. The beneficial effects were discussed, especially in terms of subsequent hand function, and it was stressed that no surgical hazards had resulted from concurrent corticotrophin therapy in these patients.

Dr. J. H. Barson (The Middlesex Hospital) described two cases of Reiter’s syndrome complicated by spondylitis and aortitis with aortic valve incompetence. The first patient, a woman aged 29, had been shown at a clinical meeting of the Society in 1950 by Dr. F. Dudley Hart, and the progressive features of the illness were listed and necropsy findings presented.

Dr. G. Brown (Westminster Hospital) presented the case history of a man suffering from classical ankylosing spondylitis complicated by iritis and aortic incompetence.

Side-Effects of Oral Corticosteroid Therapy in Adult Rheumatoid Arthritis. Dr. Oswald Savage (West London Hospital): The third M.R.C./Nuffield Steroid Trial* showed that patients on prednisolone maintained a significant advantage over those on aspirin or other analgesics throughout a 2-year period. In addition, repeated radiological examination demonstrated that the progression of joint damage was less marked in the prednisolone-treated group and that, if the dose was kept below 15 mg. daily, serious side-effects were relatively uncommon. Because of this the relative incidence of side-effects assumes increasing importance.

Figures of incidence were collected from eight centres, totalling 910 cases. The most common was rounding of the face in women, but this rarely necessitated withdrawal of the treatment. Dyspepsia was common (32 per cent.) and although peptic ulceration (10 per cent.)

cent.) was infrequent, most of the ulcers gave rise to complications. A series of 104 cases from the West London Hospital was compared with the eight-centre survey. Dyspepsia was higher (47 per cent.); of cases of dyspepsia 43 per cent. were mild and transient, 34 per cent. moderate with a negative barium meal, and 23 per cent. (11 of the 104 cases) had proven ulcers. The average dose in the cases developing ulcers was 25 mg. prednisolone per day. In the cases of dyspepsia with negative radiology the average dose differed little from those without indigestion. The importance of aspirin in addition to steroids in producing dyspepsia was discussed.

There seemed to be no doubt that, in conditions such as ulcerative colitis and asthma, where long-term steroid therapy was used without the addition of aspirin, dyspepsia was uncommon. Hypertension was quite common (13 per cent.), but very rarely necessitated withdrawal of steroids.

Other side-effects (such as fractures, peripheral neuritis, bruising, and mental changes) were under 5 per cent. It was concluded that in order to reduce the incidence of side-effects it was imperative to keep the dose below 15 mg. prednisolone per day, and to recognize that other drugs such as aspirin might play a part in their production.

When dyspepsia occurred with long-term steroid therapy aspirin should be withdrawn and replaced with enteric-coated salicylates.

Discussion.—DR. A. ST. J. DIXON (London) said that he had found no difference in faecal blood loss between patients on steroids and aspirin and on aspirin alone, during tests lasting a week or so. But one should avoid giving the two together, as rheumatoid patients receiving both aspirin and corticosteroids for long periods developed serious intestinal complications more frequently than patients suffering from skin diseases or ulcerative colitis who were given corticosteroids without aspirin.

DR. A. G. S. HILL (Aylesbury) said that sixty patients treated with a daily dose of 5 mg. prednisolone, the incidence of dyspepsia was 10 per cent., but it had been sufficiently severe to stop treatment in only two patients. Purpura was common and had been detected in 20 per cent. There was one case of peri-colic abscess and one of melaena.

The President asked whether the bruising occurred only in females.

DR. A. G. S. HILL (Aylesbury) replied that it was almost always in females.

DR. SAVAGE said that he agreed. He had never seen bruising in a male patient receiving steroids.

DR. G. D. KERSLEY (Bath) asked how far this was a controlled series. Quite a lot of women bruised without prednisolone, but 20 per cent. was a high figure. He asked if these were big patches of skin bruising.

DR. A. G. S. HILL (Aylesbury) replied that the observations were completely uncontrolled, and that all the bruises were as big as sixpences or bigger.

Alteration in Programme for 1960

The Heberden Round will be conducted by Dr. W. S. Tegner at the London Hospital on September 16, 1960, and not on September 23 as previously announced.