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Cortisone et Corticostimuline (ACTH) en Rhumatologie.

In the foreword the authors point out that, although Hench, Kendall, and their collaborators still refer to work with cortisone and ACTH as a "therapeutic experiment," this attitude is no longer tenable. These drugs are being used so widely in the field of rheumatic and other diseases that discussion on their value can no longer remain in the field of pure science.

The present work deals only with the rheumatic and para-rheumatic diseases, and is concerned with decisions as to its suitability in certain cases and the best methods of administration. The experience has been gained in the study of over 460 cases of rheumatic disease, mainly at the Hôpital Cochin in Paris, and the findings are compared with those of other workers, particularly with reports from America.

Early in the book the complications of hormone therapy are discussed, and it is pointed out that side-effects relating to the skin, locomotor system, and nerves are annoying and may be unattractive and at times even painful, but that they only rarely prove a real obstacle to the continuation of treatment. Endocrine and metabolic troubles such as steroid diabetes have been mild and tolerable. Major adverse incidents comprise vascular accidents, oedema, infections, digestive disturbances, and changes in the mental condition of the patients. Hypertension, usually mild, is occasionally progressive and may require administration to be stopped, but it is transitory and always disappears when the drugs are omitted.

The possibility of hypercholesterolaemia with a pre-disposition to athero-sclerosis as a consequence of prolonged treatment with cortisone is considered to be merely a hypothesis. Thrombo-embolic accidents are stated to be poorly evaluated in the various reports. It is believed that if their existence is confirmed a more complete study would lead to the risk being minimized. Oedema and sodium retention have been observed with both hormones. They are not considered to be serious complications and can easily be rectified by the exclusion of salt from the diet and the use of diuretics.

The possibilities of infections occurring during treatment are manifest, particularly during periods of high dosage. Staphylococcal, pneumococcal, and especially virus infections may be aggravated, even provoked. Present or recent tuberculosis is a usual contraindication to hormone therapy, and the lungs should be x-rayed at frequent intervals during extended courses of treatment. The risk of infection is lessened by the fact that the hormones do not interfere with the action of antibiotics. Gastric hypersecretion is caused by the hormones; it is necessary and easy to neutralize this and so avoid the ulceration which may complicate treatment.

The authors consider that mental risks comprise the greatest danger in this therapy. They recommend that a rigorous psychiatric examination should be carried out before treatment is started, so that any warning symptoms can be recognized at once.

It is pointed out that treatment with cortisone and ACTH is long, difficult, and full of disappointing phases, and that as much publicity has been given to the risks as to the successes, so that the patients themselves may be worried about possible complications. Continued surveillance is therefore imperative, and hormone treatment should be refused to the anxious or unstable patient. The financial aspect must also be borne in mind.

In discussing the choice of hormone, there is no doubt that cortisone is the more convenient, and possibly more exact, but that ACTH may be superior when a rapid response is required, or perhaps in the initial stage of treatment. It is recommended that the suprarenal response be checked by means of Thorn's test before treatment is started, but it is emphasized that clinical response is still the only real method of evaluation.

The importance of a gradual reduction of dosage as recommended by both Hench and Boland is confirmed, either when long-term maintenance therapy is contemplated, or when a course of treatment is being terminated. The length of remission in rheumatoid arthritis after an initial period of treatment is considered; in the authors' experience with 94 patients, it lasted more than 2 months in only 18 per cent. They incline to Hench's opinion that the 10 per cent. of cases going into remission is significant; in their experience there seems to be no correlation between the length of remission and the length of treatment, and neither the sex nor the age of the patient, nor the duration of the disease appear to be determining factors. The erythrocyte sedimentation rate gave no indication of the likelihood of a remission after treatment.

The authors have done some interesting work on the various combinations of the two hormones in rheumatoid arthritis. The figures are small, but the work has been carefully evaluated. ACTH before cortisone gave satisfactory results, as did simultaneous administration and alternate short and long courses of each drug. The results of giving cortisone and ACTH on alternate days were not impressive. The most encouraging method is to give ACTH at the end of a course of cortisone; there appears to be no danger in this, and with the possibility of stimulating the suprarenal there is more hope of preventing a relapse on withdrawal.

The phenomenon of relapse after the withdrawal of these hormones has also been studied. The authors point out the importance of objective assessment, as the patient, often forgetting his pretreatment condition, may exaggerate the activity of the disease. In their cases the
number of relapses was less after ACTH than after cortisone, but they were unable to find any correlation between either the length of disease or the sedimentation rate and the relapse rate.

The following cortisone “sparers” were tried and found ineffective: insulin, para-aminobenzoic acid, adrenaline, oestrogens, progesterone, testosterone, DOCA, and pregnenolone. The authors feel that any infection should be treated, but, in disagreement with American and English workers, are cautious about using physiotherapy as these patients are apt to do too much on their own, and the danger arises that joints may be worked too hard.

The combination of the hormones and chrysotherapy has been studied. The advantage of simultaneous administration is that under hormone protection a therapeutically active total dose can be introduced more rapidly, and they have given as much as 1-36 g. gold in 5 days with intravenous ACTH. There is, however, a danger that gold intolerance may appear in the post-hormonal phase, and this is more likely to be an urticarial than an eczematous or erythrodermal reaction. It is believed that gold becomes ineffective or harmful when given in the later stages of long-term cortisone treatment, and that it should be forbidden in the posthormonal period as it does not prevent a relapse, and there is a grave risk of serious intolerance to the metal.

These authors believe that benefit can be obtained from the combination of orthopaedic surgery, particularly arthroplasty, and the hormones, as these permit early resumption of activity and shorten the painful period of rehabilitation. They point out that surgeons have not proved that there is any delay in healing, and stress the fact that cortisone or ACTH treatment should not be interrupted during the surgical phase of treatment.

The practicability of short or long-term treatment is discussed at length. Although only one-quarter of their own cases which received successive courses of treatment, showed any appreciable benefit, the authors believe that intermittent treatment offers the arthritic patient a good chance of improvement. They suggest a number of short courses of combined cortisone and ACTH separated by short intervals; a high initial sedimentation rate is no contraindication, but where it returns rapidly to its former level on stopping, continuous treatment should be considered. They agree with Hench that intermittent therapy is indicated, particularly where posthormonal relapses are incomplete and slow, or where patients, particularly at the menopause and in adolescence, are relatively intolerant to the hormones, or where high doses are necessary for suppression of the disease.

It is considered impossible at present to say whether long-term maintenance therapy is practicable. Some authorities report very favourable results and others less favourable. The role of these hormones in rheumatoid arthritis cannot yet be compared with that of insulin in diabetes, DOCA in Addison’s disease, or thyroxine in myxoedema. It is not yet known whether the body will be able to stand indefinitely the effects of cortisone and ACTH on the haemopoietic, lymphoid, and nervous systems, or how the results of continuous hormone therapy compare with the suffering and gravity of severe polyarthritis. Neither optimism nor pessimism is justified, and conclusions will have to await the results of the further studies now being carried out in many centres.

From their experience with polyarthritis in children, these workers conclude that this form of the disease responds as well as the adult type; that the hormone dosage can be proportionately higher than for adults as the children’s power of toleration seems better; that minor side-effects, except for moon-face and obesity, are no more troublesome than in adults; and that the more serious side-effects such as hypertension and mental symptoms are less to be feared.

The results in ankylosing spondylitis have not been so good, with less effect on the pain, more severe relapses on stopping treatment, and less response to succeeding courses, so that continuous maintenance therapy is preferred in this disease. The hormones have been of great use in conjunction with arthroplasty of the hip.

In France much attention has been paid to the effects of the hormones in non-inflammatory and non-articular rheumatic conditions. In osteo-arthritis of the hip, high dosage was given for short successive periods; out of 23 cases, thirteen were relatively successful, and in these there was a history of infection, severe anatomical damage, and an alteration in the sedimentation rate.

Lesions of the intervertebral disks have been treated with success in a good proportion of cases of sciatica, lumbago, and cervical root compression. It is considered that the inflammatory element in these cases is favourably affected.

In acute peri-arthritis of the shoulder, moderate doses have often produced excellent results as long as the drug was continued for a minimum of 14 days. In the more chronic cases the response was good, though it did not appear until 12 or more days of cortisone therapy had been given. In the “frozen shoulder” group, the results were less good, and it is considered that long periods of treatment are necessary. Other series in France have shown better results.

The authors are impressed with their short experience of hydrocortisone for intra-articular injection, of which they report 149 cases, mainly into knee joints.

Professor Coste and his colleagues give an interesting appreciation of the present position of hormone therapy in the rheumatic diseases from their own experience. They believe the hormones to be valuable in the treatment of rheumatic fever, and prefer ACTH to cortisone because of its more rapid action. In gout they have no doubt of the remarkable effect, but consider that hormones should only be used where there is no response to colchicine, and that they must always be followed by this drug.

In the more chronic rheumatic conditions, the main difficulty is the possibility of complications, and they consider that there is a risk of serious psychosis in 1 per cent., and the same for digestive troubles. In long courses 10 to 15 per cent. are liable to serious complications.

On the whole they prefer continuous to intermittent treatment, and have some patients who have been on such a regime for over 2 years. They believe there to be
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This pocket edition was written with the intention of presenting rheumatism and its social aspects to the non-specialist and to the cultured public.

The difficulties of a comprehensive classification of the rheumatic diseases are fully discussed in the introduction. The author, however, comes to a compromise by closely following the nomenclature recommended by the Rheumatism Commission of the French Ministry of Health (Paris, 1937), which is in many ways similar to the British classification suggested by the Royal College of Physicians in England. A useful table is then drawn under sixteen headings of the differences existing between the inflammatory and degenerative forms of rheumatism.

Rheumatic fever (maladie de Bouillaud) is fully described, and its classical treatment by salicylates is discussed at length. The uses of ACTH and cortisone, and the prophylactic application of sulphonamides and penicillin, are briefly reviewed.

The chapter on the chronic forms of rheumatism gives to the reader a very good clinical picture of the different grades of rheumatoid arthritis, and treatment is discussed under the headings of internal medication, hygiene, diet, physical methods and orthopaedic measures. Though ACTH and cortisone may have their uses, gold remains the only drug which has stood the test of time.

Ankylosing spondylitis is included with Still’s disease, and psoriatic arthritis as a sub-variety of rheumatoid arthritis. The plan of treatment here is slightly too rigid. The use of a full plaster of paris jacket for several months would not be approved by many rheumatologists.

Tuberculous rheumatism, a French concept, is described as a clinical entity, a point of view which is hardly accepted in England and is rejected in America.

The available space has not permitted a description of the degenerative types of arthritis, but for those who can read French, this excellent little book will be found to be a helpful reference for diagnosis and treatment.

M. H. L. DESMARAI.


The Empire Rheumatism Council’s statistical investigation into thirteen possible aetiological factors and thirteen clinical features of rheumatoid arthritis was published in a special supplement to the Annals of the Rheumatic Diseases in 1950. The investigation entailed the detailed study of 532 cases and 532 controls and the analysis of the results. It was a time-consuming and expensive venture, unique in this field, and produced many interesting facts, invaluable to further workers, though perhaps disappointing in the lack of dramatic findings. The conclusions of this report occasioned a spate of critical correspondence, disagreeing with the negative findings on certain aetiological factors. Such unexpected negative findings are very valuable, as they cause people to think again, though they do not prove that these factors have no effect whatsoever on the rheumatoid state.

The sex incidence was 100 males to 162 females, and it was found that the risk of developing the disease rose between the ages of 20 and 50 years. One of the surprising features was the absence of significant increase in psychological trauma in the patients as compared with the controls. There was no tendency to association with allergic disease, but focal sepsis was slightly more common in the rheumatoid group. A familial tendency was statistically proved. 24 per cent. of cases had commenced at the menopause. In considering working and home conditions, cold appeared as the only factor which tended to increase the risk of rheumatoid arthritis. Peripheral vascular instability occurred in nearly five times as many rheumatoids as controls, and frequently antedated the onset of the arthritis.

Undue fatigue, loss of weight, transient pains, and sweating were frequent prodromal symptoms. The onset was febrile in 14 per cent. and acute in 44 per cent.; 81 per cent. consulted their doctor within 3 months of the onset of symptoms. 12 per cent. of the rheumatoid cases had nodules. Only 7 per cent. had normal sedimentation rates.

These are some of the findings discussed in the Report, which should be studied in full. G. D. KERSLEY.


This is the report of the 29 papers and the consequent discussions which were contributed to a symposium held at the University of Minnesota in November, 1951. The publication of such symposia is an increasingly common practice which often lacks adequate justification. Sometimes the delay in publication is so great that the rapid advance of research has raced ahead of the contributors; sometimes the real merit of such symposia lies in the free exchange of ideas between writers in separate but contiguous fields and the printed page fails to recapture the