Drug Treatment of Disease

CORTICOSTEROIDS IN TREATMENT OF SKIN DISEASES

I. SYSTEMIC TREATMENT

BY

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In 1953, when the supplies of steroid hormones were still meagre, a memorandum from the Ministry of Health mentioned several diseases for which priority might be given. This short list contained several diseases affecting the skin, and the promise of those days has been fulfilled. It is hardly too much to say that in respect of the more serious disorders the face of dermatology has been changed by this new method of treatment.

The steroids chiefly used in the treatment of skin diseases are A.C.T.H., cortisone, prednisone, prednisolone, and, more recently, triamcinolone. So far as their therapeutic efficiency is concerned there is not a great deal to choose between them, though of course the actual size of dose varies. More important differences are in side-effects and complications. At the present time prednisone is the one chiefly used, though perhaps before long triamcinolone will emerge as being somewhat superior. For purposes of simplicity the dose of steroids referred to below refers always to prednisone. Although reference is made to a total daily dose, it is the usual practice to divide this into two or three doses during the day.

Dangers of Steroids

The dangers attendant upon this treatment are very real, and before embarking upon steroid therapy it is essential to ascertain so far as possible the prospect of complications arising. X-ray examination of the chest should always be done to exclude latent tuberculosis; blood pressure should be taken and urine tested for albumin and sugar. Whenever there is a history suggestive of peptic ulceration, this should be looked into, and barium-meal examination made. Very often admission to hospital is necessary for the purpose of these investigations and for the start of treatment and initiation of maintenance therapy. During treatment many complications may arise; it is essential that these patients be seen by the doctor at intervals of not less than a fortnight and considerably more often in the early stages before an adjustment of maintenance dose has been made. Although, therefore, great benefits may be derived from this form of treatment, it is not one which should ever be embarked upon lightly. Fatalities resulting from the treatment are, in the present state of our knowledge, inevitable, and the price paid by the patient and by his doctor can be high.

Effective Dosage

If all these preliminary investigations give negative results, treatment may be started and an effective dose should be given at the onset. Failure to respond to the usual doses sometimes results from half-hearted underdosage at first.

The termination of therapy often requires some skill, because it is common for the original disorder to recur, at least in part, if treatment is stopped suddenly. It is

therefore, nearly always necessary to reduce the dose slowly. When doses of 40 or 50 mg. daily are being given, a reduction of 5 mg. two or three times a week may be satisfactory, but when the daily dose is in the region of 20 mg. or less it is often best to reduce by only 1 mg. a day. Even when the dose is reduced as slowly as this there may be some tendency to relapse; this does not necessarily indicate that the dose should be increased again, for after a few days on the reduced dose a minor relapse may well subside and permit further reduction. It is in this way that the level of maintenance treatment is eventually determined.

In most disorders in which maintenance is required, it is probably best to give a dose which does not entirely suppress symptoms. If very slight manifestations of the disease continue it is perhaps the best indication that, though the disorder is under control, an unnecessarily large dose of steroid is not being given. In these circumstances more severe relapse of the original disease may occur if there is any added stress. A minor illness such as coryza may impose sufficient stress to cause a relapse of a disorder which has hitherto been nicely under control. At times such as these the maintenance dose may have to be increased for a few days.

As will be seen below, there are a number of self-limiting disorders in which a short course of treatment may be given lasting three or four weeks. Many of the complications of steroid treatment may occur at the beginning of treatment, so that even such a short course should not be undertaken without adequate investigation beforehand. Sometimes the results are not so good as expected, and there is a tendency for a treatment which was originally intended to last a month or so to run into a considerably longer period, perhaps with unfortunate results. Before steroid therapy is begun, its object and limits should always be clearly defined. If the original intention has been to give a short course of four or five weeks and it is then continued beyond that time, the whole position should be reviewed and a fresh plan of campaign evolved.

A final general point of great importance is that steroid therapy should never be given as a substitute for accurate diagnosis.

THE BULLOUS DISEASES

Pemphigus vulgaris and the related disorders pemphigus foliaceus and vegetans occupy a prominent place among skin diseases. They are striking, disabling, extremely unpleasant, and dangerous; they carry perhaps the highest mortality of any cutaneous disease, being fatal in the majority of cases. Few treatments other than steroids have any value, and none are reliable. The steroid hormones, however, have a dramatic effect and quickly suppress the eruption in the great majority of cases. Without this treatment the

disease is so dangerous that steroids are imperatively indicated as soon as the diagnosis is made. There is some reason to suppose that if treatment is delayed the response may eventually not be so good, and this occurs also if initial dosage is too small. Once the diagnosis of pemphigus is made, therefore, there need be no delay. These patients may require large initial doses, often up to 100 mg. daily and sometimes 150 mg. or even more before the eruption of blisters has completely ceased. So dangerous is the disease, however, that there should be no hesitation in giving these large doses in order to achieve the initial effect; and at the same time contraindications have to be met by countermeasures rather than by withholding steroids.

The usual practice is to start dosage at 40 or 50 mg. of prednisone daily, and unless fresh blisters cease to form within three or four days the dose is rapidly increased. In this way the production of blisters can usually be checked in the course of ten or fourteen days, and once this stage is reached one may at once start to reduce the dose. This should be done cautiously in steps of 5 to 10 mg. weekly, the occurrence of fresh blisters being an indication that the reduction of dose is proceeding too quickly. Eventually, after a period of several weeks, it is usually possible to reach a maintenance dose which may be in the region of 15 mg. a day, but is sometimes less.

The results of this treatment are that the mortality of pemphigus has been reduced to about 30% or less of its previous level. Some patients die now because the disorder cannot be brought under control even with the largest doses. Others die from complications of treatment or from intercurrent diseases. Many of them are elderly.

Other Bullous Diseases

Most other bullous diseases show some response to steroids. One of the commonest is *pemphigoid*, which affects chiefly elderly people. However, the disorder is not so serious as true pemphigus, and in these elderly patients contraindications are so often present that it may be wiser to avoid steroid therapy.

Stevens-Johnson Syndrome

There is a certain mortality from this disease, but most often it is self-limiting, though unpleasant. The administration of steroids can always be expected to produce a striking improvement and to hasten recovery. The initial dose is usually in the region of 40 to 50 mg. of prednisone daily and this may quickly be reduced once the symptoms are abating. The total period of treatment will usually last not more than three or four weeks.

THE ECZEMA-DERMATITIS GROUP

This group comprises the main bulk of cases in which steroids are indicated.

Exfoliative Dermatitis

Exfoliative dermatitis affects mainly the middle-aged and elderly. In some cases it is the extension of a pre-existing skin disease, particularly of more or less localized eczema; in other cases it may be provoked by a reticulosis or by drug intoxication; in many cases it occurs as a primary condition and without ascertainable cause.

The cutaneous eruption is accompanied by a deterioration in the general health, both physical and mental. Younger patients are usually able to withstand the disorder and recovery follows after a period of

months or years. In elderly patients, however, the strain may be too great, and death may occur from exhaustion or from intercurrent disease, particularly of the respiratory system.

In the great majority of these cases the skin can be returned completely to normal by steroid treatment. The initial dose needs to be a substantial one, usually 35 to 45 mg. of prednisone a day, but it is never necessary to give the high doses which may be required for pemphigus. In the course of a few days irritation ceases, subcutaneous oedema diminishes, and in ten or fourteen days the skin has resumed a normal appearance. The dose is then gradually reduced to a maintenance level, which is usually 10 to 15 mg. a day. In favourable cases this maintenance dose can be continued with complete suppression of the disorder until eventually natural recovery makes further treatment unnecessary.

The decision to undertake steroid therapy for exfoliative dermatitis is often an extremely difficult one. In younger patients the threat to life is small and one must decide whether disability and discomfort warrant a treatment which in itself carries a mortality. In the older patient the associated diseases which constitute the principal danger are often also contraindications to steroid therapy. These elderly patients often have chronic respiratory, cardiovascular, or mental disorders which threaten life whether they are treated with steroids or not. Often one feels that without treatment they are likely to die before their skin has recovered and that the risks of steroid therapy are worth taking in order to ensure that the rest of their life will be tolerable even if it is curtailed. Even in retrospect it is often difficult to decide whether it was right to embark upon steroid therapy, and certainly the decision cannot be taken without very careful thought and appraisal of imponderable factors.

Acute Eczema

Acute contact eczema, and the sensitization eczema which sometimes complicates varicose dermatitis and other localized conditions, are distressing and disabling but essentially self-limiting and present no threat to life. In severe cases systemic steroid therapy is valuable given over a short period. 30 to 40 mg. of prednisone per day will usually suppress the acute reaction in a week or so, after which the dose may be immediately tapered off, so that a total period of four or five weeks' treatment is envisaged.

Atopic Eczema

This disorder, also known as disseminated neurodermatitis and Besnier's prurigo, occurs in all degrees of severity and may be accompanied by asthma, hay-fever, and other allergic manifestations. The symptoms can always be removed with steroid treatment. The disease is essentially inborn and can hardly be susceptible of cure, so that the benefits of steroid therapy will last only so long as the treatment is continued. These patients are, however, subject to occasional severe relapses, and sometimes at these periods steroid therapy may be justified. Apart from this there are a very few extremely severe cases in which the patient's life is a misery and both work and pleasure are impossible. In these rare cases steroid therapy maintained over months or years is justified. It should be emphasized, however, that these cases are few and far between. The dosage required for suppression of symptoms is usually in the region of 25 or 30 mg. of

prednisone daily—larger than the maintenance dose required for many other conditions. The attendant risks, therefore, must be carefully balanced against the severity of the illness.

In this condition, as in most chronic disorders, it is undesirable to give the patient a demonstration of the great benefits of steroid therapy if it is not proposed to continue them. Patients who have had a glimpse of the respite such treatment may give are only liable to be the more unhappy if afterwards this treatment is firmly, though wisely, withheld. There is, of course, a tendency to shake off this disorder as age advances. It is, however, only in the most serious cases that treatment would be given, and these are the ones where spontaneous recovery is unlikely. Occasionally in infants severe atopic eczema may be treated in this way.

Drug Eruptions

Most drug eruptions are comparatively short and sharp and are likely to subside in the course of a few days. For these, systemic steroids are not indicated. Certain drugs, however, are likely to produce eruptions of much longer duration. Notable examples are the eruptions produced by mepacrine and by gold. Cases of this sort may be treated by the method outlined for acute eczemas. The response to treatment is usually excellent and complete recovery takes place in a few days. As the dosage has to be reduced slowly, the duration of treatment is usually about a month or six weeks.

Lupus Erythematosus

Steroids do not enter into the treatment of fixed, localized, cutaneous lupus erythematosus. Although most cases of the disseminated type are in the hands of

the general physician, they occasionally come under the care of the dermatologist. The symptoms of disseminated lupus erythematosus can usually be partly or completely suppressed by steroids, but it is not certain how much the eventual outcome of the illness is influenced. D.L.E. is a disorder or syndrome which presents in many guises with a great variety of symptoms, and which runs an extremely variable course. Although it may not be difficult to assess the influence on symptoms, it is often difficult to know whether the course and the development of remissions have been much altered by treatment. While, therefore, steroid therapy is indicated for the relief of severe and intractable symptoms—provided that other safer methods of treatment have first been tried—opinions are much divided on whether it should be given in the general treatment of the disease.

Dermatomyositis

This rare disease also appears in all degrees of severity and runs a very variable course. In all but the mildest cases steroid treatment is usually given, but results are difficult to assess. Large doses may be required.

There are several other disorders in which a response to steroids can be obtained, but because of their relative mildness the risks of that treatment are not often justifiable. In this category are lichen planus, aphthous ulcers of the mouth and genital region, and a number of rarer disorders. It is not often that steroid therapy is indicated; when it is given, its effects are apt to be temporary, and we are faced with the dangers of indefinite maintenance treatment in exchange for a harmless, uncomfortable, but seldom disabling disorder.

(To be concluded.)

B.M.A. ANNUAL CLINICAL MEETING

NORWICH, OCTOBER 22-25

The final count of those who registered at the Association's Second Annual Clinical Meeting at Norwich last month was 415, and to this excellent total must be added quite an appreciable number who did not succeed in registering. Of the 415, over 200 came from outside East Anglia. All who attended the Meeting would acknowledge their debt to the local officers—Mr. J. M. RIDLEY THOMAS (chairman), Dr. R. H. SCOTT (honorary general secretary), Dr. A. BAITY SHAW (honorary science secretary), Dr. A. L. REYNARD (colour television), and Dr. B. M. MAXWELL (transatlantic clinical conference)—and to Dr. P. R. WILSON, the chairman of the Meeting's committee of management, who between them did so much to make the Meeting a success.

The first half of the Meeting was reported in our last week's issue (*Journal*, October 31, pp. 878-882). The rest of the report appears below.

SECOND GENERAL SESSION

Professor J. S. MITCHELL (Cambridge) took the chair at the Second General Session on Saturday morning, at which there were three guest speakers.

Psychiatry and Psycho-analysis

Dr. W. MAYER-GROSS (Birmingham) discussed psychiatry and psycho-analysis. Although only 20 years had elapsed since Freud's death, his doctrines and teachings had made a profound impact on everyday life and on modern

scientific medicine. They still formed a basis on which the psychoneurotic patient might be treated. It was important, therefore, that both the family doctor and the specialist in other branches of medicine should be able to understand the reaction of his patients to Freudian doctrines and the bearing they had on the treatment of psychiatric disorders.

The training of sufficient psycho-analysts presented formidable problems, and Dr. Mayer-Gross doubted if the shorter periods of training advocated by Balint at the Tavistock Clinic were sufficient to give the background of knowledge necessary to make treatment adequate. However, any doctor with patience, tolerance, wisdom, sympathy, and maturity would soon win his patients' trust, and by reassurance, explanation, and planning for the future be able to correct the majority of psychosomatic manifestations. He should, at least, be able to tide him over until a spontaneous remission of symptoms occurred. There was indeed little evidence that more complex, expert, prolonged psycho-analysis achieved results in any way better than those obtainable by simpler methods of psychotherapy.

Indications for Therapeutic Abortion

The indications for therapeutic abortion were described by Professor T. N. A. JEFFCOATE (Liverpool) on the basis of a 10-year obstetric experience at three Liverpool hospitals. The need for termination occurred only rarely: under present-day conditions probably not more frequently than one in every 1,000 pregnancies. He estimated that the problem would arise only once in every 25 years in an average practice. It should be realized that the operation was a serious one, carrying an appreciable mortality and morbidity, and inducing considerable physical and