BRITISH MEDICAL JOURNAL

LONDON SATURDAY DECEMBER 1 1956

PRESENT THERAPEUTIC STATUS OF CORTISONE AND ITS DERIVATIVES, WITH SPECIAL REFERENCE TO RHEUMATIC DISEASES*

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The multiple and various applications of cortisone and certain of its derivatives and of corticotrophin currently give these hormones a field of action and versatility "wider than that of any other therapeutic agent" (Hench, 1956). Their specific hormonal value is recognized by their use in about 20 hormonal, endocrinal, or metabolic conditions. The non-specific hormonal effects have been useful in more than 90 so-called non-hormonal conditions. In such circumstances the effects of administration of these hormones are suppressive rather than curative; but the effects are none the less valuable for purposes of treatment or further investigation. As Hench has stated, it is now no longer *if* but when, how, and for what purpose these hormones should be used.

Chief among the non-specific effects of adrenocortical hormones which have been useful clinically are their anti-inflammatory, antirheumatic, and anti-allergic activities. A few examples are given in Table I. The hormones also may have regulatory effects on haemic equilibrium and mesenchymal fibroplasia.

TABLE I.—*Usefulness of Cortisone and Its Derivatives and Corticotrophin in "Non-hormonal" Conditions**

Clinical Effect	Clinical Application: Examples	
Anti-inflammatory and antirheumatic	Rheumatic fever	Iritis, certain other ocular inflammations
	Rheumatoid arthritis	Pemphigus vulgaris
	Systemic L.E.	Acute thyroiditis
	Diffuse myositis	Non-tropical sprue
	Early periarteritis nodosa	Chronic ulcerative colitis
	Acute bursitis	
Anti-allergic ..	Status asthmaticus	Serum sickness
	Allergic ocular conditions	Sensitivity reactions to drugs
	Severe seasonal pollenosis	
Antitoxic	Snake and insect venoms	Acute viral hepatitis
	Acute delirium tremens	Severe bacterial and other toxaemias (e.g., peritonitis)
Regulatory: to regulate haemic equilibrium	Effect on eosinophils in eosinophilic pneumonia	
	Involutionary effect on lymphoid tissue in lymphomas, leukaemias	
	Acute haemolytic anaemia; thrombocytopenic purpura	
Regulatory: to inhibit mesenchymal fibroplasia	Control of formation or re-formation of adhesions, strictures, contractures, scar tissue	

* From Hench (1956), with additional examples.

Much additional investigation is needed to answer important questions pertinent to the broadening clinical applications and potentialities of these hormones. But physicians should learn to use the available hormones as effectively as possible and should obtain the consultation and supervision of experienced specialists whenever indicated.

Improved use of adrenocortical steroids has developed chiefly along two interdependent approaches. One has been by way of the various modifications of methods of administering the hormones. In a sense this has been an approach dictated by necessity, since existing measurements of adrenal cortical and pituitary function (Mason, 1955) were of limited usefulness for presumed non-hormonal diseases. Certain practical aspects of the currently advocated methods of administration are discussed below. The other approach to improved use of the hormones has been made by various chemical modifications of the steroid nucleus. This has resulted already in a number of synthetic steroidal compounds with varying degrees of metabolic and anti-inflammatory activity.

CHEMICAL DEVELOPMENTS AND STUDIES OF EFFECTS

Evolution of Antirheumatic Steroids

Cortisone, the first adrenocortical steroid found to have antirheumatic and other physiological effects, was given to patients with rheumatoid arthritis in 1948 (Hench *et al.*, 1949), and hydrocortisone, or cortisol, in 1949 (Hench *et al.*, 1950). Hydrocortisone has a more certain action than cortisone when administered locally (Young *et al.*, 1954); but it is equal to cortisone in the production of undesired metabolic effects when given systemically (Ward *et al.*, 1952). In 1954, 9α-fluorohydrocortisone was found to have an antirheumatic effect about 10 times that of cortisone, but also an effect on electrolytes about 50 times that of cortisone (Ward *et al.*, 1954; Thorn *et al.*, 1955). In the same year prednisone and prednisolone were found to have antirheumatic effects about four to five times those of cortisone (milligram per milligram) without an enhanced effect on electrolytes (Bunim *et al.*, 1955).

Trials of other compounds have included △-1,9α-fluorohydrocortisone, a combination of prednisone and 9α-fluorohydrocortisone which did not prove superior to either of these analogues (Thorn *et al.*, 1955); prednisone aldehyde, which seems to have less antirheumatic effect than prednisone (L. E. Ward, unpublished data); and aldosterone, which in doses used did not have antirheumatic properties, although it did affect electrolytes.

*Read at the Annual Meeting of the British Medical Association, Brighton, 1956.

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Undoubtedly other compounds will be introduced as a result of further intensive chemical modifications of significant portions of the steroid nucleus.

Prednisone : Metabolic Studies

Controlled metabolic balance studies in which the effects of prednisone are compared with those of cortisone or hydrocortisone have shown that prednisone has many similar and only a few different effects compared with other antirheumatically active synthetic or naturally occurring adrenocortical steroids (Ward *et al.*, 1955).

Case 1.—A woman of 51, who had had severe rheumatoid arthritis for one year, was given orally 20 mg. of prednisone daily for 36 days. It was then discontinued for 12 days, after which time hydrocortisone (free alcohol) was administered orally in a dose of 80 mg. daily for 24 days. This was followed by 20 mg. of prednisone again for six days, 17.5 mg. for six days, and 15 mg. for six days. Prednisone and hydrocortisone, in the doses used, produced marked and essentially equal antirheumatic effects.

During administration of prednisone the concentration of sodium, chloride, and carbon dioxide in the plasma remained essentially unchanged (Fig. 1). Plasma potassium increased slightly, although perhaps not significantly. The haematocrit reading increased appreciably and the body weight decreased about 5 kg., both of these changes occurring principally during diuresis of sodium and chloride in the first 12 days of the administration of prednisone.

In contrast, during the administration of hydrocortisone the average plasma concentration of sodium increased slightly and that of chloride decreased slightly, that of potassium decreased notably, and that of carbon dioxide increased greatly. The haematocrit reading and body weight remained essentially unchanged during this period.

Nitrogen balance studies (Fig. 2) revealed that, in comparison with the periods when the hormones were not being administered, the excretion of nitrogen was slightly increased during the first course of prednisone as well as when hydrocortisone was given. During the second

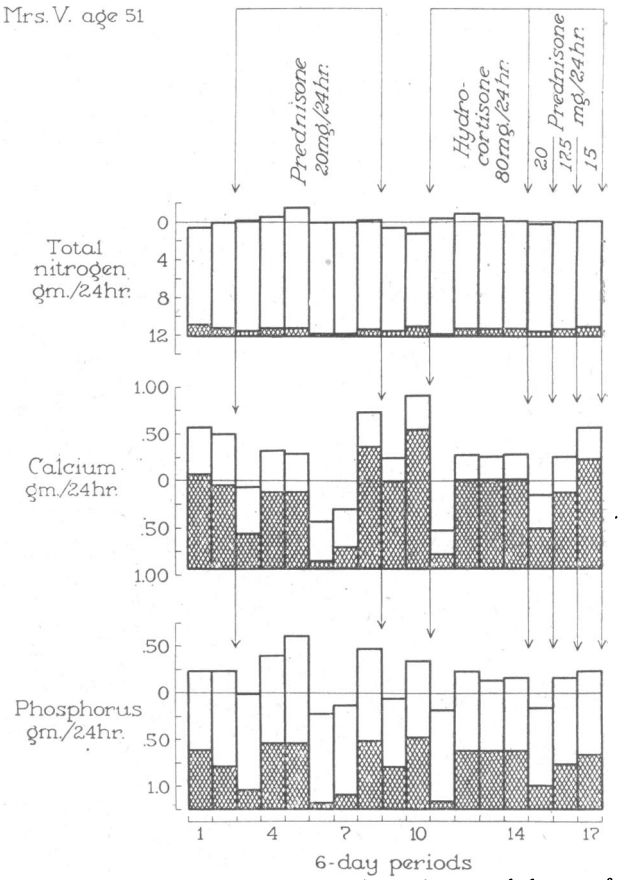

FIG. 2.—Effects of prednisone and hydrocortisone on balances of total nitrogen, calcium, and inorganic phosphorus in same patient as in Fig. 1. The daily intake is measured downward (but not blocked in) from the 0 line and is represented by the distance from the 0 line to the bottom line of the column. The average daily excretion (faecal, hatched column; urinary, clear column) is charted upward from the bottom line. Each column represents a six-day period. A negative balance is indicated by the position of the top of the column above the 0 line, a positive balance by the top of the column below the 0 line.

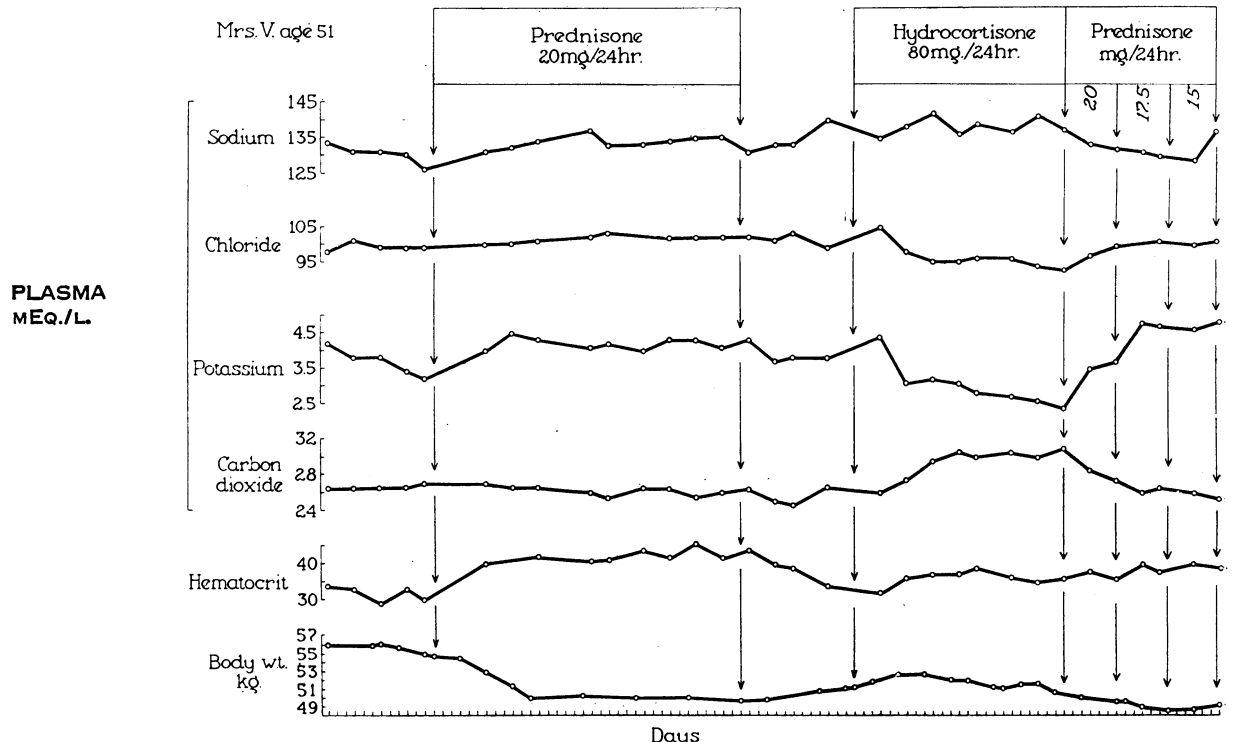

FIG. 1.—Effects of prednisone and hydrocortisone on concentration of electrolytes in plasma, on haematocrit, and on body weight determined in the course of a metabolic balance study on a woman aged 51 with rheumatoid arthritis.

course of prednisone, the nitrogen balance was in approximate equilibrium.

Calcium and phosphorus balances fluctuated irregularly during periods of administration of the hormones; interpretation of the results is difficult on the basis of these data. In general the amounts of calcium lost during the periods when prednisone and hydrocortisone were given were slightly less than in control periods when these hormones were not given.

The effects of 20 mg. of prednisone daily and of 80 mg. of hydrocortisone daily on the sedimentation rate were approximately the same (Fig. 3)—in each instance a prompt, significant decrease to normal. This paralleled the antirheumatic response.

With each of the hormones, total blood lipids increased substantially.

Urinary corticosteroids were increased less with 20 mg. of prednisone a day than with 80 mg. of hydrocortisone daily. Urinary 17-ketosteroids promptly decreased to zero during both periods of administration of prednisone, suggesting inhibition of adrenocortical function at least in respect to those substances metabolized to 17-ketosteroids. The slightly increased level of 17-ketosteroids found during the use of hydrocortisone presumably resulted from metabolism to 17-ketosteroids of part of the administered hydrocortisone.

Undesirable Hormonal Effects

Prednisone (or prednisolone) can produce most, if not all, of the so-called unwanted effects resulting from the use of cortisone, hydrocortisone, or corticotrophin. Effects which have been observed with doses of prednisone or prednisolone even smaller than those usually advocated include euphoria, insomnia, increase of appetite, facial rounding and other deposits of fat, acne, petechiae, hypertrichosis, loss of nitrogen, osteoporosis (with or without fractures), increase of blood fats, aggravation of peptic ulcer, inhibition of normal reactions in inflammation or infections, and inhibition of pituitary and adrenocortical function.

Thus, although retention of sodium and depletion of potassium may be less when prednisone is administered than when cortisone is administered, chemical alterations of steroid structure to date have not materially solved the problems of hypercortisonism.

STUDIES OF HYPERCORTISONISM

But what is hypercortisonism? The term describes exaggerated physiological hormonal effects; but as used clinically it represents more than a simple excess of cortisone. Hypercortisonism from cortisone, for example, is a composite of exogenous hypercortisonism plus endogenous hypocortisonism and hypopituitarism, while hypercortisonism from corticotrophin is a composite of endogenous hypercorticalism plus endogenous hypopituitarism. Also involved are the effects on other glands and tissues (Slocumb, Polley, Ward, and Hench, unpublished data).

Hypercortisonism was reported in 19 of the first 23 patients with rheumatoid arthritis who were given adrenocortical and anterior pituitary adrenocortical hormones at the Mayo Clinic (Hench *et al.*, 1950). It was more severe in those who had received relatively high doses for more than 50 days than in the other patients and also was more severe in women, especially post-menopausal women, than in men.

Features of Chronic Hypercortisonism, and Distinction from Rheumatoid Arthritis

With prolonged administration of excessive hormonal doses, a state of chronic hypercortisonism is likely to develop. In rheumatoid patients, particularly, this follows the initial period of stimulating effects and includes not only the familiar manifestations of overdosage but characteristically includes the cyclic occurrence of varying degrees of fatigability, emotional instability, and generalized muscular and articular aching (Slocumb, 1953; Slocumb and others, unpublished data).

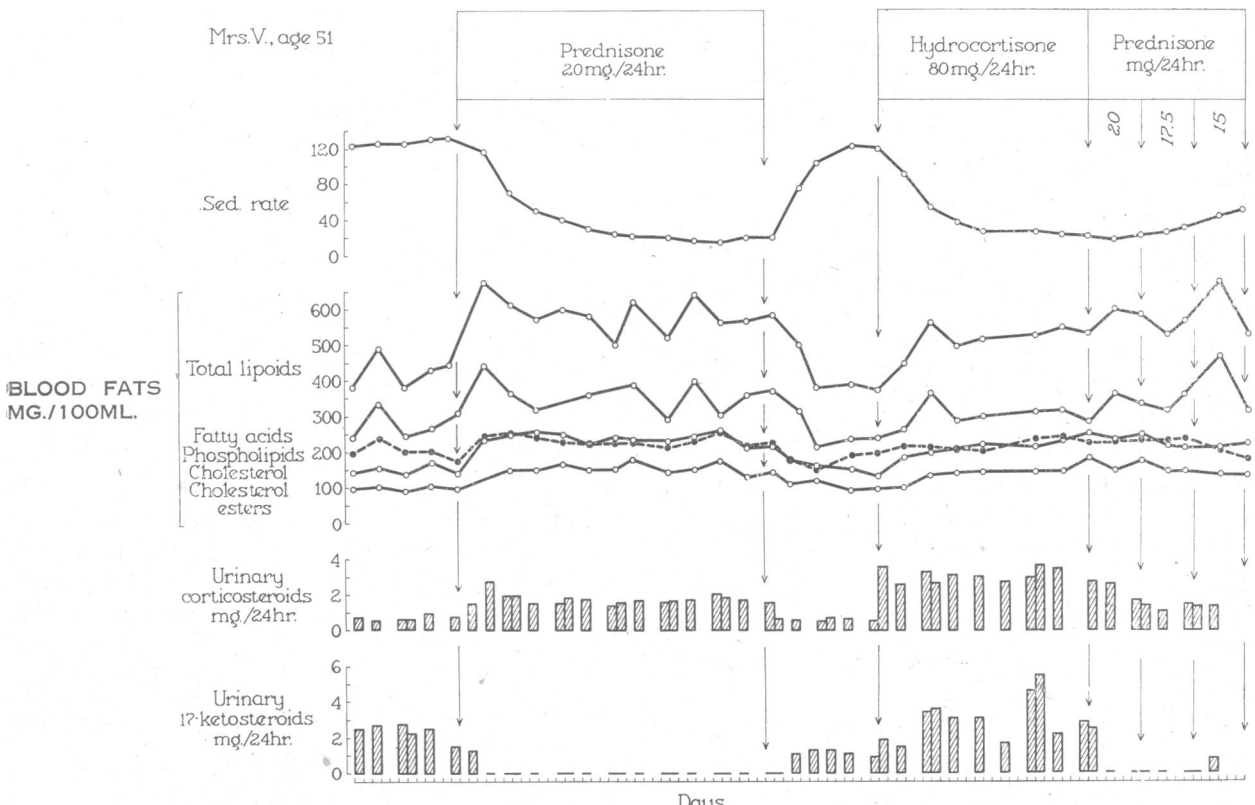

FIG. 3.—Effects of prednisone and hydrocortisone on the sedimentation rate of erythrocytes, concentration of blood fats, and urinary excretion of corticosteroids and 17-ketosteroids in same patient as in Figs. 1 and 2.

These symptoms often become accentuated toward the end of the span of time between doses of the hormone. The next dose or increases in dosage may partially improve the symptoms of chronic hypercortisonism, but only temporarily. Successive increases in dosage accentuate the cyclic variability of symptoms and may complicate the course of symptoms resulting from chronic hypercortisonism.

Detailed clinical analysis indicates that the muscular and articular aching of chronic hypercortisonism is unlike the discomfort of the increased articular inflammation associated with a flare of rheumatoid arthritis. In chronic hypercortisonism, synovitis is minimal or not increased. Symptoms of a rheumatoid flare are referable to joints and fibrous tisue; but the musculo-skeletal symptoms of chronic hypercortisonism are more diffuse and generalized, being referable more to muscles than to joints and fibrous tissue, and associated with generalized hypersensitivity and hyperalgesia.

Rest may worsen temporarily the fibrositic symptoms of a rheumatoid flare, but rest benefits the diffuse cyclic aching of chronic hypercortisonism. Physical therapy or salicylates are helpful for a rheumatoid flare but do not adequately relieve symptoms of chronic hormonal overdosage.

The sedimentation rate may increase in chronic hypercortisonism as well as in a flare of rheumatoid arthritis, and thus it is not of differential value in this problem.

A patient's remark to the effect that "my arthritis is getting worse" requires careful analysis to permit a proper decision for lowering the hormonal dosage or for raising it temporarily.

Severe Mesenchymal Reactions in Chronic Hypercortisonism

Severe diffuse mesenchymal reactions also may develop. These may simulate systemic lupus erythematosus or periarteritis nodosa. In a group of 128 rheumatoid patients with chronic hypercortisonism were 18 patients (14%) who had L.E. cells in plasma or bone marrow or both. Among these 18 patients, fever in excess of 100° F. (37.8° C.) occurred in more than 50% at some time during the reaction, nephritis occurred in 50%, transfusion reactions in 33%, leucopenia in 28%, encephalopathy in 22%, serositis in 17%, purpura in 17%, hypersensitivity to sunlight in 11%, pneumonitis in 11%, false-positive results of serological test on the blood in 7%, and phlebitis in 7% (Frerichs, 1954).

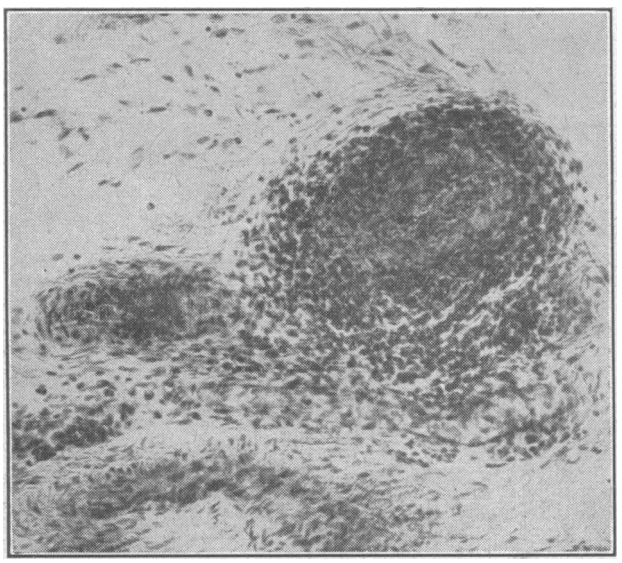

FIG. 4.—Photomicrograph of characteristic panarteritis found on muscle biopsy from the calf of a man aged 56 who had had rheumatoid arthritis for 17 years and severe chronic hypercortisonism beginning four years before this biopsy. The inflammatory reaction in endothelial, intimal, medial, and adventitial tissues is histologically indistinguishable from that characteristically present in patients with periarteritis nodosa before steroid therapy. (Haematoxylin and eosin. × 150.)

Severe mesenchymal reactions simulating periarteritis nodosa were observed in five rheumatoid patients who had diffuse panarteritis histologically characteristic of periarteritis nodosa (Fig. 4), peripheral neuritis, vascular occlusion, cutaneous ulcers, nephritis, fever, leucocytosis, and hypertension.

In incidence or severity, or in both, these various mesenchymal reactions were more pronounced in the 128 patients with chronic hypercortisonism than in either of two control groups of rheumatoid patients (105 without hormonal treatment and 166 without hormonal excess) observed during the same period.

Chronic hormonal excess seems to disarm or modify in some manner the mesenchymal tissue reactions of patients with rheumatoid arthritis and produces an incidence or severity, or both, of reactions that would not have been anticipated without excessive hormonal treatment. In some instances these severe mesenchymal reactions have been irreversible and death has resulted. In any event the seriousness of chronic hormonal overdosage is increased by severe mesenchymal reactions.

Studies on Plasma 17-hydroxycorticosteroids

Studies of hydrocortisone (cortisol) or levels of 17-hydroxycorticosteroids in the plasma of patients with rheumatic diseases have been undertaken to help determine some of the mechanisms and effects of hormonal treatment (Hench, Wu, Mason, Slocumb, Polley, Ward, and Mayne, unpublished data). Included in these studies have been certain observations on the plasma levels of 17-hydroxycorticosteroids in patients with rheumatoid arthritis and chronic hypercortisonism.

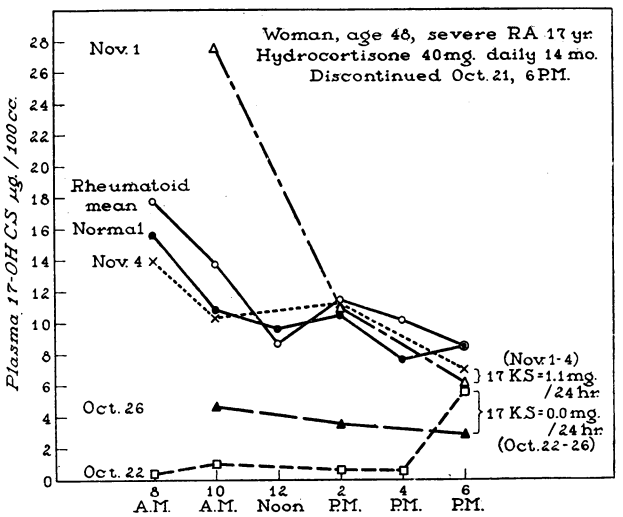

FIG. 5.—Plasma 17-hydroxycorticosteroid (17-OHCS) levels in a woman aged 48 who had had severe rheumatoid arthritis for 17 years. This patient had taken orally 40 mg. of hydrocortisone daily for 14 months and had developed most of the signs of chronic hypercortisonism in the 12 months preceding abrupt cessation of steroid therapy on October 21 at 6 p.m. The solid line with black dots shows for comparison the mean value of plasma 17-OHCS found during the day in normal patients. The solid line with clear dots shows the slightly higher mean value found in patients with rheumatoid arthritis.

Fig. 5 shows the levels of 17-hydroxycorticosteroids in plasma found as a result of abruptly stopping administration of hydrocortisone to a 48-year-old post-menopausal woman who had had severe rheumatoid arthritis for 17 years. This patient had taken 40 mg. of hydrocortisone daily for 14 months, and in the 12 months preceding cessation of the treatment most of the signs of chronic hypercortisonism had developed. Although no obvious clinical signs of adrenal insufficiency appeared when the hydrocortisone was stopped

abruptly at 6 p.m. on October 21, the level of 17-hydroxycorticosteroids in the plasma was practically zero for almost 24 hours thereafter.

The level was low on October 22 at 6 p.m., and on October 26. Normal values for plasma 17-hydroxycorticosteroids were found on November 1, 11 days after administration of hydrocortisone was stopped; but excretion of 17-ketosteroids in the urine was still negligible (1.1 mg. per 24 hours), and the clinically evident features of chronic hypercortisonism persisted for five months after treatment with the excessive doses of the hormone was stopped.

Further studies of levels of 17-hydroxycorticosteroids in plasma in rheumatoid and other patients are in progress. However, up to the present there still are no laboratory tests available which would substitute for careful clinical study of patients for whom adrenocortical steroids may be indicated.

OBSERVATIONS ON THE CLINICAL USES OF ADRENOCORTICAL HORMONES

Detailed clinical observations are needed to make treatment with adrenocortical hormones or corticotrophins as satisfactory as possible. Results of such observations over a period of more than six years of increasing use and experiences with these potent preparations have been, as stated above, one of the principal factors in improving current use of these hormones for many conditions.

The choice of hormone and doses to be used will vary with the severity of the disease, the anticipated duration of treatment, the age and sex of the patient, the presence or absence of associated medical conditions which might affect the risk of hormonal treatment, and the experience of the physician.

Indications, Dosage, and Contraindications

Since adrenocortical steroids or corticotrophin is indicated for only certain diseases, and especially only certain rheumatic diseases, an accurate diagnosis is of first importance. When the presence of a disease for which steroid therapy may be useful has been determined, the next aspect to consider is whether the stage of the disease will permit the desired alteration through hormonal treatment. Corticosteroids can affect favourably only the reversible stages of the tissue reactions of the particular diseases—that is, the pathological physiology, not the pathological anatomy of the disease. Attempts to modify the irreversible changes of a disease process by administration of steroids are generally disappointing and often result in the use of excessive hormonal doses which induce hypercortisonism, with its additional therapeutic problems.

Appropriate dosage of steroids is another important factor to be considered in hormonal treatment. Use of inadequate amounts for fulminating processes may lead to just as unsatisfactory results as the use of too large a dosage for low-grade chronic diseases when long-term hormonal administration may be needed. In general, steroid therapy is used in combination with such other treatment as may be indicated by the particular disease process.

The presence or absence of contraindications to use of adrenocortical steroids also must be considered. These deterrents may be either absolute or relative. Absolute contraindications are few: a psychotic episode or severe emotional instability or severe psychoneurosis, Cushing's syndrome, tuberculosis which is active or has been quiescent only a few years or less, and certain infectious diseases not readily controlled by antibiotics, especially those of viral origin such as acute anterior poliomyelitis and viral encephalitis.

Relative contraindications include other severe or moderately severe infections, diabetes mellitus, duodenal or peptic ulcer, pregnancy, convulsive disorders (except spontaneous hypoglycaemia), less severe degrees of psychoneurosis, osteoporosis, cardiovascular-renal disease, including hypertension, glomerulonephritis, coronary artery disease, and tendency to thrombotic or thrombo-embolic phenomena (Hench and Ward, 1954). In the presence of these conditions the indications for steroid therapy are measured against the potential disadvantages in each patient for whom it is considered.

Treatment With Relatively Large Doses for Acute Conditions

For acute self-limited disease with potentially serious damage as a result of an unchecked inflammatory reaction, it usually has seemed best to give large suppressive doses for the relatively brief period in which hormonal treatment is needed.

In *acute rheumatic fever,* 200 to 300 mg. of cortisone daily for four to six weeks or so may be needed. When control of the inflammatory reaction is established, the dose is gradually tapered off, but larger doses are resumed if signs of inflammation recur.

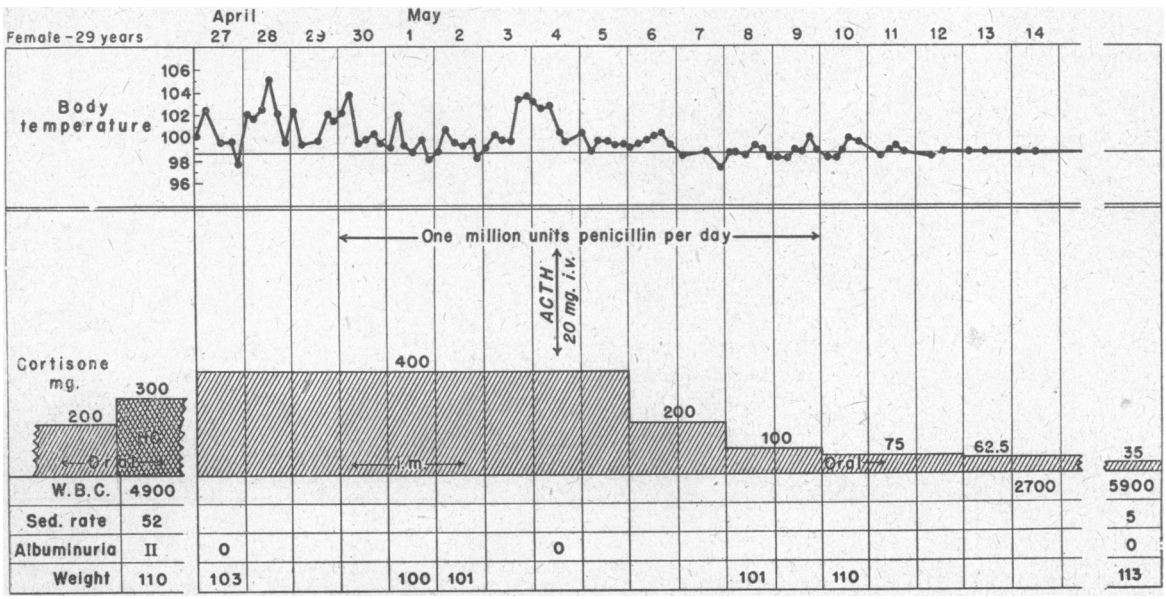

FIG. 6.—Chart showing certain aspects of the course of illness in a woman aged 29 who had had symptoms and signs of systemic lupus erythematosus for 18 months. At the time of a severe crisis with encephalopathy, hydrocortisone was administered orally in doses of 400 mg. daily for nine days and 20 units of corticotrophin (A.C.T.H.) intravenously for one day. The patient responded adequately to this treatment and the hormonal dosage was reduced to 35 mg. of hydrocortisone daily within three weeks.

Systemic lupus erythematosus is another instance in which large hormonal doses may be needed for relatively brief periods of crisis. Fig. 6 shows diagrammatically the use of 400 mg. of hydrocortisone daily for nine days plus 20 units of corticotrophin intravenously on one day, to control a severe crisis of systemic lupus erythematosus with encephalopathy in a 29-year-old woman who had had symptoms and

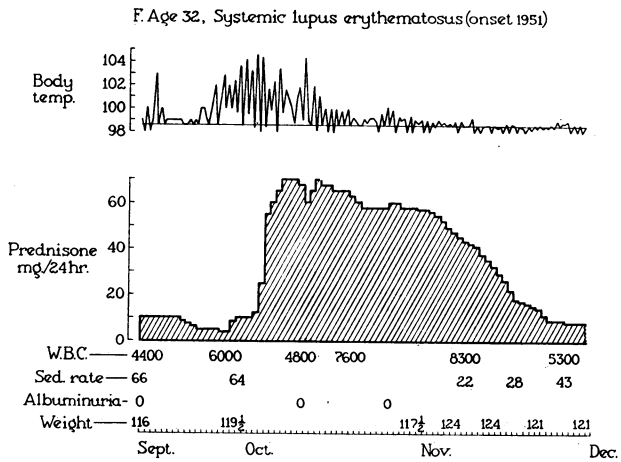

FIG. 7.—Chart of same patient as in Fig. 6 showing use of large doses of prednisone for another severe crisis of systemic lupus erythematosus two and a half years later, when patient was 32 years old. Doses of prednisone ranged from 60 to 70 mg. daily for 28 days, but as improvement occurred the dosage was gradually decreased to 8 mg. daily in the ensuing three to four weeks.

signs of that disease for 18 months previously. Within three weeks after this crisis had subsided, the hormonal dosage had been successfully reduced to 35 mg. of hydrocortisone daily; and hormonal treatment was discontinued completely in another three weeks.

The patient experienced another crisis two and a half years later (Fig. 7), at which time she was treated with prednisone in large doses—up to 70 mg. daily—followed by gradual decrease to 8 mg. of prednisone daily after three to four weeks.

Prolonged Treatment for Chronic Conditions such as Rheumatoid Arthritis

The problems of steroidal treatment for responsive chronic diseases are peculiar in that treatment may need to be greatly prolonged. Hormonal treatment for rheumatoid arthritis will serve as a suitable example.

Most rheumatologists are agreed that cortisone and related hormones are no more universally indicated for all patients with rheumatoid arthritis than is subtotal gastrectomy for all patients with duodenal ulcer or even insulin for all patients with diabetes mellitus, although in each instance the treatment is of great value when indicated properly.

When hormonal treatment is undertaken for rheumatoid arthritis the schedule of dosage as well as choice of hormone should be individualized. It also should be flexible within each patient's anticipated range of tolerance. This limitation involves use of relatively small hormonal doses. Optimal antirheumatic effects without hypercortisonism are facilitated by avoiding large, stimulating initial doses. Use of the smallest possible dose of the hormone at the start of, as well as during, treatment is advised (Ward *et al.*, 1953). Very gradual reductions of the doses—for example, only 2.5 to 5 mg. of cortisone or only 0.5 to 1 mg. of prednisone—are undertaken at varying intervals in accordance with the response. Most patients with rheumatoid arthritis should anticipate that sooner or later the inflammatory manifestations of their disease can be controlled adequately without supplemental hormonal treatment.

Increasing experience with long-term administration of adrenocortical hormones to patients with rheumatoid arthritis has led to the realization that tolerable doses are smaller than those previously considered satisfactory. These doses vary particularly with the patients' age and sex.

For post-menopausal women, 20 to 30 mg. of cortisone or 3.5 to 5 mg. of prednisone daily is usually maximal. For

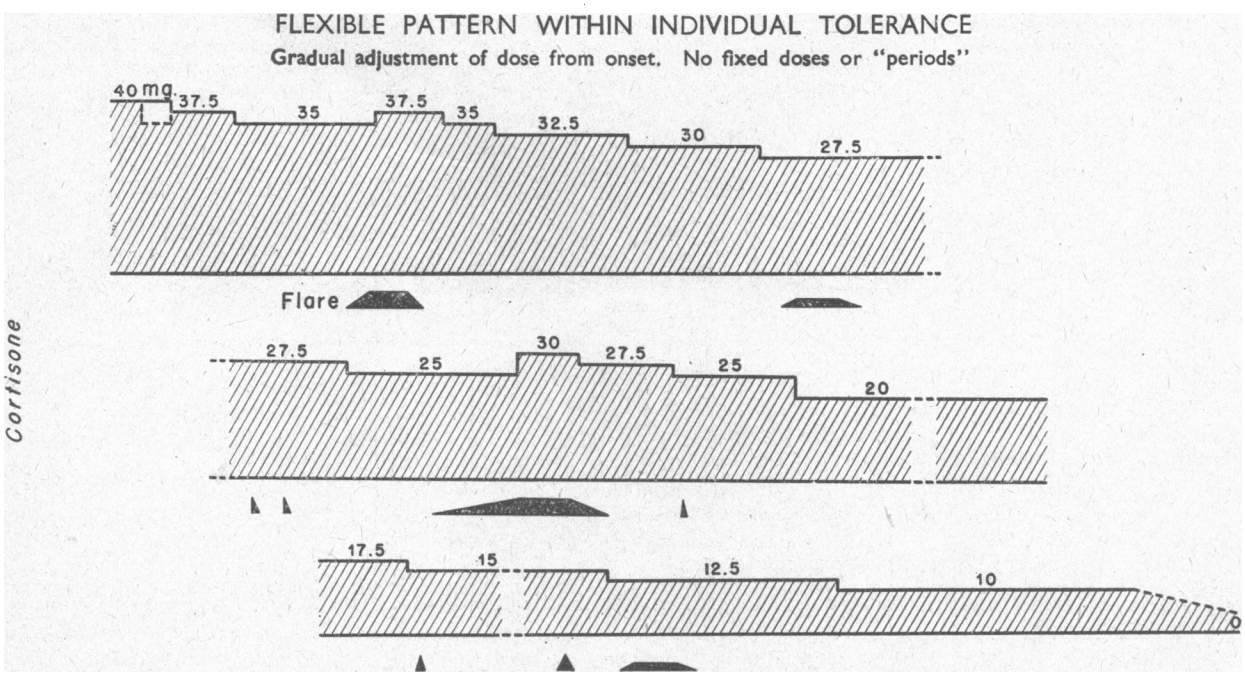

FIG. 8.—Example of flexible pattern of steroid dosage for long-term hormonal administration as used in rheumatoid arthritis. An initial dosage of 40 mg. of cortisone daily is shown. The development of a prompt antirheumatic or stimulating effect indicates the desirability of a prompt initial decrease in dosage as shown in the dotted-line insert. Small gradual reductions of dosage are undertaken in accordance with the patient's progress, but without fixed periods. For some flares, increases of dosage may be needed temporarily; for other flares, only a delay in further reduction of dosage is needed. Ultimately, the dosage for many patients with rheumatoid arthritis may be reduced to zero and control of the disease maintained, at least temporarily, with other basic treatment as indicated.

pre-menopausal women the upper limit has been in the range of 30 to 37.5 mg. of cortisone or 5 to 6.5 mg. of prednisone daily. For adult men, 37.5 to 50 mg. of cortisone or 6 to 9 mg. of prednisone may be maximal if hypercortisonism is to be avoided. In the light of current information it seems unlikely that the effects of doses within these limits are explained by the replacement of an absolute endogenous adrenocortical deficiency.

The improvement in antirheumatic effects reported sometimes on changing from one corticosteroid to another apparently results from relative differences in the dosage used or other factors in treatment rather than qualitative differences in antirheumatic effects of prednisone (or prednisolone), and cortisone (or hydrocortisone).

Use of corticotrophin to " stimulate latent adrenal cortical function " has not seemed to facilitate recovery of both adrenocortical and pituitary function sufficiently to be a routinely useful adjunct.

Individualized Treatment Schedules

An adjustable and flexible but gradually decreasing pattern of hormonal dosage may be used to reduce as well as to prevent hypercortisonism (Fig. 8).

Doses preferably are divided into equal or approximately equal amounts given regularly every six or occasionally every eight hours. Temporary increases of doses, or delays in further reductions, may be indicated for flares from time to time. But ultimately, on this programme, exogenous treatment with hormones is discontinued and the patient's disease is controlled, at least temporarily, with such other basic treatment as is indicated.

Variable and often unsatisfactory responses may be attributed to suboptimal divisions of total daily doses which do not take into account the differences of the intervals in such ordinary schedules as " night and morning " and " with meals," and the like.

When needed for different patients, more individualized symptomatic control may be provided by adjustments of dosage within the limits of the regular six-hour or eight-hour schedule (Table II).

TABLE II.—*Alternative Plans for Division of Total Daily Dose*

Time	Various Divisions of Daily Dose of 30 mg.			
	Patient 1	Patient 2	Patient 3	Patient 4
6 a.m.	7·5	10	10	10
Noon	7·5	5	7·5	
2 p.m.				10
6 „	7·5	5	5	
10 „				10
Midnight	7·5	10	7·5	
Alternative hours:	7 a.m.–1 p.m.–7 p.m.–1 a.m.			7 a.m. – 3 p.m.–11 p.m.
	8 a.m.–2 p.m.–8 p.m.–2 a.m.			8 a.m. – 4 p.m. – 12 p.m.

Results of Optimal Hormonal Usage in Rheumatoid Arthritis

Wide variability of rheumatoid inflammation in different patients, variance of indications for use of hormones, and diversity among the plans for hormonal treatment have made it difficult to correlate the data of various authors with regard to the results of hormonal treatment for rheumatoid arthritis (Ward *et al.*, 1953). Experience at the Mayo Clinic indicates that doses are well tolerated by 50 to 60% of the patients for whom hormonal treatment seems indicated, and that their signs of active rheumatoid inflammation can be satisfactorily controlled thus to the degree of 75%, more or less. In an additional 25 to 35% of such patients the results are worth while, with relief from their symptoms to the degree of approximately 50% ; but management of patients in this group is more complicated. There remain about 15% of the patients with rheumatoid inflammation for whom hormonal treatment seems indicated; but for these prolonged satisfactory control of signs is difficult if not impossible to obtain with present methods of utilizing adrenocortical and pituitary adrenocortical hormones.

SUMMARY

The potency of adrenocortical hormones and their newer effective synthetic analogues is great and generally beneficial for more than a hundred acute or chronic hormonal or non-hormonal diseases, but knowledge of how the hormones work and the safest way to use them is still far from complete. Benefits from present-day use of the hormones must still be weighed against the disadvantages, which vary for each disease and patient for whom the hormonal treatment might be helpful.

Physicians, as well as their patients, should anticipate the future development and availability of antirheumatic, anti-inflammatory, and anti-allergic hormonal preparations with increased effectiveness and fewer unwanted side-effects. However, the stage has now been reached where employment of the several potent hormonal compounds at present available can be useful and reasonably safe for a number of potentially serious diseases.

For optimal therapeutic value, use of these hormones should be supervised by physicians who have familiarized themselves with its intricacies in the same thorough manner that they would consider necessary in undertaking any complicated medical or surgical treatment.

The prednisone used in this study was generously supplied by the Schering Corporation, Dr. Edward Henderson, Medical Director.

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The newsletters, circulars, and reports published in connexion with the activities of the Australian faculties of the College of General Practitioners have now been consolidated in a quarterly journal, *Annals of General Practice*, the first number of which appeared in September. In an introductory message, Dr. W. N. PICKLES, the then president of the College of General Practitioners, wishes the *Annals* success. Besides faculty news the issue contains clinical papers on congenital heart disease and infective hepatitis. It is edited from 29, Flaumont Avenue, Lane Cove, N.S.W.