SPECIAL ARTICLE
CORTICOSTEROIDS IN MEDICINE

By
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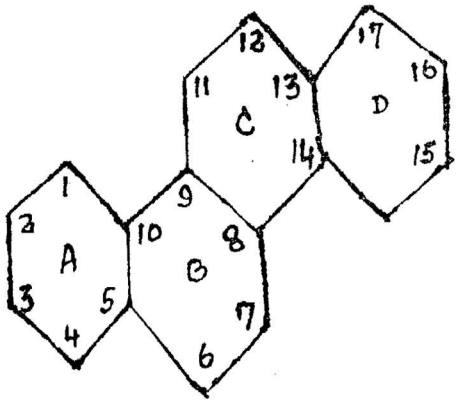
The largest number of articles are perhaps written on this subject, and also perhaps they are the most widely used drug to-day. Moreover, they are not as safe as commonly thought to be. These potentially toxic drugs may also worsen the underlying disease. Hence a revision of the subject would be in order.

NOMENCLATURE: The term "steroids" is commonly but loosely employed by many clinicians. (Stereo-solid; & OL for alcohol). "Sterols" are, therefore, a characteristic group of C_{27-29} secondary alcohols of plant or animal origin, and differ from other alcohols in being crystalline *solids* with melting point of 100° to 200°. Substances similar to sterols are termed steroids. Various steroids are (1) cholesterol from bile, (2) ergosterol from ergot of rye, from yeast, and thought to be a precursor of vit. D, (3) bile acids, (4) digitoxigenin and digitogenin-occur as glycosides, (5) sex-hormones and (6) corticchormones Thus the last named form only one of the steroids.

All of these compounds have a common nucleus called Cyclo pentano per hydrophenanthrene nucleus:—



CLASSIFICACION OF VARIOUS CORTICOSTEROIDS

(a) Old classification:— (i) Amorphous compounds & (ii) Crystalline compounds.

(b) New classification:—

This is based on recognised physiological and biochemical activities of compounds.

(I) Mineralo-corticoids:—

These are *predominantly* regulators of metabolism of minerals and water e. g. Aldosteron and Desoxycorticosterone (DOC),

(II) Glucocorticoids:—

These chiefly regulate metabolism of carbohydrates, fats and proteins, and also exert anti-inflammatory effect e. g. Hydrocortisone.

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(III) Sex-hormones:— e. g Androgens, Oestrogens and Progesterone (all cortically produced) In the present discussion these will not be dealt with,

As will be seen, the various compounds have not only glucocorticoid activity, nor only mineral-regulating property, but have both activities in varying proportions.

Glucocorticoids (Oxycorticoids):—

Here = 0 or -OH grouping is attached to the carbon atom in 11-position in the molecule.

Example: (A) Natural compounds: (i) Hydrocortisone = Cortisol = 17—hydrocorticosterone = Kendall's compound F. (B) Synthetic compound. (i) Cortisone = Kendall's compound E. (ii) Prednisolone = dehydrogenation product of hydrocortisone. (iii) Prednisone dehydrogenation product of cortisone. (iv) Methyl-prednisolone. (v) Triamcinolone, (vi) Paramethasone. (vii) Dexamethasone. (viii) Betamethasone.

Mineralocorticoids (Desoxrcorticoids):—

These substances are without = 0 or -OH groupings unlike attached in the preceeding class. Examples:—Aldosteron and DOC.

Substances having both types of activities:—

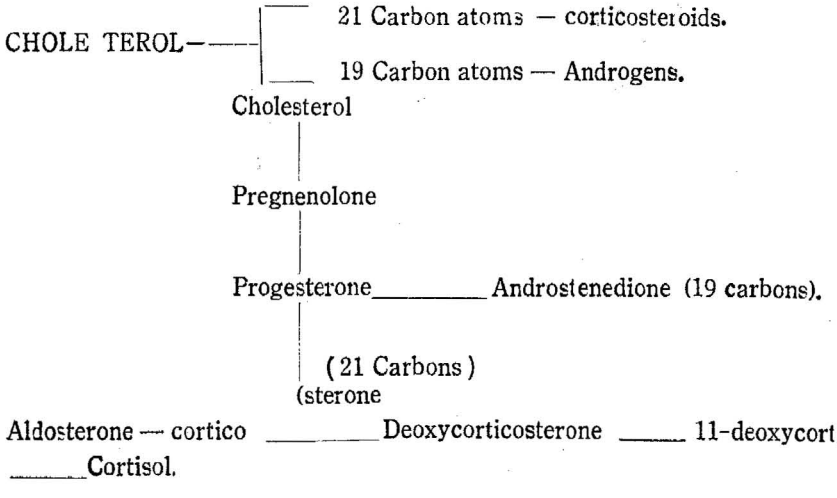
Examples:— (i) Corticosterone Kendall's compound B. (ii) 9-alpha-fluorocortisol.

STRUCTURE OF ADRENAL GLANDS

		The Zone	secrete in the species as rats.
Adrenal <	Medulla.		
	Cortex <	Outer Zone—Zona glomerulosa	aldosterone.
		Middle Zone-Zona fasciculata	hydrocortisone & corticosterone.
		Inner Lone—Zona reticularis	adrenal androgens & oestrogens.

In humans structural zones have less well-defined secretory differentiations.

BIOSYNTHESIS OF ADRENAL CORTICOIDS:-



PHYSIOLOGICAL OR BIOCHEMICAL EFFECTS OF CORTICOIDS:-

The compounds referred to below are corticoids in general without any special reference to whether they belong to glucocorticoid group or mineralocorticoid one, or both.

I) Effects on carbohydrate metabolism :-

(a) Glycogenesis :- increase deposition of glycogen mainly in liver. (b) Gluconeogenesis :- increase formation of sugar from non-carbohydrate sources like proteins and fats. (c) antiinsulin action i. e. increase the resistance to action of insulin. Thus they increase the blood levels of glucose.

II) On protein metabolism :-

The effect is catabolism of proteins. (a) increased excretion of nitrogen. (b) reduction and wasting of muscle mass. (c) gluconeogenesis. (d) osteoporosis i. e. reduction of proteinous matrix of bone followed by decalcification. (e) atrophy of skin.

III) On fat metabolism

(a) increased mobilization of fats from perepheral fat depots. (b) increased oxidation of fats; ketonaemia and ketonuria. (c) increased transportation of fats to the liver. (d) increased deposition of fats in neck (bufallo hump); in supraclavicular area; cheek (moon face), and loss of fat from the extremities

(IV) Electrolyte and water balance :-

a) Na^{++} retention b) K^{++} excretion c) fluid retention in extracellular space d) shrinkage of cells.

V) Effects on lymphoid tissues (action by glucocorticoids only):-

a) decreased mass of lymphoid tissues b) lymphocytopenia

VI) Effect on formed elements of blood :-

a) eosinopenia b) polymorphonuclear leucocytosis c) mild polycythaemia (if excessive corticoids are given).

VII) Effect on mesenchymal tissues:—

Suppression of inflammatory changes i e. (anti-inflammatory effect) a) Clinically. Prevention of local heat, swelling and pain. b) Microscopically· Early—suppression of cedema, fibrin deposition, capillary dilatation and migration of phagocytes. Late—suppression of capillary proliferation, fibroblastic prolifera tion, deposition of collagen and cicatrization.

No satisfactory explanations are available for this anti-inflammatory effect but general formulations are that they inhibit intlammation irrespective of the nature of the inciting agent viz. whether the latter is chemical, mechanical or immunological. Also, this effect is made use of only palliatively and the underlying disease remains unchanged. Moreover, the antiinflammatory effect is exerted only locally and that some steroids have local tissue affinity e g. skin or eyes.

VIII) Effect on Immune response :-

Only fixed tissues reactivity like Tuberculin reaction or homotransplant reaction are suppressed. The corticoids have no effect in :-

i) suppressing formation of antibodies, ii) preventing union of antigen--antibody, (iii) preventing the release of histamine, and (iv) in anaphylaxis.

They merely prevent the inflammatory response leading to cell-injury and hence have the well known therapeutic benefits. Available facts do not establish their so-called specific role as a therapy in severe allergic reactions inspite of the occasional dramatic responses seen.

COMPOUNDS

I) Mineralocorticoids :—

(i) DOCA. Desoxycorticosterone acetate : has no glucocorticoid activity at all, not absorbed from G I tract, hence only injections and buccal pellets effective. Formerly used in adrenal insufficiency, but better compounds are now available.

(ii) 9-alpha-fluoro-cortisol : it is synthetic, has also glucocorticoid activity, hence used in Addison's disease, but not used as a glucocorticoid because of salt retention.

(II) Glucocorticoids :—

Compound	*Comparative Dosage for glucocorticoid activity)*
Cortisone	25 mgm.
Hydrocortisone	20 mgm.
Prednisone	5 mgm.
Prednisolone	5 mgm.
Methyl prednisolone ...	4 mgm.
Triamcinolone	4 mgm.
Parame.hasone	2 mgm.
Dexamethasone	0.75 mgm.
Betamethasone	0:6 mgm.

THERAPEUTIC USES

The clinician should be aware that the glucocorticoids *do not* cure even ONE disease ! Even in Addison's disease, only where their use is rational, the therapy is only substitutive. In all other diseases or conditions, their usage is empirical They prevent the destructive or fibrotic complications of inflammation. Also by suppressing inflammation they allow time for other therapeutic measures or natural body defences to become effective. However, they do not correct the basic cause of the abnormality in any disease.

Thorn et al recommend the use of glucocorticoids in four general types of patients :—

(i) Patients with fatal diseases such as pemphigus whose life may be saved or significantly prolonged.

(ii) Patients with destructive inflammatory diseases such as in certain diseases of eye and nervous system, where essential function can be preserved.

(iii) Patients with acute, self-limited disease, such as status asthmaticus, in whom suppression of allergic component of the condition until a natural remission occurs is life-saving or is very effective in relieving disability.

(iv) Patients with chronic diseases such as rheumatoid arthritis, in whom steroid therapy may delay or prevent development of the usual sequelae (also see below).

General guidelines for the therapy :-

(a) Dosages have to be worked out for each patient by trial and error

(b) A single dose, even a large one is harmless.

(c) A few days' therapy is unlikely to produce harmful effects except when given in high doses

(d) As the therapy is prolonged over period of months, the incidence of disabling and potentially lethal effects increases.

(e) Abrupt cessation of prolonged, high dosage therapy leads to severe adrenal insufficiency endangering life.

(f) They should be used as a last resort.

Two Types of Dosage Schedules are employed :-

(i) Smaller starting doses and gradually increasing till the desired effect is achieved e g. control of pain in diseases like arthritis

(ii) High initial dosage and then gradually reducing till the manitenance dose is reached to control the condition e. g. In all crisis like pemphigus.

Clinical conditions where the therapy is considered :-

1) Adrenal insufficiancy.

2) Arthritis :

(a) Osteoarthritis : here sometimes intra-articular route is employed. The danger is that there may be intraarticular destruction as in Charcot's joints

(b) Rheumatioid arthritis : in this, the rate of progression of joint-disease, when determined objectively, has been the same in steroid-treated and non-steroidtreated patients (controls). Systemic therapy is reserved for acute episodes and for severe disease not responding to other measures like rest, physiotherapy, gold, salicylates etc., and is generally necessary in only about 10% to 20%. "What is gained if the patient becomes asymptomatic from rheumatoid arthritis, but dies of haemorrage from a steroid-induced peptic ulcer? ".

(3) Rheumatic carditis :- The therapy is reserved only for patients not responding to salicylates or those severely ill with fever, acute CCF, arrhythmias. pericarditis.

(4) Kidney diseases :—

(a)	Acute glomerulonephritis	... ...	No effect.
(b)	Chronic ,,	... ...	,,
(c)	Subacute ,, or nephrotic syndrome	...	somewhat useful.

(5) Bronchial asthma :—
should not be used in milder forms of the disease or in presence of infections. Useful in status asthmaticus.

(6) Eye conditions :—
Used in allergic conditions of eye structures. The danger is that topical therapy often induces intraocular hypertension, and visual defects of glaucoma result.
In bacterial or fungal conjunctivitis, when used with antibiotic to which the organisms are not sensitive, the masking of inflammation by the steroids may lead to progression of the infection until the eye sight is lost from panophthalmitis.
The drug is contra-indicated in herpes simplex of eye.

(7) Chronic ulcerative colitis :—
used in severe cases only However, they may mask the signs and symptoms of perforation.

(8) Leukemias :- In acute, and autoimmune haemolytic anaemia, Thrombocytopenic purpura (idiopathic), and granulopenia.

(9) In shock :- Their use is debatable.

SKIN-CONDITIONS

Locally :— in eczematous dermmatitis, contact dermatitis, numular eczema, lichens simplex; in pruritic conditions like pruritis ani, all alleregic conditions especially during reactions and some collagen diseases chiefly SLE.

Systemically:- Pemphigus (here upto 120 mgm. of prednisolone per day may be given).

TOXICITY

Na^{++} retention, water retention, CCF, K^{++} excretion, muscular weakness, and corresponding ECG changes, hyperglycaemia, precipitation of latent diabetes, susceptibility to infections, flaring up of tuberculosis perforation of peptic ulcer and bleeding from it, osteoporosis, psychosis, moon face, central obesity, bluish striae ecchymoses, acne, hirsuitism etc.

ACKNOWELEDGMENTS

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