EFFECTS OF 9-ALPHA-FLUORO HYDROCORTISONE ACETATE ON ADRENAL FUNCTION

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Boland and Headley (1954) described their clinical trials of 9- α -fluoro hydrocortisone acetate (9- α -FF) in the treatment of rheumatoid arthritis. Although salt-retention made the use of this drug in the treatment of rheumatoid arthritis impracticable, they saw in it a new hope, since its existence demonstrated the possibility of producing analogues of hydrocortisone with physiological properties differentially enhanced. The properties studied were the "anti-inflammatory" (anti-rheumatoid in this instance) and

the salt retaining. The former was approximately ten times as great as that of hydrocortisone and the latter more like fifty times as great. How does the 9- α -fluoro substitution affect the adrenocortical suppressive action? It would be a great advantage to have a cortisone-like steroid that would supplement the adrenocortical secretion instead of suppressing it and providing a single qualitatively different substitute.

The Figure shows the results of an experiment

Figure.—Effect of 9- α -fluoro hydrocortisone acetate (given orally to a woman aged 29 with rheumatoid arthritis) on adrenal function measured by daily urinary excretion of 17-hydroxycorticosteroids.

designed to throw light on this question. The patient had early rheumatoid arthritis. She was on a salt-free diet, to minimize fluid retention, during the first period of treatment, but not during the second. The urinary "total 17-hydroxy-corticosteroids (17-OH CS)" assay used was that developed by Dr. J. K. Norymberski at this Centre (Appleby and others, 1954, 1955). The figures recorded on the diagram for 17-OH CS represent the number of mg. excreted daily, less the theoretical recovery, as 17-OH CS, of the administered 9- α -fF (40 per cent.). The patient's control assays show a below average output of 17-OH CS, representing an endogenous secretion of approximately 20 mg. hydrocortisone a day. The results show that as little as 2 mg. 9- α -fF profoundly suppresses the endogenous secretion, suppressing it to the same extent as would ten times as much hydrocortisone. That the suppression was mediated through the inhibition of pituitary ACTH is shown by the excellent response to the administration of ACTH.

Summary

The substitution of a fluorine atom at the 9- α position in the hydrocortisone molecule enhances its ability to suppress adrenocortical function through

pituitary ACTH inhibition. The degree of enhancement parallels that of its anti-rheumatic potency.

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Effet de l'acétate de 9- α -fluoro hydrocortisone sur la fonction surrénale

RÉSUMÉ

La substitution d'un atome de fluor en position 9- α de la molécule d'hydrocortisone renforce sa faculté de supprimer la fonction corticosurrénale par l'inhibition pituitaire de l'ACTH. Son pouvoir antirhumatismal est renforcé au même degré.

Efecto del acetato de 9- α -fluoro hidrocortisona sobre la función suprarrenal

SUMARIO

La substitución de un átomo de fluor en posición 9- α de la molécula de hidrocortisona acrecenta su poder supresor de la función adrenocortical por inhibición pituitaria de la ACTH. Su poder antirreumático sube paralelamente.