Effect of Desoxycorticosterone Acetate on Insulin Sensitivity in Diabetes Mellitus.* (17582)

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(Introduced by Paul K. Smith)

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It has been shown by Cheng and Sayers(1) that desoxycorticosterone acetate (DOCA) increases the sensitivity of rats to insulin, presumably through the previously demonstrated ability of adrenal cortical hormones to inhibit the pituitary output of ACTH.(2) The demonstration of a similar effect of DOCA should theoretically be possible in the type of human diabetes mellitus where the activity of a pituitary factor appears to play a role. Himsworth(3) has suggested that this type of diabetes is present when the glucose-insulin tolerance curve indicates a relative insensitivity to insulin, in contrast to the variety of diabetes in which the glucose-insulin tolerance curve shows a sensitivity to insulin. The present study was undertaken to determine whether insulin insensitive type of curves, as observed in certain patients with diabetes mellitus, can be converted to insulin sensitive type.

Methods and Procedures. Six adult diabetics found to be insulin insensitive by the Himsworth glucose-insulin tolerance test(3) were given 10 mg of DOCA, intramuscularly, daily. In 5 of these patients the injections were continued for 10 days, in one for 4 days. The glucose-insulin tolerance and glucose tolerance tests were done consecutively on successive days before the administration of DOCA and directly after its discontinuance.

Results. In this report only the effects on the glucose-insulin tolerance test are included. The effects of the administration of DOCA on the glucose tolerance, glucose excretion in the urine, fasting blood sugar and insulin requirements will be reported at a later date. From Fig. 1 it can be seen that 5 of the 6 patients showed greater degree of sensitivity to insulin after receiving DOCA than they had before. The curves, which before treatment were characteristic of insulin resistance, changed to those typical of insulin sensitivity. The curves of the sixth patient (G. E.) showed minimal changes, which were in the direction of increased insulin sensitivity, but not beyond the range of spontaneous variability.

Comment. The data presented here seem to show that administration of DOCA to insulin insensitive diabetic patients is followed by increased sensitivity to insulin. This par-

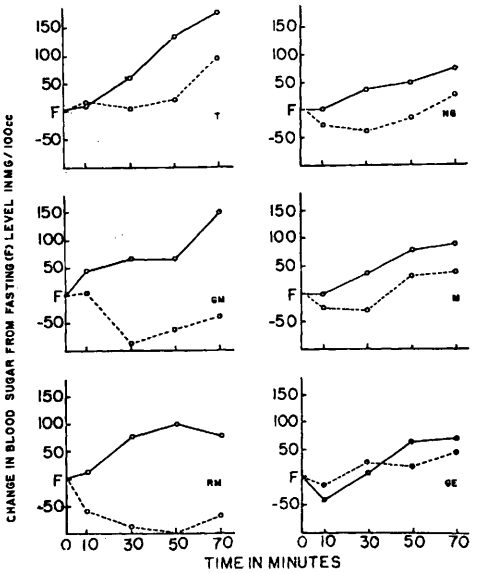

FIG. 1 EFFECT OF CONTINUED ADMINISTRATION OF DOCA ON THE GLUCOSE-INSULIN TOLERANCE TEST

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allels the observation of Cheng and Sayers(1) in non-diabetic rats. These authors suggest that the mechanism of this change is most likely through inhibition of the pituitary output of diabetogenic factors, although direct competition with 11-oxy-steroids must also be considered. The estimation of the changes in output of 11-oxy-steroids by diabetics receiving DOCA will throw additional light on this problem. Further observations on the dynamics of this reaction in humans are in progress.

Summary. The effect of DOCA on the insulin sensitivity of 6 insulin insensitive patients was studied. Five showed a marked increase, and one an equivocal increase in insulin sensitivity.

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Production of Hypertension in the Rat by Substituting Hypertonic Sodium Chloride Solutions for Drinking Water.* (17583)

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A disturbance in the metabolism and distribution of salt and water in animals made hypertensive by the Goldblatt technique and its modifications and in essential hypertension may be inferred from a considerable body of recent work. An increase in the volume of extracellular fluid has been demonstrated in the muscles of hypertensive dogs;(1) polyuria and polydipsia are noted in renally hypertensive rats;(2) increased excretion of antidiuretic hormone has been reported in hypertensive dogs, rats and men;(3) the movements of extracellular fluids in rats made hypertensive by subtotal nephrectomy in response to the administration of hypertonic solutions are altered from the normal.(4) In free choice experiments hypertensive rats voluntarily reduce their sodium chloride intakes,(5) and rigid sodium chloride restriction lowers the blood pressures of hypertensive rats.(6) The utilization of low sodium diets in the therapy of hypertensive disease in man has been reviewed recently,(7) and the hypertensive patient reacts to the withdrawal of dietary sodium chloride in a manner different from the normal.(8) It appears possible, from a consideration of the known effects of adrenal steroids on the extracellular fluid, that the hypertension resulting from the administration of desoxycorticosterone acetate and sodium chloride(9) may also be associated with a disturbance in the extracellular fluids. Although it was originally believed that this type of hypertension might be explained by the renal lesion resulting from the procedure,(10) this view has become untenable in the light of recent evidence which indicates that such

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