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Action of Desoxycorticosterone on Non-Protein Nitrogen Content of Blood During Experimental Uremia.*

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Previous experiments in the mouse and rat showed that desoxycorticosterone in the form of its acetate exerts a beneficial effect during experimental uremia inasmuch as it prolongs the survival time following bilateral nephrectomy.[1] The question arose whether this effect is due to an increased resistance to uremia or whether desoxycorticosterone actually prevents the development of the uremic condition. In order to clarify this problem, we determined the N.P.N. of bilaterally nephrectomized desoxycorticosterone acetate (D.C.A.) treated rats simultaneously with that of nephrectomized but otherwise untreated controls. In order to eliminate the possibility of complicating the experiment by injury to the adrenals, the nephrectomy was performed following careful decapsulation of the kidney, a precaution which makes any adrenal injury highly improbable. As an added safety measure, the right kidney, which is especially close to the adrenal was removed several days before ablation of the left kidney. Thus even if there had been some interference with the right adrenal at the time of the first intervention, sufficient time was allowed for its recovery.

Twenty male albino rats weighing 55 to 100 g were divided into 2 equal groups of 10 animals in such a manner that the average weight was 87 g in both groups. In a first operation, the right kidney was removed in all animals. Three days later, subcutaneous injections with 10 mg of D.C.A. in 0.25 cc of peanut oil were given to the first group on 4 successive days, the second group remained untreated, acting as controls. Six days after the ablation of the right kidney, the left kidney was removed in all animals. Twenty-four hours after the second operation, all the control animals showed obvious signs of uremia (muscular weakness, tremor) and one animal succumbed, while the D.C.A.-treated group was still

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1 Selye, Hans, *Canad. Med. Assn. J.*, 1940, **43**, 333.

in good condition. During the following 6 hours, 6 of the untreated controls went into deep coma and respiration became so shallow that it was obvious they were dying. Therefore, in order to obtain blood for N.P.N. determination (Folin and Wu method modified for microdetermination with the Evelyn photo-electric colorimeter) these animals were killed. Thirty-two hours after the second nephrectomy, the only 3 surviving controls were killed simultaneously with the D.C.A.-treated animals which were still in fairly good condition even at this time. The blood N.P.N. of the untreated controls varied from 180-268 mg %, average 204 mg %, while that of the D.C.A.-treated animals varied from 148-188 mg %, average 170 mg %, although most of the animals in the latter group were sacrificed later than the controls. The significance of this apparent difference between the treated and untreated animals was evaluated by "Student's" method for small samples and is expressed in terms of probability estimated by graphic interpolation in Fisher's table of t.[2] It is generally agreed that differences may be regarded as significant if P is smaller than 0.05 and in our experimental series, $P =$ less than 0.01, consequently the inhibition of the N.P.N. rise must be regarded as highly significant. This conclusion is supported by 2 additional experimental series which were carried out under similar circumstances and gave essentially the same results.

We feel that on the basis of these observations, one may say that D.C.A. tends to counteract the development of uremia in the nephrectomized rat. It remains to be seen whether this action is due to an inhibition of protein catabolism.

Summary. Experiments on rats indicate that treatment with desoxycorticosterone acetate not only prolongs the survival time and delays the clinical signs of uremia, but actually inhibits the rise in the non-protein nitrogen content of the blood after complete nephrectomy.

[2] Fisher, R. A., *Statistical Methods for Research Workers*, 6th ed., Edinburgh, 1936, p. 128.