

MINIMUM OBSERVATIONS NECESSARY TO ADVANCE KNOWLEDGE OF THE ACTION OF ACTH AND CORTISONE

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THE MINIMUM observations for safety are the daily weight, the daily blood pressure, the bi-weekly urinalysis for sugar and constant watchfulness for odd behavior or personality changes.

What I should like to discuss is how we may advance our knowledge by using subtraction. This method has been used twice today. We don't know which of the many metabolic effects of ACTH or cortisone are responsible for the therapeutic effect we want. There is something to be learned by antagonizing some of their different actions individually. For example these agents deplete the body of potassium. Yet one can offset some of this potassium depletion by a high intake and avoid some of its deleterious effects on the heart and the brain without diminishing the therapeutic effect of the hormone. A second example mentioned was the use of insulin to counteract the diabetogenic action of ACTH, which again did not appear to make it less therapeutic.

Moreover, if you give ACTH you produce all the steroids that the adrenal can produce. The patient treated with it shows a marked increase in urinary 17-ketosteroids as well as in corticosteroids. Since we know that cortisone is therapeutic as well as ACTH, we can immediately subtract from the things we have to investigate those effects which we believe are due to the androgen produced by the adrenal, represented by the index of increased ketosteroids in the urine. This is another example of the way we are picking off things from the mass of information at hand to throw out. The next example is taken from a paper by Bartter and associates.¹

One of the most constant effects of either ACTH or cortisone seen in a balance study is a negative nitrogen balance. Now that is very gross measurement; it simply means that more nitrogen comes out of the body than goes in and does not tell which cells it comes from, which cells that is an advantage to, and which cells a disadvantage to. They thought it would be of interest to add to ACTH an agent which has the reverse effect, namely, causes the body to put on tissue and retain nitrogen, and see what the combination of the two did. Metabolic data on a patient with ovarian agenesis (a condition which is of no importance to this experiment) were studied. This patient was first given ACTH alone; then she was given ACTH plus methyl testosterone, then methyl testosterone alone. While she was receiving

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1. Bartter, F. C.; Fourman, P.; Albright, F.; Jefferies, W. McK.; Dempsey, E., and Carroll, E. L.: Does Methyl Testosterone Modify the Effects of Adrenocorticotrophic Hormone (ACTH) and of Desoxycorticosterone Glucoside (DOCG)? in Symposium on Pituitary-Adrenal Function, Baltimore, Horn-Shafer Company, 1951.