THE CLINICAL SIGNIFICANCE OF ESTIMATIONS OF ALDOSTERONE

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A proper appraisal of the clinical significance of estimations of aldosterone must depend on a knowledge of its secretion and metabolism and the mode of transport, including renal clearance, of the hormone and its metabolites. The object of this paper will be to review this field and to illustrate particularly by examples from the studies of the authors and their collaborators in normal and pregnant subjects.

Recently, teams from the Worcester Foundation and the Montreal Children's Hospital have prepared appreciable quantities of (7-3H) aldosterone of about 20μc/μg specific activity. Using this material, which is in many ways more suitable than that previously used, a reinvestigation of some of the problems will be described and it is hoped that the simple methods which have been evolved will be of general application particularly in view of the availability of this tritiated aldosterone.

One of the most important urinary metabolites of aldosterone is an unidentified conjugate of the hormone itself (previously referred to as the 3-oxo-conjugate) which is not hydrolysed by β-glucuronidase. This comprises about 15% of the secretion rate in the normal subject and increases to as much as 50% in pregnancy. Hydrolysis of this conjugate and estimation of the aldosterone released has been the most commonly used clinical method since the first classical studies of Axelrad et al. (1955). It has recently been emphasized that specificity in the estimation of this fraction is not easy to achieve and the methods presently available will be critically reviewed.

Aldosterone is also excreted as metabolites conjugated with glucuronic acid. The total glucuronide fraction has been measured in certain conditions. Ulick & Lieberman (1957) have described one of the compounds which are...
released from this fraction by $\beta$-glucuronidase and claim that it is $3\beta, 18,21$-trihydroxy-5$\beta$-pregnane-11,20-dione.

Following injection of labelled aldosterone and measurements of the specific activity of urinary metabolites, the secretion rate of aldosterone can be calculated. Some workers have measured the specific activity of the aldosterone released from the 3-oxo-conjugate and others that of a tetrahydroderivative of aldosterone. The principles and assumptions of the method will be discussed.

A method will be described which estimates the excretion of aldosterone released from the 3-oxo-conjugate, the secretion rate from the specific activity of this fraction after injection of (7-3H) aldosterone and the quantities and pattern of metabolites after $\beta$-glucuronidase incubation of the urine. The secretion rate and pattern of metabolites of cortisol can be simultaneously estimated after injecting a mixture of tritiated aldosterone and (4-14C) cortisol. The method involves one partition column and paper chromatogram for the aldosterone released from the 3-oxo-conjugate and one partition column plus Porter-Silber reaction for the metabolites of aldosterone and cortisol conjugated with glucuronic acid. Assay of radioactivity can be carried out with a liquid scintillator or flow counter. Following the simultaneous injection of the two labelled steroids their metabolism has been directly compared in the same subjects. Future possibilities for the analysis of aldosterone in body fluids, such as in blood, and their significance will be discussed.

REFERENCES