Increased Renal Pressor Activity (Renin) in Sodium Deficient Rats and Correlation with Juxtaglomerular Cell Granulation.* (24807)

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(Introduced by W. Stanley Hartroft)
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Groups of cells in the media of the afferent glomerular arteriole have attracted attention since they were initially described by Ruyter (1). Goormaghtigh proposed that these juxtaglomerular (JG) cells were the site of the pressor substance, renin(2). In addition to indirect evidence(3), studies of dog kidney coupled wtih assays of renin suggest this theory might be true but statistical data concerning the relationship are lacking(4). Recently a series of studies with the rat has shown changes in pressor activity (renin) of kidneys under a variety of experimental conditions which, as Gross pointed out (personal communication), parallel degree of granulation of JG cells under the same conditions. Pressor activity of renal extracts is increased in adrenalectomized rats and dogs(5,6), decreased with high dietary intake of salt and by desoxycorticosterone acetate administration (7,8), and decreased in the contralateral kidney when the other renal artery is constricted (9). Similar studies have shown parallel changes in granulation of JG cells(10,11,12). In addition, an increase in granulation of JG cells has been produced by dietary sodium deficiency(13,14). To extend these observations, in the present experiment pressor activity in kidneys of sodium-deficient animals has been measured and compared to granulation of their JG cells.

Methods. Fourteen young (65-90 g) male rats of the Wistar strain were fed a semi-synthetic diet deficient in sodium but otherwise nutritionally adequate(15). Fourteen comparable rats consumed the same amounts of diet to which 0.6% sodium chloride was added. After 6 months, the animals were killed and one kidney from each was taken for histologic study. It was fixed in Helly's solution, paraffin sections prepared and stained by a modification of Bowie's technic(16). Degree of granulation of JG cells was estimated by a semi-quantitative procedure to obtain an index (JGI)(14). The higher the JGI, the more JG granules are present in the kidney. A saline extract was prepared from the other kidney by homogenizing the tissue with an equal volume of isotonic saline in a glass homogenizer. The homogenate was centrifuged, the supernatant removed and assayed by the method of Gross and Sulser(17). Test rats were bilaterally nephrectomized one day prior to use. The femoral artery was cannulated and level of blood pressure measured with a mercury manometer. After control readings were obtained, 0.1 ml of a 1 to 50 dilution of the extract was injected into the opposite femoral vein. Animals with either very high or very low blood pressure readings during the control period were not used. The peak of the rise in level of blood pressure was usually obtained in 1 to 3 minutes. A correlation coefficient between maximum pressure elevation and JGI was determined.

Results. Kidneys of sodium-deficient animals contained greater amounts of pressor material (Avg. Δ P = 48 mm., S. D. = $\pm$ 11) than did control animals (Avg. Δ P = 24, S. D. = $\pm$ 7) and in addition had more granules in their JG cells (Avg. JGI = 38, S. D. = $\pm$ 16; *cf.* Avg. JGI for controls = 13, S. D. = $\pm$ 6). The relationship demonstrated in Fig. 1 shows that even within groups, the greater the number of granules in JG cells, the greater was the degree of pressor activity in extracts of these same kidneys. In the small range of overlapping values between the two groups, both JGI's and degree of pressor activity overlapped. JGI correlates with pressor activity of the kidney with a coefficient of 0.80, $p<0.01$.

Discussion. These data strongly suggest that juxtaglomerular cells elaborate the

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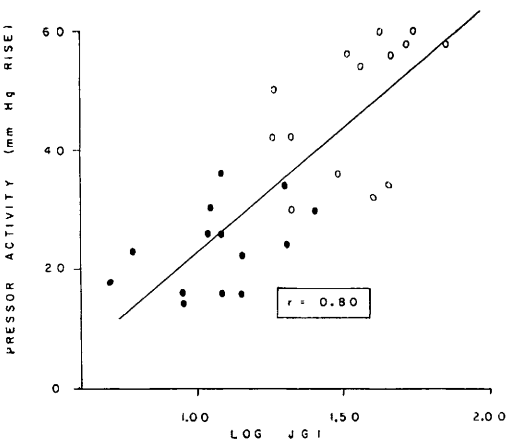

FIG. 1. Graph showing correlation of pressor activity of renal extracts (renin) and degree of granulation of juxtaglomerular cells (JGI). ○ sodium-deficient rats; ● control rats. $p < .01$.

pressor substance, renin, and that the granules seen within them are either renin or a precursor. Tobian *et al.*(18) using similar methods, found that when juxtaglomerular granulation decreased, so did extractable renin in kidneys of hypertensive rats (desoxycorticosterone hypertension and "untouched kidneys" of rats with unilateral renal hypertension) and suggested the same conclusion. Such a suggestion supports the concept that renin may function as a trophic hormone for the zona glomerulosa of the adrenal cortex. This hypothesis is supported further by the following: JGI correlates with width of the zona glomerulosa under conditions of high and low dietary intake of sodium; JGI falls when mineralocorticoids are administered; and hyperplasia with hypergranulation of JG cells occurs when its (alleged) target organ, the adrenal, is extirpated. The observation of Deane and Masson(19) that renin produces thickening of zona glomerulosa is also pertinent. This concept of the function of juxtaglomerular cells would explain how focal circulatory and/or electrolyte disturbances within a kidney could influence mineralocorticoid (aldosterone) secretion.

Summary. Pressor activity (renin) and degree of granulation of juxtaglomerular cells (JGI) of kidneys from normal and sodium-deficient rats were measured. Pressor activity was increased in sodium-deficient animals and correlated ($r = 0.80$) with degree of granulation of JG cells.

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