Compensatory Renal Hypertrophy in Fasted and Fasted-Refed Rats[1] (35947)

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Previous studies from this laboratory have indicated that compensatory renal hypertrophy following uninephrectomy is not diminished in hypophysectomized rats or affected by growth hormone replacement therapy in such animals (1). In addition, more recent work has demonstrated that insulin deficiency produced by streptozotocin diabetes does not inhibit compensatory hypertrophy (2). In these same studies, the process of compensatory hypertrophy was accompanied by increases in long-chain fatty acid oxidation by homogenized kidney cortex.

The present studies were undertaken to further investigate controlling factors in compensatory hypertrophy, the relationship between hypertrophy and increased fatty acid oxidation, and the role of hyperplasia in these phenomena.

Materials and Methods. Male rats (Charles River Laboratories) were fed chow *ad libitum* for 3–5 days until time of unilateral nephrectomy. In Expt. 1, rats weighing 94 ± 4 g were then fasted for 24 hr and refed (S-R) or continued on *ad libitum* food intake (F). Forty-eight hours after the first operation, the remaining kidney in all animals was removed. Following uninephrectomy in Expt. 2, rats (132 ± 2 g) were fasted (S) or fed (F) for 48 hr at which time the remaining kidney was removed. All rats received water *ad libitum* throughout the experiment. In both experiments rats were weighed at the time of surgery. Kidneys were weighed and cortices were isolated and homogenized in oxygenated Krebs–Ringer phosphate buffer (KRP) (1 ml/200 mg). Aliquots were taken for protein determination (1, 2) and 0.5 ml was added to 25 ml flasks containing 0.5 ml of KRP and 125 nmoles of 1-^{14}C-ammonium palmitate (1 μCi/μmole). Incubation of tissues, collection of $^{14}CO_2$, extraction and isolation of media lipids were performed as previously described (1, 2).

Results. Results in Table I were calculated for individual rats and the means and standard error of the mean was obtained. Body weight increased in fed but not fasted or fasted-refed animals. The ratio of kidney weight to body weight rose with nephrectomy in all rats, but in fasted animals this increase was mainly due to body weight loss and therefore might not reflect actual kidney hypertrophy. That such is indeed the case is indicated by our findings that after nephrectomy absolute kidney weight rose more in fed than in fasted-refed rats and actually decreased in 48 hr fasted animals. Compensatory hypertrophy in fasted-refed animals was accompanied by increased palmitate oxidation similar to that seen in fed rats, whereas 48 hr of fasting blocked the increase seen after nephrectomy.

Discussion. Compensatory renal growth during the first 48 hr after uninephrectomy consists mainly of hypertrophy rather than hyperplasia (3). This is substantiated by the observation that hydroxyurea administration which blocks DNA synthesis does not inhibit compensatory renal growth or increases in RNA and protein (4). Similarly, 24 hr of fasting after nephrectomy blocks the mitotic response but not kidney enlargement at 48 hr (5). These data are in accord with our findings in nephrectomized rats fasted 24 hr and refed until 48 hr after nephrectomy. The fact that palmitate oxidation parallels kidney growth and RNA-protein accretion suggests a relationship between these changes.

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TABLE I. Responses to Unilateral Nephrectomy in Fed, Fasted, and Fasted-Refed Rats.

Expt.:	1		2	
	S-R (6)[a]	F (6)	S (7)	F (7)
Body wt change (g)	−2 ± 1.2[c]	7 ± 3[b]	−37 ± 1[b c]	10 ± 1[b]
Kidney wt change (mg)	86 ± 22[b]	132 ± 22[b]	−18 ± 14[c]	180 ± 18[b]
Change in kidney wt/body wt	106 ± 24[b]	120 ± 14[b]	176 ± 18[b c]	110 ± 14[b]
Change in palmitate oxidized (dpm/mg of protein)	206 ± 94[b]	258 ± 94[b]	−80 ± 38[c]	338 ± 68[b]

[a] Number of animals in each group is given in parentheses.
[b] Significantly different from zero.
[c] Significantly different from result in fed animals.

However, palmitate oxidation seems unrelated to changes in DNA metabolism.

Total fasting after nephrectomy does block compensatory growth. Our findings in this regard confirm those of other workers (6) who also noted as did we that body weight loss was much greater than kidney weight loss. We have noted in addition that increases in palmitate oxidation are not seen in states where compensatory renal hypertrophy is blocked by fasting.

In summary, our results indicate that increases in palmitate oxidation are more closely associated with the hypertrophic than with the hyperplastic component of compensatory renal enlargement.

Summary. Following uninephrectomy rats were fed, fasted, or fasted (24 hr) and refed (24 hr) until the time of removal of the second kidney. Fasting for 24 hr with subsequent refeeding did not appreciably affect the process of compensatory hypertrophy or the increase in fatty acid oxidation by cortical homogenate of the hypertrophied kidney. Fasting for 48 hr after uninephrectomy not only blocked both processes, but even resulted in renal weight loss and a decrease in palmitate oxidation. The relationship between hypertrophy and fatty acid oxidation noted in this and previous studies is discussed.

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