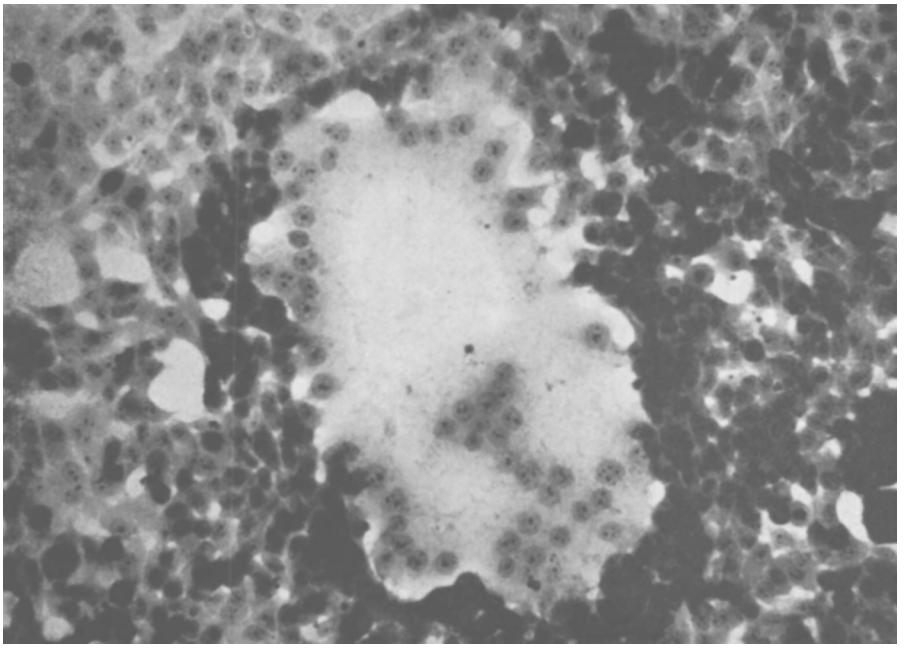

FIG. 1.

the KB strain of human carcinoma cells.

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Lipid Metabolism in Kidney Undergoing Compensatory Hypertrophy.* (22644)

ELINOR LEVIN,† S. ALBERT, AND RALPH M. JOHNSON.
(Introduced by James M. Orten.)
Richard Cohn Radiobiology Laboratory, Detroit Institute of Cancer Research, and the Department of Physiological Chemistry, Wayne State University, College of Medicine, Detroit, Mich.

Previous studies involving "regenerating" liver in rats(1), and the prostate and seminal vesicle tissue of non-castrated and castrated rats with and without testosterone treatment (2), suggested that there was an increased P^{32} uptake in all of the Schmidt-Thannhauser (3) fractions that was associated with cellular hypertrophy. Neither of these conditions can be considered as a hypertrophy, pure and simple, however, since the hypertrophy seen in the first 24 hours in regenerating liver is, in a sense, a preparative state for an ensuing cellular hyperplasia in that it occurs prior to the appearance of mitosis, while that in the prostates and seminal vesicles occurred in the

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presence of actively dividing cells. It was desirable to study the phosphorus metabolism associated with a pure hypertrophy in order to determine whether the changes observed to occur during cell growth were related to or were independent of mitosis.

When one kidney of an experimental animal is surgically removed, the remaining kidney is observed to undergo compensatory hypertrophy(4,5). In this case the complicating factors mentioned above appear to be absent or greatly minimized, and thus this tissue presents itself as one which might profitably be studied.

Experimental. Six male Fisher strain rats, 3-4 months old, were used in each experimental group. The animals were maintained on a stock diet of Purina laboratory chow and water *ad libitum* before and after unilateral nephrectomy. Nephrectomy was accomplished by making a lateral incision about ¾ inches long on the left flank, just below the inferior border of the rib cage. The kidney was raised from the incision and the adrenal gland stripped away and pushed back into the cavity. The pedicle of the kidney was ligated, the kidney excised, and the incision closed in 2 layers.

Preliminary experiments(6) were carried out to determine the percent increase of the intact kidney weight over that of the excised kidney at various times following nephrectomy. The results, calculated on both a moist and dry basis, showed that the greatest increase in weight of the intact kidney occurred about the third day, and rate of increase leveled off at about the seventh day. Therefore, the animals were sacrificed either 3 or 7 days following nephrectomy. Kidneys taken from the right side of non-nephrectomized animals served as controls.

Four hours after giving each rat a subcutaneous injection of 0.45 μc of radioactive phosphorus‡ per g body weight the animal was sacrificed. The abdominal cavity was exposed, and the intact kidney was perfused with ice cold physiological saline *in situ* via the inferior vena cava. The kidney was removed, cut into small pieces, and homogenized in 10% trichloroacetic acid containing 0.4 M $MgCl_2$(7). The phosphorus-containing fractions shown in Table I were then prepared by methods previously described(8,9, 10).

One kidney did not provide enough tissue for the fractionation described above and also for unsaturated fatty acid determinations. Therefore, additional groups of control and experimental animals were prepared in a manner identical to that described, and dienoic, trienoic, tetraenoic, and pentaenoic acids were determined on the perfused kidneys following their homogenization in physiological saline (11).

Results. Three days after nephrectomy the intact kidneys weighed an average of 10% more than those removed; after 7 days they weighed 23% more, and after 20 days they were 27% heavier than the controls. Increases in the amount of cephalin and lecithin in the hypertrophying kidneys were usually apparent 7 days after nephrectomy. However, there was a decreased P^{32} uptake by these 2 phospholipids 3 days after nephrectomy, that had returned to the normal (control) levels by 7 days (Table I). No changes in either amounts of phosphorus or of P^{32} uptake by any of the remaining fractions studied were observed either 3 or 7 days after unilateral nephrectomy (Table I). These results, especially those concerning P^{32} uptake by the phospholipid and acid-soluble fractions, were in contrast to those seen in the experiments involving hypertrophying liver 24 hours after partial hepatectomy(1) and seminal vesicles and prostates of castrated rats following testosterone treatment(2).

Samples of all tissues used in the study were fixed in Bouin's solution and prepared for histological examination(1). The mitotic activity of the kidney 3 and 7 days after nephrectomy was no greater than that seen in organs taken from the unoperated controls. While not enough is known to postulate that there are biochemically distinct types of hypertrophy, it seems possible tentatively to hypothesize as follows: If a tissue is subjected to a stimulus capable of eliciting cellu-

‡ The radioactive phosphorus used in these experiments was furnished by the Oak Ridge National Laboratory, Oak Ridge, Tenn.

TABLE I. P^{32} Uptake and Concentration of Phosphorus in Rat Kidney Undergoing Compensatory Hypertrophy.

Fractions	Controls		3-day nephrectomy		7-day nephrectomy	
	P^{32} uptake*	μg P/mg N	P^{32} uptake	μg P/mg N	P^{32} uptake	μg P/mg N
Acid-soluble	1706 (79)†	26.7 (1.3)	1604 (70)	25.7 (.8)	1776 (58)	30.2 (.9)
Total phospholipids	488 (18)	29.5 (.8)	501 (15)	30.3 (1.0)	519 (23)	33.1 (.4)
Cephalin	333 (14)	14.1 (.4)	284 (10)	12.5 (.2)	346 (20)	16.1 (.3)
Lecithin	809 (52)	11.5 (.4)	780 (21)	13.0 (.4)	877 (90)	12.9 (.3)
Sphingomyelin	93 (4)	3.6 (.1)	87 (3)	3.5 (.2)	99 (4)	3.6 (.1)

* Figures for P^{32} uptake are concentration coefficients calculated as follows:

$$\frac{\text{Counts/min. in fraction}/\mu\text{g phosphorus in fraction}}{\text{Counts/min. injected}/\mu\text{g of body wt}}$$

† Figures within parentheses are stand. errors of mean values.

lar growth (hypertrophy) that is accompanied or followed closely by cellular increase (hyperplasia), it may be expected to show an increased P^{32} uptake in the fractions isolated by the Schmidt-Thannhauser procedure. If, however, the stimulus elicits cell hypertrophy only, it need not produce a change in the rate of uptake of P^{32} in these fractions.

The changes in the concentrations of the unsaturated fatty acids were greater in the presence of compensatory hypertrophy of kidneys, seen in the present experiments, than were observed in the case of liver hypertrophy following partial hepatectomy(12). The dienoic and tetraenoic acid contents were increased, and the trienoic and pentaenoic acids decreased 3 days after nephrectomy (Table II). By the seventh day the amounts had essentially returned to normal. The changes observed then, seemed to be associated with a cell that was rapidly enlarging in size at 3 days, rather than with the enlarged cell itself (at seven days). It is of interest, and perhaps significant, that the compensatory response in the intact kidney 3 days after nephrectomy, whatever its nature, was associated with an increase in only those fatty acids essential for growth, *i.e.*, dienoic and tetraenoic acids, and a decrease in trienoic and pentaenoic acids.

TABLE II. Concentration of Unsaturated Fatty Acids in Rat Kidneys Undergoing Compensatory Hypertrophy.*

	Control (4 animals)	3-day nephrectomy (6 animals)	7-day nephrectomy (4 animals)
Dienoic	94 (4)	112 (6)	86 (2)
Trienoic	16 (4)	4 (2)	9 (2)
Tetraenoic	123 (2)	137 (2)	109 (2)
Pentaenoic	22 (3)	14 (1)	16 (1)

* μg of unsaturated fatty acid/mg nitrogen. Figures in parentheses are stand. errors of the mean values.

Summary. The increased P^{32} uptake of the various phosphorus-containing fractions during hypertrophy in liver and prostatic tissue is not exhibited during renal hypertrophy. It is suggested that the P^{32} increases seen in the liver and prostatic tissue during hypertrophy are associated with subsequent mitotic activity found in these tissues.

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