

Water-soluble antioxidant content of skin of animals receiving the supplemental diet, compared to controls, was higher as seen in the figure. Control animal skin contained an average of 1.08 microequivalents of antioxidant per mg of protein. The maximum increase (50%) in skin antioxidant content of those animals receiving the supplemental diet occurred in the first 2 weeks of feeding, after which the level decreased and remained approximately 10% above controls. No distinct morphological differences were observed in the skin of those animals receiving the supplemental diet when skin biopsies were sectioned and examined under the light microscope.

The average body weight of animals on supplemental diet was slightly higher than that of animals on regular diet. However, the liver weight of animals on supplemental diet was significantly higher than controls (table). The liver weight of these animals reached a maximum in 2 weeks, at a level about 50% higher than the animals on regular diet, and maintained this higher level throughout the period of the experiment. Light microscopic examination of liver biopsies did not reveal any distinct histological differences.

It has been suggested that liver enlargement in rats chronically fed BHT was associated with increased activity of drug metabolizing microsomal enzymes¹³. The increases in liver weight observed in the current studies may also reflect an enhanced or altered ability to metabolize UVL-induced carcinogens of biogenic origin and thus explain the tumor-inhibiting properties of these antioxidants. On the other hand, elevated levels of skin antioxidants may suppress initiation and development of UVL-induced skin tumors by protecting against the direct deleterious effects of UVL. In support of the latter a recent study reported that the same antioxidant mixture protected against UVL-mediated erythema in hairless mouse skin¹⁴. Regardless, dietary antioxidants should provide a useful tool in elucidation of the mechanism(s) of UVL-carcinogenesis.

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Impaired proximal tubular transport functions in anaesthetized splanchnicotomized dogs

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Summary. The maximal tubular transport of inorganic phosphate, D-glucose and para-aminohippuric acid, respectively, was depressed on the denervated side in unilaterally splanchnicotomized, anaesthetized dogs. It is concluded that renal sympathetic activity might in general regulate proximal tubular transport functions.

The importance of sympathetic nervous activity in the regulation of salt and water balance by influencing the renal handling of sodium has been suggested in several studies. An increase of sympathetic activity achieved by low frequency stimulation of the renal nerves^{2,3} or by haemorrhage⁴, as well as by constriction of the thoracic inferior vena cava⁵, were shown to decrease sodium excretion.

On the other hand, interruption of renal sympathetics by different procedures in different species⁶⁻¹¹ or administration of sympathetic blocking agents^{2,10,12-14} were followed by an increase in urinary sodium excretion. The sodium retaining effect of sympathetic activation as well as the natriuresis following renal denervation are not related to any changes in glomerular filtration rate (GFR), renal blood flow (RBF), and/or in their intrarenal distribution. Micropuncture studies have yielded evidence that the primary site of action of both adrenergic activation and sympathectomy is the proximal tubule^{3,5,8,10,11}.

The urinary excretion of inorganic phosphate (Pi) results from filtration and active tubular reabsorption in mammals¹⁵. A predominant part of the reabsorptive process takes place in the proximal tubule¹⁶, but distal tubular reabsorption has also been demonstrated¹⁷. The renal transport of D-glucose (G) by an active reabsorptive process can be localized mainly to the proximal tubule^{18,19}, but recent data raised the possibility of some distal reabsorption²⁰. Para-aminohippuric acid (PAH) is excreted both in vivo²¹ and in vitro²² by active secretion at the proximal tubular level. However, following the verification of bidirectional transport in *Necturus* kidneys²³, such a process has been proved also in other species^{24,25}.

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Material and methods. In our present experiments the effects of Pi, of G and of PAH loading were studied by clearance techniques in anaesthetized dogs with one kidney denervated. Denervation was performed by left splanchnicotomy 10–70 days prior to the experiments.

GFR was measured by the clearance of ^{51}Cr -EDTA, except for the PAH loading series where clearance of inulin²⁶ was used. The concentration of Pi and PAH, in plasma and urine samples, were determined by methods of FISKE and SUBBAROW²⁷ and of BRATTON and MARSHALL²⁸, respectively, that of G was measured enzymatically (GOD-Perid, Boehringer).

Results and discussion. Tubular transport was calculated from the filtered and excreted quantities. Plasma (P) Pi, G and PAH levels (mean values and range), GFR, rate of tubular transport of innervated (inn) and denervated (den) kidneys with standard errors (S.E.), respectively, and results of statistical evaluation by Student's *t*-test are presented in the table.

Effect of inorganic phosphate, D-glucose and para-aminohippuric acid loading on their transport in denervated and innervated kidneys.

	Pi	G	PAH
m	5	9	9
n	17	15	15
P _{mg} % range	10.6–51.3	727–1058	20.8–36.8
\bar{x}	27.8 ± 3.3	886 ± 30	29.3 ± 1.3
GFR	inn 49.9 ± 2.5	55.2 ± 3.1	45.4 ± 3.5
ml/min/100 g	den 50.0 ± 2.3	57.2 ± 2.3	50.4 ± 3.8
Tm	inn 10.2 ± 1.6	349 ± 31	34.1 ± 4.7
mg/100 ml GFR	den 6.5 ± 1.3*	326 ± 27*	26.6 ± 3.8*

m = number of dogs, n = number of clearance periods, P = plasma concentrations of inorganic phosphate (Pi), D-glucose (G) and para-aminohippuric acid (PAH), respectively; GFR = glomerular filtration rate, Tm = maximal tubular transport of Pi, of G and of PAH, inn = innervated kidney, den = denervated kidney, * *p* < 0.01.

Denervation phenomenon, i.e. significantly increased urine flow and sodium excretion from denervated kidneys, was present in all the experimental series with no difference in GFR between intact and splanchnicotomized side.

The results show that maximum transport (Tm) of Pi, of G and of PAH, respectively, was depressed after denervation. Considering that, in addition to diminished proximal tubular sodium reabsorption, a decrease in other mainly proximal tubular active secretory or reabsorptive transport processes without any change in GFR was observed, an impairment of proximal tubular transport function after denervation can be suggested. The mechanism of this phenomenon is not clear as yet. However, the defect of essentially different transport processes allows one to conclude that renal sympathetic activity might in general regulate proximal tubular transport functions.

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Sensitivity of the developing chick myocardium to the positive inotropic effects of calcium and isoproterenol¹

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Summary. The present results show that the sensitivity of the chick myocardium to the positive inotropic effect of Ca^{++} decreases during development and that the Ca^{++} concentration of the physiological solution used must be lowered below 'normal' to study the effects of positive inotropic agents in preparations from younger embryos. Isoproterenol elicits positive inotropic responses in 7–9-day embryonic ventricle and in newborn chick atria; however, the 4-day embryonic myocardium is unresponsive to isoproterenol.

Although the first studies on the effects of acetylcholine and epinephrine on the embryonic chick heart were reported more than 40 years ago, it was not until 1950 that BARRY⁴ reported the first quantitative studies on isolated, spontaneously beating embryonic chick hearts. The present report deals with studies of the positive inotropic effects of Ca^{++} and isoproterenol on isolated, electrically paced preparations of embryonic and newborn chick myocardium.

Materials and methods. Hearts were isolated from embryos obtained from fertilized eggs (White Leghorn) at

various times during development or from newborn chicks within 1 week of hatching. Most studies employed whole 7–9 day embryonic ventricle or newborn chick left

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