

The Effect of Intravascular Volume Expansion on Proximal Tubular Reabsorption during Development (40978)

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Abstract. This study was designed to assess the contribution of the proximal convoluted tubule to the blunted natriuretic response of the newborn to volume expansion. Guinea pigs ($n = 17$) ranging in age between 1 and 56 days were subjected to similar degrees of vascular volume expansion by infusion of an isoncotic albumin solution. Measurements of TF/P inulin in proximal tubular fluid were made by the recollection technique prior to and following the expansion. A decrease in proximal fractional reabsorption of fluid ($P < 0.01$) was observed at all ages, but there were no significant differences in TF/P inulin between various age groups under both control and experimental conditions. Whole kidney fractional reabsorption of sodium, which was similar in all groups during control conditions, was significantly lower ($P < .001$) in the oldest than in the two younger groups of animals during volume expansion. These results demonstrate that the proximal convoluted tubule is not the site responsible for the age related differences in sodium reabsorption. The tendency to retain a sodium load observed during maturation appears therefore to be due solely to enhanced reabsorption in segments of the nephron located beyond the proximal convoluted tubule.

It is well recognized that newborn animals lack the ability to dispose efficiently of a sodium load (1-5). Experiments performed in our laboratories have demonstrated that within 2 hr after the administration of an isotonic sodium solution equal to 10% of body weight, 1-week-old puppies excrete only about 5% of the load while adult dogs excrete about 50% of the total amount infused (3). Clearance experiments performed in puppies (6) have provided suggestive evidence that enhanced reabsorption of sodium at the level of the distal nephron contributes to this blunted response. The role played by the proximal convoluted tubule in this phenomenon has been investigated only in rats older than 3 weeks of age (7). It is for this reason that we decided to study the behavior of this nephron segment in guinea pigs of various ages subjected to volume expansion. Unlike the rat, this animal species is born with functional superficial nephrons which are amenable to micro-puncture from the first day of life.

Methods. The study was performed in 17 guinea pigs, ranging in age between 4 hr and 56 days, and in weight between 70 and 406 g. The animals were divided into three

groups corresponding to specific stages of postnatal development of renal function: 1 to 14 days of age, characterized by very low glomerular filtration rates (GFR) of the superficial nephrons; 15 to 22 days of age, representing the period of rapid rise in superficial nephron GFR; and a third group, 23 to 56 days of age, characterized by a slow rise in superficial nephron GFR (8).

The preparation of the animals for micro-puncture was similar to that described previously (9). Isotonic saline (0.9% NaCl solution), containing [*carboxyl*- ^{14}C]inulin in concentrations calculated to deliver 60 $\mu\text{Ci/hr}$ in the first week of life, 50 $\mu\text{Ci/hr}$ during the second week, and 40 $\mu\text{Ci/hr}$ thereafter, was infused at a rate of 0.6 ml/100 g body wt per hour. Blood samples were obtained from the arterial catheter, which was also used to record mean arterial pressure. Ureteral catheterization was performed for collection of urine samples, which were used for measurements of inulin and sodium.

After a 30-min period of equilibration, fluid collections from randomly selected proximal tubules were obtained. Special care was taken to avoid the use of negative pressure during the collections and to pre-

TABLE I. CHANGES IN HEMATOCRIT ASSOCIATED WITH INTRAVENOUS INFUSION OF A 4% ALBUMIN SOLUTION EQUAL TO 5% OF BODY WEIGHT

Age (days)	Decrease in Hct (%)
1-10	20.2 ± 4.8 ^a
15-22	21.1 ± 5.7
27-56	22.1 ± 6.8

^a Mean ± SEM.

vent retrograde leak by insuring that the length of the mineral oil block was equal to at least two tubular diameters.

The animals were then volume-expanded by adding salt-poor human albumin (4 g/dl) to the infusing solution. The rate was adjusted such as to deliver a load equivalent to 5% of body weight in 30 min. After a 15-min period of equilibration, fluid was collected again from the same tubular site (recollection technique).

The concentration of radioactively labeled inulin in tubular fluid, final urine,

and plasma was determined in a liquid scintillation spectrometer (ABAC SL40, Intertechnique). All samples in which the total count was not at least twice that of the background were discarded. The concentration of sodium in plasma and urine was determined by flame photometry.

Fractional reabsorption of sodium was calculated from the formula: $1 - (U/P \text{ sodium} \times P/U \text{ inulin})$, where U and P are the urinary and plasma concentrations of sodium and inulin, respectively.

The effect of volume expansion on sodium reabsorption was assessed by comparing control values with those obtained 1 hr after the infusion of albumin was completed.

Statistical analysis was done by using the Student's t test (10).

Results. The degree of intravascular volume expansion was similar in all groups, as indicated by the fall in hematocrit (Table I). TF/P inulin ratios did not differ significantly with age, under control conditions (Table II). There was a significant decrease ($P <$

TABLE II. TF/P INULIN RATIOS OBTAINED BY THE RECOLLECTION TECHNIQUE BEFORE AND AFTER INTRAVENOUS INFUSION OF A 4% ALBUMIN SOLUTION EQUAL TO 5% OF BODY WEIGHT

Age (days)	Body weight (g)	TF/P inulin ^a	
		Control	Experimental
1	101	1.59	1.01
2	70	1.78	1.73
2	89	1.22	1.16
5	93	1.31	1.28
5	85	1.38	1.01
10	160	2.20	1.28
10	213	2.21	1.39
Mean ± SEM		1.67 ± 0.15	1.28 ± 0.08
15	217	1.48	1.11
17	194	1.46	1.22
19	211	2.01	1.01
21	228	2.28	1.72
22	200	1.27	1.01
Mean ± SEM		1.70 ± 0.19	1.21 ± 0.13
27	142	1.24	1.01
28	208	1.40	1.29
35	191	1.89	1.09
42	227	1.59	1.30
56	406	2.70	1.56
Mean ± SEM		1.76 ± 0.26	1.25 ± 0.09

^a Each value represents a mean of two to four individual measurements. There was an overall significant decrease in TF/P inulin, similar in all age groups, in response to isoncotic volume expansion ($P < 0.01$). There was no significant difference in TF/P inulin between various age groups, under both control and experimental conditions.

0.01) in TF/P inulin ratios in response to isoncotic volume expansion, but the magnitude of the change did not vary from one age group to another (Fig. 1). In spite of the similar inhibition of sodium reabsorption in the proximal tubule, whole kidney fractional reabsorption of sodium (Table III) decreased more in the oldest than in the younger animals ($P < 0.01$).

Discussion. Studies performed under hypoxic conditions in guinea pigs and dogs have demonstrated that the fractional reabsorption of sodium in the proximal tubule remains stable during development (8, 13). Whether or not the same applies to the conditions induced by volume expansion has been ascertained only in rats (7). Baker and Solomon found no difference in the proximal fractional reabsorption of sodium between the 20- to 30-day-old and the more than 50-day-old animals subjected to an infusion of hypertonic saline solution. The relevance of this finding to the study of renal sodium handling during development is difficult to ascertain. It is indeed possible that a significant stage of maturation is missed in this animal species due to the inability to use micropuncture techniques until nephrogenesis is completed in the superficial cortex. Moreover, measurements of hydraulic permeability of the proximal tubule as well as those of hydrostatic and oncotic pressure gradients across the proximal tubular epithelium have demonstrated age-related differences which would

TABLE III. CHANGES IN FRACTIONAL REABSORPTION OF SODIUM ASSOCIATED WITH INTRAVENOUS INFUSION OF A 4% ALBUMIN SOLUTION EQUAL TO 5% OF BODY WEIGHT^a

Age (days)	Control	Experimental
1-10	0.986 ± 0.010 ^b	0.938 ± 0.030
15-22	0.990 ± 0.010	0.947 ± 0.060
27-56	0.990 ± 0.004	0.879 ± 0.160

^a There was a significant decrease in fractional sodium reabsorption in response to isoncotic volume expansion in all groups ($P < 0.05$). The fractional sodium reabsorption after volume expansion in the oldest group was significantly less ($P < 0.01$) than that in the other two age groups.

^b Mean ± SEM.

be expected to affect sodium reabsorption at least under certain experimental conditions (9, 11-14). Our results demonstrated that despite these differences the degree of inhibition of proximal tubular reabsorption in response to volume expansion remains constant during the development of the guinea pig. However, in this, like other animal species (1-3, 5-7), and in the human (4), the excretion of sodium was less in the two younger than in the oldest group. It is therefore reasonable to surmise that the age-related differences in Starling forces are balanced by those in tubular permeability resulting in similar degrees of proximal fractional reabsorption of sodium and water both under conditions of hyponemia and volume expansion. The retention of sodium observed in the young should, therefore, be a consequence of enhanced reabsorption at more distal sites of the nephron. The behavior of the proximal tubule neither blunts nor exaggerates this phenomenon.

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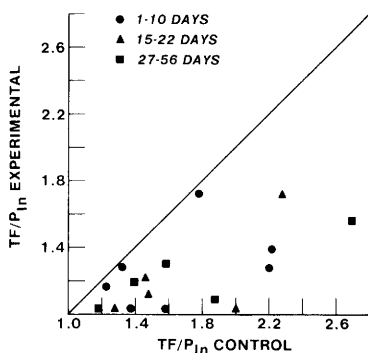


FIG. 1. TF/P inulin ratios in three different age groups of guinea pigs, before (Control) and after (Experimental) intravascular volume expansion. Note that all points are below the line of identity.

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