EFFECTS OF ACUTE CHANGES IN DIETARY PROTEIN ON RENAL CONCENTRATING MECHANISM AND RENAL MEDULLARY WATER AND SOLUTE CONTENT IN RATTUS NORVEGICUS

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As discussed earlier (B.Schmidt-Nielsen, J.M.Barrett, B.Crossley, B.Graves, MDI Biol. Lab. Bull. 23:68-71,1983; B.Schmidt-Nielsen, J.M.Barrett, B.Graves, B. Crossley, Am. J. Physiol. in press) rats maintained on a reduced protein (LP) diet exhibited a number of physiological changes in kidney function which are accompanied by renal morphological changes. The changes, in urea clearance and distribution of solutes in the renal medulla, were found to develop gradually during 3 to 4 weeks on the LP diet, and they specifically affected the renal handling of urea and the morphology of the thin limbs of the loops of Henle. The slow development of the changes occurring when the diet is changed from normal (NP) to a reduced protein diet appears to contrast remarkably with the sudden increase in urea urine/plasma ratio which takes place when the protein intake is suddenly increased (in man, H.V.Murdaugh Jr.,B.Schmidt-Nielsen, E.M.Doyle, R. O' Dell, J. Appl. Physiol. 13:263-268,1958; in camel, B.Schmidt-Nielsen, T.R.Houpt, S.A.Jarum, Am. J. Physiol. 188:477-484,1957). To investigate this question in more detail, measurements of solute content of the renal medula and other physiological studies (to be complemented by morphological studies) were made on rats maintained on a reduced protein diet for four weeks followed by a normal protein diet for a few days. Six groups of young Wistar rats were studied: NP for 4 weeks,LP for 4 weeks,LP for 3 weeks,LP for 4 weeks switched to NP for either 2, 3, or 4 days. In this report the results from three of these groups only will be reported in detail: Group 1, NP diet for 4 weeks (NP rats), Group 2, LP diet for 4 weeks (LP rats), Group 3, LP diet for 4 weeks, then NP diet for 2 days (LPNP).

The rats were dehydrated for 18-20 hours, and killed in CO_2. Urine and plasma samples were collected and the kidneys removed and sectioned. The inner medulla was divided into three zones, IM1, IM2, and IM3 as shown previously (B. Schmidt-Nielsen, J.M.Barrett, B.Crossley, B.Graves, MDI Biol. Lab. Bull. 23:68-71, 1983). The outer medulla was divided into two parts: outer stripe of outer medulla, OM1, and inner stripe of outer medulla, OM2. The tissues were dried and analysed as previously described (B.Schmidt-Nielsen, B.Graves, J.Roth, Am. J. Physiol.244:F472-F482,1983) for determination of water and solute content. Plasma urea concentration (Table 1) was significantly higher and urine/plasma urea ratio was significantly lower in the LP compared to the NP rats (Table 1). This is due to the effective urea conservation in LP rats. In the LPNP rats the plasma urea remained high, while the urine/plasma urea ratio rose significantly (similar results were seen after 3 and 4 days).

Table 1
(n = 6)

	Plasma concentration			Urine concentration			
	Osm mOs	Urea mM	Na mEq	Osm mOs	Urea mM	Na mEq	Urea U/P
NP	318.7 ± 2.7	9.15 ±0.39	158.4 ± 1.7	2594 ±118	1456 ± 64	124 ±15	140.4 ±34.4
LP	323.3 ± 3.0	12.13 ±0.86	158.8 ± 1.7	1457 ± 70	314 ±47	254 ±35	25.9 ±5.4
LPNP	316.3 ± 2.2	14.00 ±1.04	156.6 ± 2.0	2135 ±103	1111 ± 47	104 ±52	84.3 ±4.4

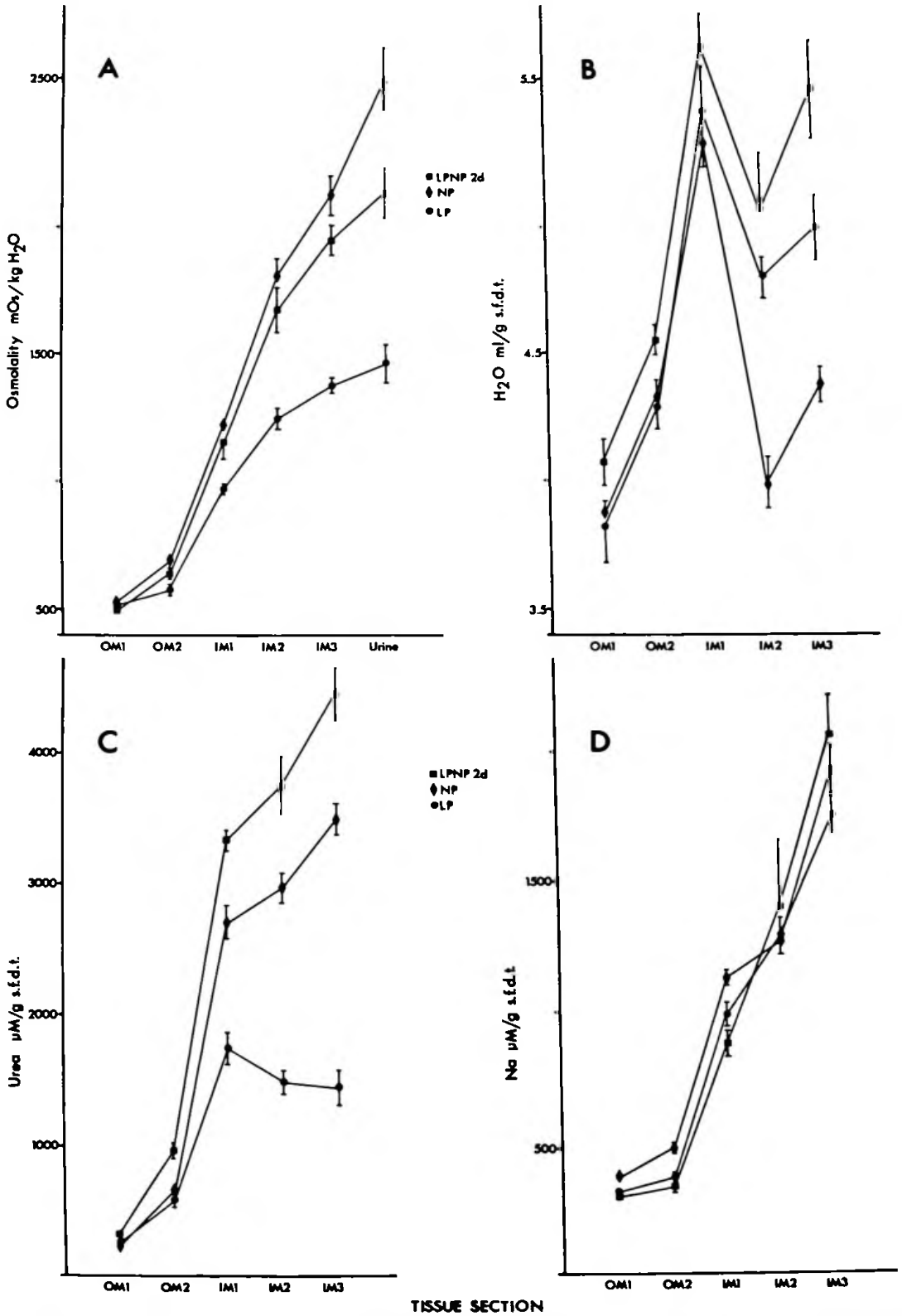

Fig. 1. Renal medullary osmolalities (mOs/kg water) and amounts of water and solutes. A) Osmolality of outer (OM1,OM2) and inner medulla (IM1,IM2,IM3) as well as the osmolality of urine. B) Amounts of water in ml/g s.f.d.t. in the zones of the outer and inner medulla. C) Amounts of urea (mM/g s.f.d.t.) in the renal medulla of three groups of rats. D) Amounts of sodium in the medulla.

The osmotic concentration of the renal tissue was lower in the inner medulla of the LP compared to the NP rats (Fig. 1). In the LPNP rats (Group 3) the osmotic concentration of the tissue and urine was almost as high as in the NP rats. The difference in the water content of the tissues per gram solute free dry tissue (g s.f.d.t.) between LP and NP rats was as expected (Fig. 1), since the water content of the tissue increases with decreasing osmolality (B.Schmidt-Nielsen, B.Graves, J. Roth, Am. J. Physiol. 244:F472-F482,1983). There was, however, an unexpected and highly significant difference in the water content (ml/g s.f.d.t.) of the tissue in LPNP rats. In spite of the fact that the osmolality was as high in the tissues of LPNP rats as in the NP rats, the water content was significantly higher in all tissue zones in LPNP rats than in both LP and NP rats. In the rats changed from an LP diet to a NP diet for the 3 and 4 days, the water content of the inner medulla gradually decreased but did not reach the level in the NP rats. The amount of urea (mM/g s.f.d.t.) was also significantly higher in the inner and outer medullary tissue of the LPNP rats than in both LP and NP rats (Fig. 1). The amount of sodium (mEq/g s.f.d.t.) in the renal medullary tissues was not significantly different in the three groups.

The change which occurred in renal function following a change in diet from LP to NP for two days restored the ability to concentrate the osmolality and urea concentration in the renal medulla and in the urine. However, the handling of water in the renal medulla was profoundly affected in the LPNP rats, i.e., less water was removed from the inner and outer medulla of these rats compared to rats maintained for 4 weeks on either an NP or LP diet. The removal of water from the inner medulla is an important component of the counter-current concentrating mechanism of the mammalian kidney and the change observed may involve a change in water permeability of medullary structures. Studies in collaboration with Dr. J. M. Barrett are in progress to determine changes in morphology of the kidneys associated with these physiological changes. Supported by NIH grant # R01 AM15972.