NEPHROLOGY

The natural history of renal tubular acidosis: Lightwood's syndrome revisited. MARTIN A. NASH, ANTONIO D. TORRADO, EDDIE S. MOORE, JUAN RODRIGUEZ-SORIANO, IRA GREIFER, ADRIAN SPITZER, and CHESTER M. EDELMANN, JR. *Albert Einstein Coll. of Med., N. Y., N. Y.*

Twelve children with primary renal tubular acidosis (RTA) studied with HCO_3^- titration and NH_4Cl loading have been observed 1½–8 yrs. These include 7 ♂ with proximal RTA (PRTA) dx'd at 7–18 mos, and 3 ♂ and 2 ♀ with distal RTA dx'd at 3–13 yrs. Bone disease and/or nephrocalcinosis were present in DRTA but not PRTA. GFR (C_{IN}) at onset was normal or slightly decreased in PRTA, but 40–60% of normal in DRTA. GFR is now normal in all patients. With rx pts had accelerated growth, reaching at least the 3rd percentile in 2–3 yrs, with some achieving the 50th percentile. Five with PRTA have normal blood pH and HCO_3^- off rx, 5–8 yrs after dx. Two remain on rx <2 yrs after dx. The acidification defect in pts with DRTA persists. Thus PRTA appears to be a self-limited disease of bicarbonate reabsorption in male infants, characterized by growth retardation and acidemia, without bone disease and nephrocalcinosis. DRTA appears to be a permanent defect in urinary acidification, with acidemia, growth retardation, bone disease, and nephrocalcinosis. Response to rx in both groups is good, with marked improvement in growth, and normalization of GFR in DRTA despite severe degrees of initial nephrocalcinosis. On the basis of these observations, it seems likely that Lightwood's syndrome was proximal RTA—not distal RTA as has been considered heretofore.

Maturation of intrarenal blood flow distribution in newborn puppies. LEONARD I. KLEINMAN and JOHN H. REUTER (Intr. by I. Light). *Univ. of Cincinnati Coll. of Med., Cincinnati, Ohio.*

Intrarenal glomerular blood flow distribution was studied in 34 newborn puppies ranging in age from 1 to 40 days using radio-labeled carbonated microspheres 15–25 μ . The technique was validated by histological sectioning, dual labeling of microspheres and multiple sectioning of the same kidney. Relative blood flow per gram tissue to juxtamedullary inner cortical (IC) and outer cortical (OC) glomeruli was determined by the ratio of microspheres trapped in the respective region. IC/OC ratios fell from 1.2 at birth to 0.25 at 14 days and remained relatively constant thereafter. There was no correlation between IC/OC ratio and EPAH extraction (EPAH). EPAH remained constant at 0.50 during the first 40 days of life (adult EPAH = 0.85). IC/OC ratio declined as blood pressure rose from 30 to 70 mm Hg and remained relatively constant at blood pressures above 70 mm Hg. These results suggest that there is a marked change in intrarenal blood flow distribution during the first two weeks of life as more blood is delivered to outer cortical nephrons with maturation. The early large flow to juxtamedullary glomeruli suggests a large post-glomerular medullary flow. The lack of correlation between IC/OC ratio and EPAH suggests that the low EPAH in the newborn period is not due solely to a large medullary flow. Finally, intrarenal flow distribution maturation is closely related to blood pressure maturation.

The effect of Na_2SO_4 on urinary acidification in the intact fetal lamb. EDDIE S. MOORE, CLARENCE W. DELANNOY, and JOHN B. PATON (Intr. by Richard Behrman). *Univ. of Ill. Coll. of Med., Chicago, Ill.*

Recent studies have shown that the fetal kidney is limited in its ability to acidify the urine and to secrete hydrogen ions when compared to the adult kidney. To further study H^+ secretion and the ability of the fetal kidney to establish a pH gradient between blood and urine, Na_2SO_4 was infused into the intact fetus.

Studies were done on 7 near-term pregnant sheep and their fetal lambs. The ewes were injected with DOCA and the fetuses were given cortisone acetate. This served to enhance renal tubular reabsorption of Na^+ . Caesarean sections were performed and 75cc of 8% Na_2SO_4 was infused into each fetus. Blood and urine samples were collected from the ewe and fetus. There were no significant changes in fetal or maternal blood pressure, pulse, temperature or pCO_2 .

The mean initial urine and blood pH in the fetus was 7.075 and 7.352 respectively. The mean minimum urine pH in the fetus after Na_2SO_4 was 5.2 with a range of 4.7–5.7. The mean minimum blood pH in the fetus after Na_2SO_4 was 7.362. The mean urine pH in the ewe before and after Na_2SO_4 was 5.824 and 5.920 respectively. This is consistent with little or no transfer of $\text{SO}_4 =$ across the placenta. The mean maximum TA and NH_4 excretion in the fetus was 4.35 and 8.21 $\mu\text{Eq}/\text{min}/\text{kg}$ respectively. There was no correlation between fetal weight and response time before production of an acid urine.

These studies indicate that in the intact fetal lamb, a stimulus (DOCA) to the fetal kidney to reabsorb Na^+ without equivalent amount of anion results in intense acidification of the urine. The fetal kidney is thus able to establish a pH gradient with no evidence of intrinsic limitation of hydrogen ion secretion.

Pressure gradients for filtration in the developing kidney. ADRIAN SPITZER (Intr. by Chester M. Edelmann, Jr.). *Albert Einstein Coll. of Med., N. Y., N. Y.*

It is well documented, both in humans and animals, that low rates of glomerular filtration prevail during early postnatal life. Although several explanations for this phenomenon have been offered, no direct measurements of the forces responsible for glomerular filtration in the developing animal are available. This information was sought in the present study by micro-puncture techniques. Free flow proximal intratubular pressure (P_t), "stop flow" (P_s), mean arterial, and colloid-osmotic pressure of the plasma protein (P_{co}), were determined in guinea pigs ranging in age from 1 to 56 days (27 animals). The values obtained were used in the calculation of glomerular capillary pressure, $P_{cap} = P_s + P_{co}$, and of the effective filtration pressure, $P_{eff} = P_{cap} - (P_t + P_{co})$. Free flow intratubular pressure increased from 5.5 ± 0.3 during the 1st to 9.2 ± 0.2 (mean $\pm$ S. E.) during the 8th week of life, whereas capillary pressure increased from 21.2 ± 1.8 to 29.3 ± 1.0 mm Hg. Since the actual increase in capillary pressure was about twice the increase in intratubular pressure, effective filtration pressure rose accordingly from 4.9 ± 0.4 to 9.4 ± 0.8 mm Hg. During the same period mean arterial pressure changed from 42.9 ± 2.2 to 58.5 ± 7.9 mm Hg. It appears, therefore, that an increase in glomerular capillary pressure is an important factor in the increase in glomerular filtration rate that is observed with age.

Ontogeny of amino acid transport sites in kidney: specific and total activity. K. BAERLOCHER, C. CLOW, S. MACKENZIE and C. SCRIVER. *McGill Univ.-Montreal Children's Hosp. Res. Inst., Montreal, Que., Can.*

Urinary hyperexcretion of proline, hydroxyproline and glycine is a defined component of the transient impairment in tubular