1642 RENAL INVOLVEMENT IN ARTERIOHEPATIC DYSPLASIA (AHD). Kumudchandra J. Sheth & Steven L. Werlin, Med Coll of Wis, Dept of Peds, Milwaukee, WI.

The syndrome of AHD consists of cholestasis secondary to paucity of intrahepatic bile ducts, pulmonic stenosis, vertebral abnormalities, mental retardation, and a characteristic facies. Although renal involvement has been infrequently reported, a spectrum of changes including congenital small kidney with renal failure, cystic kidney disease, tubulointerstitial nephropathy and renal lipidosis have been noted. To better define renal functions in AHD, we evaluated 8 children(2M,6F;ages2-16yr). Glomerular filtration rate (GFR) was reduced in 2/5(<10%;<50%). One of 2 pts with proteinuria had nephrotic syndrome and reduced GFR; 1 had mild proteinuria and normal GFR. Proximal and distal renal tubular functions including concentration and acidifiation tests were normal(5/5). Initially serum electrolytes, calcium, magnesium, uric acid and acid-base status were normal, but hyperchloremic metabolic acidosis developed with cholestyramine therapy in 3. Rickets developed in 1. Blood pressure was normal in all. Renal tissue(1 biopsy, 3 postmortem) examination showed normal kidney(1), glomerulosclerosis(1), calcium deposits(1) and renal lipidosis(1). On electron microscopic examination, the lipid deposits showed granular and lamellar electron-dense bodies, while X-ray dispersive analysis showed them to be rich in chromium, silicon, calcium, phosphorus and iron. Conclusions: 1) A spectrum of renal changes are found in AHD. 2) Renal functions may be variably reduced. 3) Renal lipidosis may be related to long standing hyperlipidemia as a result of intrahepatic cholestasis. 4) Trace elements are accumulated in electron-dense bodies.

●1643 POSTISCHEMIC ATP-MGCL2 PROVIDES PRECURSORS FOR THE RESYNTHESIS OF CELLULAR ATP. Norman J. Siegel, M. Stromski, M. Avison, G. Thulin, R.G. Shulman, Yale Univ. Sch. of Med., Dept. of Peds, and Molec Biophy and Biochem, New Haven, CT 06510.

Accelerated recovery of renal ATP levels have been documented in rats given a postischemic infusion of ATP-$MgCl_2$. This observation could be related to a direct entry of ATP as a source of metabolic energy or to augmentation of the resynthesis of cellular ATP. To distinguish between these possibilities, rats were infused with either ATP-$MgCl_2$ (25 μmoles), AMP-$MgCl_2$ (25 μmoles) or normal saline (NS) after 45 min of renal ischemia. Renal cortical ATP levels were determined continuously in vivo, prior to, during and for 120 min after the ischemic injury using ^{31}P NMR spectroscopy (TMR-32; 32.5 MHz for ^{31}P).

During the ischemia, cellular ATP levels fell rapidly and remained <10% of control values in all rats. ATP levels returned to 50% of control values within 10 min after the ischemic insult in all animals. In rats given NS, renal cortical levels of ATP recovered to only 65±2% at 2 hrs indicating a very slow and incomplete regeneration of cellular nucleotides. In contrast, the animals infused with ATP-$MgCl_2$ (81±3%) or AMP-$MgCl_2$ (83±4%) had significantly better ($P<0.01$) recovery of cellular ATP.

Since ATP-$MgCl_2$ and AMP-$MgCl_2$ produced a similar result, it would appear that the infused ATP was not necessarily a direct source of cellular energy. Moreover, these findings would suggest that the postischemic infusion of ATP-$MgCl_2$ provides precursors for the repletion of the tissue nucleotide pool and resynthesis of cellular ATP.

1644 PROSTACYCLIN PRODUCTION AND VITAMIN E IN THE HEMOLYTIC UREMIC SYNDROME. RL Siegler, JB Smith, MB Lynch, SF Mohammad, Departments of Pediatrics and Pathology, University of Utah School of Medicine, Salt Lake City, Utah.

Preliminary reports suggest that Hemolytic Uremic Syndrome (HUS) plasma is unable to stimulate endothelial cells to produce normal amounts of prostacyclin (PGI_2), a substance known to inhibit platelet aggregation and thrombosis. Some children with HUS have been reported to have low levels of Vitamin E. Neonatal plasma reportedly is unable to stimulate normal PGI_2 production. This can be corrected by the in vitro addition of Vitamin E.

We, therefore, tested the hypothesis that HUS sera have an impaired ability to stimulate PGI_2 production and that this abnormality is associated with Vitamin E deficiency. HUS (n=19) and normal children sera (n=22) were incubated with cultured endothelial cells, and PGI_2 generation was determined by radioimmunoassay of its stable metabolite, 6-keto $PGF_{1\alpha}$. Vitamin E and total lipids were also measured in HUS (n=15) and normal sera (n=19). The following results (mean ± SD) were obtained:

	6-keto $PGF_{1\alpha}$ (ng/ml)	Vitamin E (ng/dl)	Vitamin E/Total Lipids
HUS Children	6.7±3.6	1.30±0.40	1.60±0.69
Normal Children	11.1±3.8	1.15±0.45	1.92±0.73

Sera from children with HUS residing in the Intermountain Region have a significantly ($p<0.001$) decreased ability to stimulate PGI_2 production by cultured endothelial cells. However, the lack of significant difference in the Vitamin E and Vitamin E/Total Lipids ratios fails to support a role for Vitamin E in the pathogenesis of HUS.

●1645 CELLULAR MECHANISM OF RENAL PHOSPHATE (Pi) TRANSPORT BY THE NEWBORN. Yong Choi, Rolf Kinne and Adrian Spitzer. Albert Einstein College of Medicine, Departments of Pediatrics and Physiology, Bronx, New York.

We have provided evidence that the enhanced renal reabsorption of Pi in growing animals is due to a large extent to an increase in the fractional reabsorption of Pi by the proximal tubule. This prompted us to explore the cellular mechanism responsible for this phenomenon. Vesicles of proximal tubule brush border membranes obtained from guinea pigs of either 1-7 or > 30 days of age were used to assess the kinetics of the Na^+-Pi cotransporter. No significant differences were found between these two age groups either in the Km (0.61 vs 0.75 mM, $p>.4$) or in the Vmax (1282 vs 1960 pmole/mg protein at 12 sec, $p>.2$). The Ki, measured in the presence of arsenate in the incubation media, was also found to be similar (3.0 vs. 2.3 mM, $p>.2$). To assess the Pi concentration gradient across the luminal membrane, we measured intracellular concentration of Pi by spectrophotometry (SP) and by nuclear magnetic resonance (NMR) and found it to be ≈ 3-fold lower in the newborn than in the adult. The exchangeable Pi, measured by NMR, was found to represent only ≈ 25% of the total intracellular Pi, measured by SP (.25±.6 vs 1.0±0.10 mM, $p<.001$ in the newborn and .60±.07 vs 2.06±.09 mM in the adult, $p<.005$). In addition, the Na^+-independent uptake of Pi by brush border microvesicles was significantly higher in the newborn than in the adult ($p<0.05$) at concentrations of Pi in the media varying between 0.1 and 4.0 mM. We surmise that, contrary to previous assumptions, a steep downhill Pi concentration gradient exists across the luminal membrane of the proximal tubule and that passive diffusion along this concentration gradient may contribute to the enhanced renal reabsorption of Pi observed in growing animals.

●1646 THE ROLE OF ALDOSTERONE IN RENAL ELECTROLYTE TRANSPORT DURING DEVELOPMENT. Yuhei Ito, David I. Goldsmith, and Adrian Spitzer. Albert Einstein College of Medicine, Department of Pediatrics, Bronx, New York.

Indirect evidence has led us to postulate a cause and effect relationship between the high levels of plasma aldosterone concentration (PAC) and the positive electrolyte balance prevailing during infancy. The purpose of this study was to assess directly the relationship between PAC and renal transport of Na^+ and K^+. PAC measurements and renal clearance of Na^+ and K^+ were performed in 1 and 6-week-old puppies that received a 5% saline solution, 15 ml/kg b.w. for 3 consecutive days i.p. (E), and in age matched sham operated controls (C). The same variables were then measured during i.v. infusion of increasing amounts of aldosterone (5,10, and 20 μg/kg b.w. for 2 hrs each). In sodium loaded animals, the changes in urinary Na^+/K^+ ratio were inversely proportional to those in PAC and significantly larger ($p<.01$) in newborn (from 1.22±.32 to 2.38±.60) than in mature dogs (.71±.52 to .98±.17). The relationship between PAC and Na^+/K^+ during aldosterone infusion differed between C and E being described respectively by the equations $y=1.35-.002x$ ($r=.89$) and $y=2.25-.005x$ ($r=.94$) in the 1-week-old ($p<.05$), and $y=.71-.0002x$ ($r=.99$) and $y=1.36+.006x$ ($r=.67$) in the 6-week-old ($p<.05$). A direct relationship was observed in each group between PAC and K^+ excretion ($\Delta U_K V$). However, the slope of the regression line describing the relationship between PAC and $\Delta U_K V$ was significantly steeper ($p<.01$) in adults ($y=1.32+.02x$, $r=.73$) than in newborn puppies ($y=1.04+.003x$, $r=.64$). Thus, the effect of aldosterone on renal Na^+ reabsorption is maximal, while the effect on K^+ secretion is minimal, during the neonatal period. The resulting retention of both Na^+ and K^+ is concordant with the needs of the growing organism.

†1647 RENAL TUBULAR REABSORPTION OF PHOSPHATE (Pi) DURING DEVELOPMENT. Frederick J. Kaskel, Adarsh M. Kumar, Leonard Feld and Adrian Spitzer. Albert Einstein College of Medicine, Department of Pediatrics, Bronx, New York.

Studies from our laboratories have demonstrated that the rate of renal Pi reabsorption is significantly greater in the newborn than in the adult guinea pig. In order to determine the location of this enhanced reabsorption along the nephron, micropuncture experiments were performed on euvolemic, non-fasted guinea pigs, 5-14 days and 42-49 days of age, maintained on standard guinea pig chow diet (0.76% Pi). Inulin concentrations were determined by the method of Viet, while Pi concentrations were measured by electron probe analysis*.

		Newborn	Adult	p
n		9	10	
GFR	ml/gK	0.58±0.11	1.13±0.08	<.001
SNGFR	nl/min	5.18±0.49	19.55±1.56	<.001
TF/Pin		1.92±0.15	1.85±0.12	>.90
TRPi	%	88.44±2.58	78.99±2.77	<.05
$SN_{Prox}FRPi$	%	77.31±3.28	63.99±3.05	<.05
$SN_{Dist}FRPi$	%	17.54±2.13	8.51±1.64	<.01

Maximal TRPi was reached in both age groups at a TF/Pin of 1.5. The results demonstrate that the proximal as well as the distal segments of the renal tubule contribute to the enhanced reabsorption of Pi characteristic of the growing subject, and that most of the reabsorption is achieved in the newborn, like in the adult, in the early segment of the proximal convoluted tubule.

*Performed at the National Biotechnology Resource in Electron Probe Microanalysis, Harvard Medical School, Boston, Mass. (C. Lechene, Director).