1093 DEVELOPMENT OF GLOMERULAR PERMEABILITY IN THE NEWBORN LAMB. Mary O. Lim, Carl W. Trygstad, UCLA-Harbor General Hospital, Dept. of Pediatrics, Torrance, Ca.

Following birth there are changes in glomerular morphology and function reflected by an increased glomerular filtration rate (GFR). We wanted to determine if there are developmental changes in glomerular permeability associated with the increased GFR seen during early life.

Clearance studies were performed in 12 lambs and compared to 4 adult ewes. Studies were performed shortly after birth and weekly where possible during the first 6 weeks of life. Creatinine (Cr), I^{125}-Iodothalamate (I) and inulin (In) were administered as a bolus followed by constant infusion. The urine/plasma (U/P) ratio of I to Cr and In was determined. Then fluorescein labelled dextrans (D) mol. wgt. 3-70,000 daltons were infused. The D were chromatographed on LKB Ultrogel to separate them by mol. wgt. and analyzed by spectrophotoflurometry. U/P D / U/P I was plotted against effective D radius (A).

Correlations of I versus Cr and In were C_I=1.1 x C_{Cr}+6.7, r=0.9 and C_I=0.9 x C_{In}+4.9, r=0.9 respectively. There was no significant difference in the D curves between the newborn, young or adult ewes.

We conclude 1) changes in glomerular permeability for small molecules can not account for the increase in glomerular filtration rate seen during early extrauterine life. 2) Fluorescein labelled D can be used to determine glomerular sieving.

1094 CHANGES IN RENAL TUBULAR PERMEABILITY DURING DEVELOPMENT. Earle A. Lockhart and Adrian Spitzer, Albert Einstein College of Medicine and Lincoln Hospital, Department of Pediatrics, Bronx, New York.

Measurements of hydrostatic and oncotic pressure gradients across the proximal tubular epithelium have suggested that changes in permeability characteristics of the membrane might occur during development. In order to test the possible role of the intercellular channels in this phenomenon, microperfusion experiments were performed in guinea-pigs ranging in age from 1 to 52 days. Known amounts of metabolically inert radioactive substances of several molecular weights were injected into the proximal tubule, close to the glomerulus, and collected in the final urine. Simultaneously injected ^3H inulin served as a reference substance. The results are expressed as recovery of the substance, compared to inulin (y) as a function of age in days (x). Whereas a small and constant amount of creatinine (mol. wt. 113, Stokes-Einstein radius (r) 3.0 Å) leaked out of the tubule at all ages (y = 0.95 - 0.0007x, r=0.2, n=31), sucrose (mol. wt. 342, r = 4.5 Å) behaved similarly to the marker (y=0.98 - 0.0001x, r=0.05, n=14). The recovery of an intermediate size molecule, mannitol (mol. wt. 180, r = 4.0 Å), while incomplete immediately after birth, increased progressively reaching values comparable to those of inulin by 40 days of age, (y =0.93 + 0.002x, r=0.65, p<0.001, n=22). These data demonstrate that a tightening of the intercellular spaces occurs during development. By applying Poisseuille's law, which describes lamellar flow through narrow channels, we can calculate that the back-leak might be about 25% larger in the newborn than adult.

1095 A COMPARATIVE SHORT COURSE TREATMENT FOR BACTERIURIA IN GIRLS WITH RECURRENT URINARY TRACT INFECTIONS WITH AMPICILLIN, CEPHALEXIN, AND SULFAMETHOXAZOLE-TRIMETHOPRIM. Manop Luengnaruemitchai, Robert S. Fennell, III, R. Dixon Walker, Eduardo Garin, George A. Richard (Spon. by M. Schulkind), Univ. of Fla. College of Med., Dept. of Pediatrics, Gainesville.

55 Girls ages 3 to 16 years with recurrent urinary tract infections were randomly treated with sulphamethoxazole-trimethoprim (ST), Ampicillin (A), and Cephalexin (C) for 10 days. Criteria included two consecutive urine cultures greater than 100,000 col./ml., no history of allergy to Penicillin or sulfa, and bacteria sensitive to the assigned medication. Therapeutic success (Rx. Success) was defined as a sterile urine culture at the fourth day after completion of therapy. Recurrent infection (Rec. inf.) was defined as two consecutive positive urine cultures during the first 80 days following an initial documented therapeutic success. E. coli was the most common organism; found in 19/28 (67.8%) in ST group, 15/17 (88.2%) in A group, and 8/10 (80%) in C group.

	ST	A	C
Rx. Success	27/28 (96.4%)	10/17 (58.8%)	7/10 (70%)
Rec. Inf. (days)			
1-20	3 (11.11%)	4 (40.0%)	3 (42.85%)
21-40	8 (29.62%)	3 (30.0%)	0 (0.0%)
41-60	3 (11.11%)	0 (0.0%)	2 (28.67%)
61-80	0 (0.0%)	0 (0.0%)	1 (14.28%)
Total Rec. Inf.	14/27 (51.84%)	7/10 (70.0%)	6/7 (85.8%)

The total Rec. Inf. rate was statistically significant (p<0.05) between groups ST and C.

1096 RENAL TRANSPORT OF PAH AND GLOMERULO-TUBULAR(GT) RELATIONSHIPS DURING DEVELOPMENT IN PUPPIES UNINEPHRECTOMIZED AT BIRTH. Teresa M. Mantaring and Billy S. Arant,Jr.(Spon. by J.N. Etteldorf), University of Tennessee Center for the Health Sciences, Department of Pediatrics,Memphis.

The ability of the developing kidney to compensate for a reduction in functioning nephron mass and changes in GT balance following nephron loss were studied in puppies uninephrectomized at birth and in paired sham controls at ages(n) 0(3), 2(3), 4(4), 6(4) and 8(3) weeks of age. TmPAH, Cin, CPAH, PAH extraction (EPAH) and dry kidney weight(DKW) were determined. In the paired control animals, TmPAH(r=.95)*, Cin(r=.97)*, CPAH(r=.92)*, CPAH/EPAH(r=.95)* and TmPAH/Cin(r=.90)* increased with age. Filtration fraction(FF) and CPAH/EPAH/gDKW did not change with age. Immediately after nephrectomy and at 2 weeks, the experimental animals exhibited significant differences from controls in DKW, TmPAH and Cin, however, these differences were not apparent at or beyond 4 weeks. Neither TmPAH/gDKW, TmPAH/Cin, EPAH, FF nor CPAH/EPAH/g DKW were different between studies at any age, even though DKW was always less than controls and the DKW of the intact right experimental kidney was significantly greater than the right kidney of controls. It is apparent that the developing kidney is appropriate and adequate to functionally compensate for nephron loss at birth and does so while maintaining normal developmental GT relationships for PAH.

* p<.001

1097 CELL METABOLISM IN UREMIA. Jack Metcoff, Robert Lindeman, & Don Baxter. University of Oklahoma Health Sciences Center & Veteran's Administration Hosp., Depts. of Pediatrics & Medicine, Oklahoma City, Oklahoma.

Carbohydrate and protein metabolism are often impaired during uremia. We hypothesize this results from some imbalance of positive and/or negative effectors of key enzymes which regulate these pathways, rather than from uremic "toxins". To test this hypothesis, the effects of hemodialysis on cell metabolism in uremic patients was measured using the circulating neutrophil as a cell model. 60 paired studies have been completed. A 6 hour hemodialysis period was associated with significant (p<0.05) increases in the activities of the regulatory glycolytic enzymes in leukocytes: glucose-6-phosphate dehydrogenase, phosphofructokinase (PFK) & pyruvate kinase (PK). Nucleotide energy charge was correlated with PFK & PK. An accumulation of triosephosphates at the level of the PFK-catalyzed step was noted. Protein synthesis (^3H-leucine) increased (p<0.05), while RNA synthesis fell slightly. Cellular concentrations of 13 free amino acids increased. 7 patients with predialysis hyperglycemia (m=160 mg/dl) had increased leukocyte PFK & protein synthesis, with decreased blood glucose, postdialysis. This did not occur in normoglycemic patients. The removal of a dialyzable uremic toxin should have affected cell metabolism in both groups equally. Thus a reversible defect of regulatory enzyme activities in glycolytic and protein synthesis pathways is evident in uremics with carbohydrate intolerance, consistent with some imbalance of metabolic effectors regulating key enzymes.

Supported by Eaton Laboratories, Norwich, N.Y.

1098 RENAL PHOSPHATE CLEARANCE IN FETAL LAMBS. E.S. Moore, E.E. Chung, E.E. Cevallos, B.J. McMann, M. Ocampo and E. Lyons. Dept. of Pediatrics, Pritzker School Med., University of Chicago at Michael Reese Medical Center, Chicago.

The renal clearance of phosphate (P) was studied in 4 groups of fetal lambs. In group I, acute extracellular fluid (ECF) expansion was done in 4 fetuses by infusing Ringer's lactate without Ca++. In group II, ECF expansion with added Ca++ was done in 3 animals. In group III, the effect of exogenous bovine parathyroid harmone (PTH) was studied in 5 fetuses. In group IV, the response to endogenous fetal PTH was studied by infusing EDTA into 5 fetuses to produce hypocalcemia. In group I, plasma Ca++ (P_{Ca}) decreased by 10%. Fractional clearance of P (FC_p) increased 3-fold (P<.001). P excretion factored by sodium clearance (E_p/C_{Na}) did not change. In group II, P_{Ca} did not change. FC_p however, increased 2-fold (P<.01) while E_p/C_{Na} again did not change. Plasma levels of immunoreactive PTH (iPTH) remained stable in groups I and II. In group III, tubular reabsorption of P decreased from a mean control of 96 to 78% and FC_p increased 3-fold (P<.001). In group IV, P_{Ca++} fell from a mean control of 12.8 to 5.6 mgm/dl. Plasma iPTH increased from 0.071 to 0.723 ng/dl. FC_p increased 10-fold (P<.001) and P excretion increased independent of C_{Na} (P>.05). These studies demonstrate that acute ECF expansion in the fetus results in an increased FC_p independent of P_{Ca++} and iPTH but related to C_{Na}. Fetal hypocalcemia stimulates production of fetal PTH and the fetal renal tubule is responsive to endogenous as well as exogenous PTH.