61 RENAL CLEARANCE OF URIC ACID(CUA) DURING DEVELOPMENT IN THE PUPPY. Stapleton, F.B. and Arant, B.S., Jr.

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The human kidney excretes uric acid(UA) by glomerular filtration, tubular reabsorption and secretion. Maturational patterns of UA transport in the developing kidney have not been defined. Renal transport of UA in the mongrel dog is qualitatively similar to the adult human; therefore, CUA, inulin(Cin), plasma volume (PV) and sodium clearance(CNa) were studied in puppies aged 1-90 days and compared to an adult dog. Results are mean±SE.

Age, days(n)	1-2(6)	30(5)	60(8)	90(4)	Adult
Cin, ml/min	0.46±.10	5.68±.35	9.27±.86	12.15±2.66	61.88
Serum UA, mg/dl	0.9 ±.17	0.35±.02	0.31±.03	0.34±.08	0.19
Filtered UA, µg/min	4.5 ±.9	20±1.4	28±3.5	42±0.8	117
CUA, ml/min	0.37±.004	3.77±.29	5.43±.66	6.3±1.3	25.94
CUA/Cin, %	78±6	67±4.3	59±.05	51±3	42
PV, ml/kg	132.8±20	77.4±6.4	73.7±9.2	67.3	59.7
CNa/Cin, %	1.2±4	0.49±.12	1.14±.26	1.03±.19	1.16

Cin, filtered UA, CUA and CUA/gDKW increased with age(r=.835***, .731***, .790***, .630***). Serum UA and CUA/Cin decreased with age(r=-.596*, -.588*); whereas, CNa/CUA did not vary with age(r=-.23, P=.3). PV expansion with 10ml/kg 5% albumin/0.9% NaCl increased CUA/Cin by 6,7,13 and 49% in the respective age groups of the puppies compared to 41% in the adult. It is concluded that 1) renal tubular UA reabsorption increases or secretion decreases, or both, as PV decreases during development, 2) the effect of PV expansion on CUA/Cin increases with age, and 3) CUA is unrelated to CNa in the puppy. *P<.05; **P<.005; ***P<.001; DKW=dry kidney wt.

62 Na AND Cl PERMEABILITY IN NEWBORN RABBIT PROXIMAL CONVOLUTED TUBULES (PCT). Holmberg, C., Tisher, C., and Kokko, J.P., Children's Hospital, Univ. of

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Ionic permeabilities differ in adult superficial (SF) and juxtamedullary (JM) PCT with Na>Cl=HCO₃ in JM and Cl>Na=HCO₃ in SF. These permeability differences are known to affect passive reabsorption in these nephron populations. To address the question of when these differences develop, PCT from the corticomedullary junction (JM) and cortical surface (SF) of newborn were perfused in vitro with serum ultrafiltrate and bathed in rabbit serum. The immediate subcapsular PCT were too immature to perfuse (no lumens) so that the immediate subadjacent PCT were studied and designated SF. Potential difference (PD) was recorded before and after introduction of a 50mm outward gradient for NaCl (A=50) and the Na/Cl permeability (PNa/PCl) calculated. Five kidneys were also fixed for ultrastructural studies.

Results:	PD (mv)	ΔPD (A=50)	PNa/PCl
SFPCT (n=5)	-0.9±0.1	+3.5±0.6	0.55±0.06
JMPCT (n=5)	-2.5±0.1	-2.2±0.4	1.37±0.11

JMPCT had PNa>PCl while SF had PCl>PNa. Also morphologic differences were observed between SF and JM. We conclude: 1) Intrinsic heterogeneity of PCT is present at birth. 2) PNa/PCl approximates free solution mobilities for these ions (0.66) in SF while JM have developed Na permeability. 3) Since JM PCT develop earlier than SFPCT these findings suggest that epithelial discrimination between ions is part of the maturation process.

63 ANALYSIS OF NEPHRON SEGMENTAL FUNCTIONS IN VIVO AND IN VITRO DURING EPITHELIAL ONTOGENY

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The expression of segmental functions during renal epithelial ontogeny depends on cell intrinsic mechanisms and on extracellular factors. Differential segmental changes of ion transport, osmotic permeability and enzyme activities have been studied in this laboratory by micropuncture in vivo, perfusion of isolated nephron segments in vitro and, recently, by primary cultures of renal epithelia from defined nephron segments.

The contributions of loop of Henle epithelia to renal osmoregulation during ontogeny are given as an example. In vivo, net fluid transport increases by a factor of 2.5 while proximal volume delivery to the loop changes from 4.3 to 7.1 nl/min, and luminal osmotic activity at the macula densa site decreases from 284 to 181 mOsm. In vitro, the thick ascending segment is characterized by a low and constant osmotic permeability during ontogeny while the maximal transepithelial gradient for Na⁺ increases from 40 to 75 mM with differentiation. Segmental activities of glycolytic and Na⁺-transfer enzymes increase greatly. In culture, epithelial cell proliferation from the ascending loop is stimulated selectively by hormonal supplements. Appropriate techniques may thus provide insight into the mechanisms by which segmental functions are expressed during nephron ontogeny.

64 CHANGES IN GLOMERULAR CAPILLARY PERMEABILITY TO DEXTRANS (D) DURING DEVELOPMENT. Jodorkovsky, R.A., Goldsmith, D.I., Kleeman, S.R., Sherwinter, J., and Spitzer, A. Albert Einstein College of Medicine, Bronx, New York.

An increase in the permeability of the glomerular capillaries has been suggested to contribute to the rise in GFR occurring during maturation. This is difficult to reconcile with the observation that the urine of the newborn contains more protein than that of the adult. It is this inconsistency that prompted us to measure the clearance of polydisperse tritiated D (Einstein-Stokes radius (r) 18-58Å) in 6 newborn and 7 six-week old puppies. The separation of D according to molecular size was accomplished by fractionating samples of plasma and urine on a Sephacryl gel column. At both ages, the permeance of D molecules with radii less than 23Å was similar to that of ¹²⁵I iothalamate (r~5Å), while larger molecules were restricted to a progressively greater degree. The relative clearance of D ranging in size from 24-40Å was 21±1% (SE) greater in the newborn than in the more mature puppy. No significant differences between the two age groups were found in the relative clearances of D smaller than 23Å or larger than 41Å. Although these data are open to various interpretations, the simplest is that the number of pores per unit of glomerular capillary surface area is larger in the newborn than in the older puppy. Electrical charge notwithstanding, the existence of a greater pore density would explain the presence of relatively large amounts of protein in the urine of the newborn, but it cannot be construed to account for the low GFR prevailing at early age.

65 DEVELOPMENT OF GLOMERULAR PERFUSION RATE (GPR) IN FETAL AND NEWBORN LAMBS. Robillard, J.E., Weismann, D.N. and Smith, F.G., Jr., Dept Pediatrics, University of Iowa, Iowa City, Iowa, U.S.A.

The developmental pattern of regional glomerular density (GD) and glomerular perfusion rate (GPR) was studied in 29 fetal kidneys between 103-142 days of gestation (term 145 days) and in 8 newborn kidneys (3 to 19 days) using 15µ microspheres. The relative distribution of GD, measured in four cortical zones (zone 1 being the most outer portion) decreased in zone 1 from 44±3% in fetuses <120 days to 31±1.5% in newborns (p<0.01) and increased from 17±1.5% to 25±1.2% in zone 3 (p<0.05). No significant changes were seen in GD in zones 2 or 4. GPR values (nl/min), computed for each cortical zone, did not increase during fetal life (see Table). However, after birth, GPR increased three times in zones 1 and 2, doubled in zone 3 and did not change in zone 4 when compared to mean fetal GPR values.

Fetuses	n	Zone 1	Zone 2	Zone 3	Zone 4
120	10	6.14±0.81	7.25±0.72	7.11±0.76	7.05±0.93
120-130	10	8.17±1.55	6.88±0.82	6.16±0.63	6.96±0.75
130	9	6.92±0.89	4.36±0.42	5.56±1.00	5.97±0.47
newborns	8	*20.69±1.68	*16.13±2.07	*11.95±0.89	7.92±1.38

*p<0.001 by analysis of variance
The increase in GPR in zones 1 and 2 followed the increase in glomerular filtration rate (GFR) very closely (r=0.82 and 0.86) in newborns. The present results suggest that the rapid increase in GFR following birth may depend on the increase in GPR in the outer portion of the cortex.

66 Clearance studies suggest that the attenuated natriuretic response to volume expansion (VE) in neonates can be explained by an overcapacity of the distal tubule (DT) resulting in a high fractional reabsorption (FR) of Na even under VE. This possibility is examined in micropuncture studies from proximal tubules (PT), early and late DT in 24 (R24) and 40 (R40) days old rats during hydropenia (HP) and VE. Preliminary results:

		Early DT	Late DT
		TF/P-Na	TF/P-In
PT TF/P-Na was	HP R24	0.6±0.1	5.3±0.5
consistently =	HP R40	0.3±0.1	6.0±0.6
1. From the va-	VE R24	0.5±0.1	2.5±0.5
lues in the ta-	VE R40	0.6±0.1	4.1±0.5
		0.2±0.1	16.4±1.4
		0.2±0.1	11.1±1.4
		0.2±0.1	7.3±0.6
		0.5±0.1	7.4±1.0

ble, the fractional delivery (FD) and the fractional reabsorption (FR) of Na in early and late DT can be calculated. FR Na in proximal tubule and loop of Henle was lower in R24 than in R40 both during HP and VE. During transition from HP to VE, FD-Na to the early DT was increased more in R40 than in R24. FD-Na from the late DT in the volume expanded rats was 2.3% in the R24 and 6.6 in the R40. Fractional Na excretion in the urine was 0.8% in R24 and 3.4% in R40. It is concluded that there is a heterogeneous functional development of the nephron which can explain many aspects of the different relationship between Na balance and Na excretion in neonates compared to the adult.