55 THE EFFECT OF NORMAL DEVELOPMENT ON COMPENSATORY RENAL GROWTH. Wilton, P., Larsson, L. Karolinska Institute, Stockholm, Sweden.

Rats were nephrectomized (Nx) or sham-operated (S) at the age of 5, 12 and 40 days. One group of rats was Nx in utero 3-4 days before delivery. Light microscopy studies of renal structural development were carried out in the postnatal Nx and S rats at the age of 6-26 days. Renal structural development followed the same pattern in Nx as in S rats. The formation of new nephrons was completed at the age of 6-7 days. There was no structural evidence of formation of new nephrons. Furthermore, glomerular counting showed the same number of glomeruli in Nx and S rats at the age of 60 days. The number of glomeruli in fetal nephrectomized rats was the same as in control animals from the same litter. GFR, SNGFR and kidney weight were estimated at 60 days of age in Nx and S rats. The compensatory increase in renal weight and GFR was most pronounced in rats Nx at the age of 5 days, i.e. just before the formation of nephrons was completed.

The quotient between the recorded SNGFR and GFR was the same in all groups studied, indicating a homogenous increase in SNGFR of the nephrons at all cortical levels.

56 AGE RELATED DIFFERENCES IN ANGIOTENSIN II (A-II) METABOLISM IN RAT TISSUES. Bailie, M.D., Wallace, K. B., and Oparil, S. Michigan State University, East Lansing, Michigan and University of Alabama, Birmingham, Alabama, USA.

In order to attempt to account for age-related differences in plasma angiotensin II concentration, the activity of angiotensinases in developing rat tissues was examined. The rate of degradation of A-II was determined in vitro during incubation of tissue homogenates with 125-I-tyrosine labeled angiotensin II. Peptide fragments were separated electrophoretically and quantified by gamma scintillation counting. Half-life of labeled A-II in plasma or liver homogenates did not change with age. In contrast, the half-life in renal tissue homogenates decreased from 8.4 ± 1.2 minutes in two-week-old rats to 4.7 ± 0.7 minutes in eight-week-old rats and 2.8 ± 1.8 minutes in adults. This change in the rate of disappearance was accompanied by concomitant increase in the rate of appearance of labeled peptide fragments. Peptide mapping revealed that the principal metabolite of 125-AII was tyrosine. The only other detectable metabolites of A-II were the amino-terminus tetrapeptide and the carboxy-terminus hexapeptide. The appearance of these fragments was highly variable, suggesting that endopeptidases did not constitute the ultimate cleavage of AII degradation. The increased rate of metabolism of angiotensin II during development is consistent with the age-related increases in the concentration of angiotensin II in plasma of developing rats as demonstrated by previous studies from our laboratory.(Supported by NIH Grants HD06290 & HL22544)

57 PROSTAGLANDINS (PG) MODULATING RENAL BLOOD FLOW (RBF) AND PLASMA RENIN ACTIVITY (PRA) DURING FETAL LIFE. Matson, J.R. and Robillard, J.E., Dept. Pediatrics, University of Iowa College of Medicine, Iowa City, Iowa, U.S.A.

The effect of PG synthesis inhibition by indomethacin (I) (5.7 ±0.70 mg/kg fetal wt., i.v. bolus) on RBF and intracortical blood flow distribution was studied in 8 chronically catheterized fetal lambs (117-137 days gestation; term 145 days) using 15μ microspheres. Following I urinary PGE and PGF decreased significantly ($p<0.01$) from 0.72±0.12 to 0.27±0.04 ng/min and from 0.93±0.16 to 0.36±0.09 ng/min respectively. Fetal blood pressure increased significantly from 40±1 to 45±2 mmHg ($p<0.01$) and heart rate decreased significantly from 173±5 to 142±6 beats/min ($p<0.05$). Fetal arterial pH, blood gases, Na^+, K^+ and Cl^- remained within normal limits. A significant decrease in RBF and increase in glomerular filtration rate (GFR), filtration fraction (FF) and renal vascular resistance (RVR) were observed following I.

	RBF cc/min	GFR cc/min	FF	RVR mmHg/cc/min
Control	42.8±2.63	2.5±0.19	0.08±0.01	0.87±0.17
Post I	34.3±2.02	3.0±0.21	0.13±0.01	1.29±0.16
p value	<0.05	<0.05	<0.001	<0.05

No change in intracortical blood flow distribution was seen following I. PRA decreased significantly from 6.3±1.2 to 3.1±0.7 ng/cc/hr following I ($p<0.01$). The present results suggest that during fetal life, renal PG's: a) have an important role in maintaining RBF by decreasing efferent arteriolar constriction and b) may modulate renin secretion.

58 ALLOMETRIC APPROACH TO POSTNATAL RENAL GROWTH - NORMAL AND COMPENSATORY. HUTSON, J. DEPARTMENT OF SURGERY, ROYAL CHILDREN'S HOSPITAL, MELBOURNE, AUSTRALIA.

Normal renal growth in the mouse was determined by removal of kidneys in mice aged 20 - 50 days. Kidney weight was compared with body weight by plotting on a graph with logarithmic co-ordinates. Kidney weight was linearly related to body weight on this scale. Unilateral nephrectomies were then performed on neonatal (5 days old), juvenile (15 days old) and adolescent (35 days old) animals, with the opposite kidney being removed 15 days later. In a second experiment kidneys were removed 30 or 45 days after neonatal nephrectomy. The kidney weight after compensatory growth was also linearly related to body weight, the regression line being parallel to that of the controls in females, and having a greater slope than that of the controls in males. The kidneys removed after a long interval were not statistically heavier than those after 15 days. These conclusions are contrary to others reporting increased compensatory growth in neonatal animals. However the principles of allometry, which consider the changing forms of the body and organs with growth, have rarely been applied to compensatory growth. This experiment suggests that allometry is a useful technique to study compensatory growth, and the conclusions reached may be more meaningful in understanding compensatory renal growth.

59 MATURATION OF RENAL TUBULAR TRANSPORT OF DIGOXIN Aladjem, M., Kaplinsky, Ch., Laufer, Y., Wolfish, N., Halkin, H., Pediatric Renal Unit, Chaim Sheba Medical Center, Tel-Hashomer, Israel.

Previous data have suggested an age related increase in renal tubular secretion of digoxin in infants and children receiving long term digoxin therapy. This phenomenon could be the result of a maturational process or secondary to chronic substrate stimulation. To investigate this question two groups of 2 week old paired litter-mate rats received intraperitoneal injections of either digoxin or an equal volume of normal seline (control) an alternate days until sacrificed at 4, 6, and 8 weeks of age. An additional group of 12 week old rats were studied as controls. I^{125} digoxin uptake was measured in renal cortical slices as the CPM/mg wet tissue slice to medium ratio (S/M). Both digoxin treated and control rats demonstrated significant age related increment in digoxin uptake. S/M ratios at 4, 6, 8, and 12 weeks in the control group were (mean ± S.D) 1.34 ± 0.06, 1.39 ± 0.14, 1.62 ± 0.18 and 1.93 ± 0.25 respectively ($r = 0.81$, $p < 0.001$) but did not differ significantly at each age from those in the control group. I^{125} uptake was significantly reduced by both Dinitrophenol (DNP) and sodium azide, as well as by a 100% nitrogen atmosphere.

These results indicate that renal tubular transport of digoxin is an age related energy dependent process, which probably is not subject to substrate stimulation.

60 THE EFFECT OF CHRONIC PARTIAL URETERAL OBSTRUCTION (CPUO) ON RENAL TUBULAR TRANSPORT DURING MATURATION. Taki, M., Goldsmith, D.I. and Spitzer, A. Albert Einstein College of Medicine, Bronx, New York

These studies were designed to determine whether the effect of CPUO on the renal tubule is dependent upon the pattern of transport prevailing at various stages of development. Guinea pigs (n=78) underwent CPUO at birth, 1,2,3 or 4 wks of life and were studied 4 wks later (E). Sham operated littermates served as controls (C). The degree of CPUO, measured by the resistance to a constant flow of fluid, was similar in all groups. TRP averaged 87% in C, was slightly lower in the contralateral kidney (CK) of E (82%) and did not vary with age, whereas it increased with age ($p<.05$) from 46.6 ± 6.1 to 68.0 ± 6.3% in the affected kidney (AK). FeNa in AK was 7.5 ± .5 when CPUO was produced at birth and 4.8 ± 1.0 when surgery was done at 4 weeks ($p<.05$). In C and CK, FeNa was much lower than in AK ($p<.001$), similar to each other and also decreased with age. UkV (mEq/min/g KW) varied inversely with FeNa in AK. Umax/Posm of C and CK in E were similar (range 4.0-4.3), while the ratio was not different from 1.0 ($p>0.9$) in AK at all ages. UV (μl/min/100 ml GFR) of the AK was 22.4 ± 3.7 when surgery was performed at birth, 26.7 ± 4.0, when surgery was done at 1 wk, and then decreased rapidly to reach 5.8 ± 1.2 when CPUO was produced at 4 wks ($p<.001$); no significant differences in UV were observed between C and the CK of E at any age. The results demonstrate an inverse relationship between age at time of CPUO and severity of tubular damage, and suggest the possibility of a major role for the distal nephron in P transport during early life.