1486 FOLLOW-UP OF HYPERVENTILATED NEONATES. C. Brett, M. Dekle, C.H. Leonard, C. Clark, S. Sniderman, R. Roth, R. Ballard, and R.I. Clyman. Mt. Zion Medical Center, Department of Pediatrics, San Francisco, California.

Hyperventilation has been advocated for treatment of newborn infants with pulmonary hypertension; however, there are theoretical harmful effects of hyperventilation on the immature nervous system. From March 1977 to May 1979, 13 infants > 37 weeks gestation were selected to be hyperventilated because of severe hypoxemia refractory to conventional mechanical ventilation, i.e., failure to maintain PaO_2 > 50 torr with an FiO_2 1.0, despite $PaCO_2$ <40 and pH >7.40. Eleven survived, 9 were available for follow-up evaluation. Seven infants had meconium aspiration syndrome, one had HMD, one had Gp B strep sepsis. All infants eventually required a decrease in $PaCO_2$ to <20 torr and increase in pH to >7.50 before a change in $AaDO_2$ became evident. As a group, the 9 infants were exposed to a $PaCO_2$<20 torr for 51.8±11.8 hrs (mean± SEM), to $PaCO_2$ <15 torr for 11.8±3.3 hrs, to a pH 7.50 for 64.4± 18.6 hrs, and to a pH>7.60 for 6.1±2.9 hrs. One infant was lost to follow-up after a normal assessment at 9 mos. The other 8 infants (7 AGA, 1 markedly SGA) were at least 1¾ years at the time of evaluation. The 7 AGA infants had a normal developmental quotient (mean±110, range 96-130) by Stanford Binet or Bayley; the one SGA infant had a Bayley of 89. All 8 had normal neurological examinations. All AGA infants are growing normally. Although only 9 infants with short term follow-up are reported here, these preliminary observations are reassuring with respect to neurological and developmental outcome following prolonged hyperventilation.

1487 MECHANISM OF ANTINATRIURESIS AFTER SYSTEMIC VASODILATION.

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To investigate the role of the sympathetic nervous system in the sodium retention after systemic vasodilation, 15 hypophysectomized dogs undergoing saline diuresis (5 ml/min) had the left kidney denervated (5% phenol in 70% ethanol). After stable urine flows were obtained, control clearances for inulin, PAH, free-water, distal chloride delivery and fractional distal chloride reabsorption were obtained. In 8 dogs, diazoxide (D) as a bolus (5 mgm/kg) was infused; in 7, sodium nitroprusside (N) was infused. During both infusions, mean arterial pressure dropped from 133±6 (x±SEM) to 83±7 torr ($p < .01$). With D, $U_{Na}V$ from the right kidney fell from 23±7 to 7±2 uEq/min ($p < .01$). C_{IN} and C_{PAH} decreased slightly but significantly ($p < .05$). $C_{H_2O} + C_{Cl}$ decreased from 6.1±.3 to 2.1±.8 ($p < .01$) and 6.7±.1 to 3.1±.1 ($p < .01$) ml/min/100 GFR, respectively. $C_{H_2O} + C_{Cl}/C_{H_2O}$ was not affected. No significant changes on the left were noted. With N, no changes occurred in C_{IN} or C_{PAH}. $U_{Na}V$ decreased on the right from 20±4 to 12±3 uEq/min ($p < .05$). C_{H_2O} and $C_{H_2O} + C_{Cl}$ decreased from 8.5±1.0 to 4.7±1.3 and 8.9±1.0 to 4.4±1.5 ml/min/100 GFR respectively ($p < .05$), no changes were noted on the left. The data indicate that the renal sympathetic nerves increase sodium reabsorption in the proximal nephron during acute systemic vasodilation.

1488 PATHOGENESIS OF EXPERIMENTAL FOCAL SEGMENTAL GLOMERULOSCLEROSIS (FSG) Manju Chandra, Myron Susin and Saul Teichberg (Spon. by Joseph Kochen) Cornell Univ. Medical College, New York, N.Y., North Shore Univ. Hosp., Manhasset, N.Y., Depts. of Pediatrics and Pathology

Repeated aminonucleoside (A) injections have been shown to produce FSG in rats and this effect is enhanced by uninephrectomy. Since this increase in FSG may be a result of increased GFR or a higher dose of A reaching a solitary kidney, the following study was done. Rats were injected with A, (5 mg/100 gm body wt), intraperitoneally on days 0, 21 and 28. On day 49, experimental (E) rats (10) received an additional 15 mg of A selectively to the left kidney (L). Controls (4) received saline. On day 110, $C_{Iothalamate}$, $C_{Hippuran}$ and histologic alterations were studied. In E, percentage of FSG was higher in the right kidney (R), that was not perfused with additional A, than in the Left. (R, 7.8 ± 2.6% vs L, 3.9 ± 1.8%, $p < 0.01$). The effective renal plasma flow (R, 2968 ± 532 µl/min, L, 1945 ± 315) as well as GFR were also higher in the Right (GFR, R, 1515 ± 291 µl/min vs L, 1021 ± 170, $p < 0.05$). Controls which did not receive the additional unilateral A perfusion showed equal percentage of FSG in both kidneys and also showed equal GFR and effective renal plasma flow. Our data suggest that increase in the cumulative filtered load of protein may be more important than direct injury to epithelial cells by A in the pathogenesis of FSG.

● **1489** APPARENT INCREASE IN NUMBER OF GLOMERULI (NG) DURING NORMAL AND COMPENSATORY RENAL GROWTH. Robert L. Chevalier (Spon. by Thaddeus Kelly), University of Virginia Medical Center, Dept of Pediatrics, Charlottesville, VA.

The question of whether new nephrons are formed during postnatal renal development continues to be actively debated, but remains unresolved. Guinea pigs were uninephrectomized (N) or sham-operated (S) at birth or at 12 wks of age. 3 wks later, NG was determined by counting India ink (I)-containing glomeruli in acid digests of kidneys after in vivo arterial perfusion with I. Additional glomeruli not identified with I were revealed by Camco (C) counterstaining. The percent of NG(I) in the inner compared with outer cortex did not differ in 3 wk S and N groups.

	1 day	3 wks of age		15 wks of age	
		S @ birth	N @ birth	S @ 12 wks	N @ 12 wks
NG(I)	72±1 (6)	70±2 (8)	83±3 (8)*	86±3 (5)*	88±2 (5)*
NG(C)	8.1±1.1(5)	9.0±0.7(5)	1.3±0.4(5)*	1.4±0.2(5)*	------

Mean ± SEM x 10^3 (number of animals). *$p<0.005$ compared with 1 day and 3 wk S groups.

Conclusions: At least 12% of glomeruli are not identifiable by I in the first 3 wks of life, while 98% contain detectable I in adulthood. An apparent increase in NG during maturation may therefore result from altered perfusion in a subpopulation of glomeruli rather than from de novo formation of nephrons, and takes place throughout the cortex. This process is accelerated by N in early development, but is unaffected by N in adulthood.

● **1490** ADAPTATION OF RENAL SULFATE (SO_4) REABSORPTION TO SULFUR INTAKE. David E.C. Cole and Charles R. Scriver. MRC Genetics Group, McGill Univ.-Montreal Children's Hosp. Res. Inst., Montreal, Quebec, Canada.

Restriction of dietary sulfur results in reduced renal SO_4 excretion, a finding attributed to decreased sulfur amino acid oxidation and filtered load of SO_4. We found serum [SO_4] in C57Bl/6J adult male mice fed a "low-protein" (LP) diet (8% casein; 0.2% Met., 0.03% Cys) and in those fed a "high-protein" (HP) diet (27% casein; 0.68% Met., 0.1% Cys) for two weeks was not different (1.24±0.11 mM ($\bar{x}$±SEM, n=6) vs 1.34±0.11 (n=7)). Reduced fractional SO_4 excretion index (FEI SO_4) was found in the LP group (LP=0.11±0.04 vs HP=0.50±0.14, $p < .01$). Evidence for adapted renal reabsorption was confirmed by assaying Na^+-dependent uptake of 50 µM SO_4 into renal brush border membrane vesicles (BBMV). Na^+-dependent uptakes of 5 µM glucose and 50 µM phosphate served as internal markers; initial rates (15s) were normalized to those at equilibrium (60 min.). SO_4 uptake was higher (361±39% of equilib. value n=10) in LP BBMV vs HP BBMV (270±16% n=10, p=0.023). No differences were noted with D-glucose (709±47% vs 698±30% n=5) or phosphate (193±17% vs 191±11%, n=11). The response to selective deficiency of dietary SO_4 was studied using soybean-based diets with 1% NaCl (diet 1); 0.5% DL-methionine and 0.5% taurine (diet 2); and 1% Na_2SO_4 (diet 3). FEI_{SO_4} was 0.09± 0.01, 0.39±0.09, and 0.56±0.08, respectively. Adaptation was significant only with diet 1 ($p < 0.01$). These findings indicate renal adaptation in BBM to depletion of SO_4 *per se*.

1491 ELEVATED SERUM SULFATE (SO_4) AFTER 1,25-$(OH)_2D_3$ TREATMENT: A MARKER FOR DECREASED GLOMERULAR FILTRATION (GF) WITH HYPERCALCEMIA? David E.C. Cole, Harriet S. Tenenhouse and Charles R. Scriver. MRC Genetics Group, McGill Univ.-Montreal Children's Hosp. Res. Inst., Montreal, Que.

The most frequent cause of elevated serum [SO_4] is reduced renal sulfate clearance secondary to decreased GF. We have observed that 1,25-$(OH)_2D_3$ treatment in man results in an increase of serum [SO_4] that correlates inversely with decreased creatinine clearance (Ped. Res. 14,570, 1980). With osmotic mini-infusion pumps implanted subcutaneously into normal (+/Y) C57Bl/6J adult male mice and their hypophosphatemic (Hyp/Y) littermates, we examined the effect of 1,25-$(OH)_2D_3$ treatment (83 ng/g·dy x 10 dy) on serum calcium and serum [SO_4]. Sham-operated animals receiving propylene glycol only served as controls. 1,25-$(OH)_2D_3$ treatment in +/Y mice, resulted in significant hypercalcemia compared to controls: 11.34±.07 (n=8) vs 10.05±0.12 mg/dl (n=9), respectively; $p < .001$. Serum [SO_4] was also elevated (1.35±.07 vs 1.17±.05 mmol/l; $p < .025$). In contrast, the same dose administered to the Hyp/Y mouse failed to change either serum Ca [9.57±.05 (n=6) vs 9.46±.05 mg/dl (n=6)] or SO_4 (1.03± .02 vs 1.06±.07 mmol/l). These observations support the hypothesis that 1,25-$(OH)_2D_3$ reduces sulfate clearance (and presumably GF). This effect is apparently mediated by changes in serum calcium and is not necessarily the direct result of hormone action on glomerular filtration. This study indicates that avoidance of hypercalcemia will minimize adverse effects of 1,25-$(OH)_2D_3$ on renal function.