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RESPONSE OF THE NEWBORN TO INDUCED HYPOTENSION.

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The response of vasoactive mediators in the neonate to a 20% fall in mean arterial blood pressure (MBP) was studied in six chronically catheterized lambs 4-7 days old, following infusion of sodium nitroprusside (SNP). No significant change in pHa, PaCO₂, plasma sodium or osmolality was observed following the infusion of SNP. However, the fall in MBP from 65.3±3.90 to 53.8±2.82 mmHg (Mean ±S.E.) at the end of sixty minutes infusion was associated with the following changes in vasopressin (VP), renin activity (PRA) and catecholamine concentrations (CA) (*p<0.01):

ΔVP (pg/ml)	ΔPRA (ng/ml/hr)	ΔCA (pg/ml)
+32.70±16.28*	+18.97±7.97*	+345.0±100.52*

These levels remained significantly elevated for at least thirty minutes after the end of infusion while MBP rose above control values and was still elevated (72.8±2.95 mmHg) after sixty minutes. These experiments demonstrate that as in the adult, the newborn sheep responds promptly to a hypotensive episode by secreting vasoactive mediators which may play an important role in blood pressure homeostasis. The prolonged hypertension that followed suggests that as in the fetus, blood pressure is not well regulated due to either slower metabolism or immaturity of feedback mechanisms controlling the release of vasoactive mediators.

NEPHROLOGY

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PREDICTION OF PROTEINURIA BY RANDOM AND 24 HOUR URINE PROTEIN:CREATININE RATIOS (U P/Cr) IN NEPHROTIC CHILDREN.

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The feasibility of using the U P/Cr to predict daily protein excretion in nephrotic patients was tested in 125, 24 hour urine collections from 47 children with nephrotic syndrome (aged 19 mos - 16 years). Six patients were steroid non-responsive and had focal segmental sclerosis by biopsy; all others were considered to have minimal change disease either by biopsy or Prednisone responsiveness. Urine protein was measured by the Coomassie blue binding technique (Bio-Rad Lab) and creatinine by the spectrophotometric Pierce Test Kit. Total protein excretion (TP) ranged from 2 mg to 32 g/m²/day. U P/Cr ranged from .002 to 33 in 24 hour urine samples. The correlation between daily protein excretion and U P/Cr was highly significant (n = 125, r = 0.57, p < 0.001). However, the scattergram of all data suggested non-linearity when proteinuria was minimal (< 100 mg/m²/d) or excessive (> 1 g/m²/d). Logarithmic conversion improved the correlation of data at both extremes of TP:

TP	Correlation Coefficients (r)	U P/Cr vs. TP
(n)	Linear Regression	Log Conversion
<100 mg/m ² /d (38)	.64	.72
>100-1000 mg/m ² /d (32)	.81	.85
>1000 mg/m ² /d (55)	.49	.77

Logarithmic conversion of all data enabled accurate prediction of TP from U P/Cr (n = 125, r = .97, Log TP = 0.9 (Log U P/Cr) - 0.51. Random U P/Cr from 9 specimens collected on the day following a 24 hour urine were also predictive of TP (r = 0.96, p < .001). These data support the concept that U P/Cr can accurately predict proteinuria although non-linearity outside moderate ranges requires logarithmic conversion.

1569 AMINOGLYCOSIDE NEPHROTOXICITY IN THE NEONATE.

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Nephrotoxicity due to aminoglycosides is infrequently recognized in the neonate, in part because aminoglycosides may cause subtle increases in serum creatinine that are superimposed upon a postnatal decline in serum creatinine and rise in creatinine clearance. The present study was designed to evaluate changes in renal function in infants receiving either mezlocillin or the aminoglycoside amikacin + ampicillin for presumed neonatal sepsis.

113 neonates were randomly allocated to either mezlocillin or ampicillin + amikacin in a controlled study. There were no significant differences between groups in clinical condition, number (58 vs. 55), gestational age (30.5 vs. 30.8 weeks), birthweight (1490 vs. 1509 grams), duration of therapy (6.2 vs. 5.8 days), or baseline creatinine clearance (0.50 vs. 0.52 ml/min), fractional excretion of sodium (3.1 vs. 3.2%), and urinary excretion of the enzymes alanine aminopeptidase (AAP), lysozyme (Lys), and NAG, expressed as units per milligram of urinary creatinine.

On the final day of therapy there were no differences between mezlocillin and ampicillin + amikacin groups in fractional excretion of sodium, urinary activities of AAP, Lys, and NAG, or clinical status. However, creatinine clearance/kg significantly increased by 30% in mezlocillin treated infants (p < .001) but only by 8.6% in the ampicillin + amikacin treated infants (p NS).

In summary, amikacin therapy in neonates appears to be associated with nephrotoxicity as demonstrated by a diminished postnatal rise in creatinine clearance.

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HYDROCHLOROTHIAZIDE, AMILORIDE AND TOLMETIN IN THE TREATMENT OF DIABETES INSIPIDUS OF BRATTLEBORO RATS. Uri Alon, Martha D. Wellons, James C. M. Chan. Medical College of Virginia, Richmond, VA.

To test the effects of hydrochlorothiazide (HCTZ) alone and in combination with amiloride or tolmetin in the treatment of nephrogenic diabetes insipidus, metabolic studies of 12 days each were carried out in 36 male, Brattleboro rats. They were divided into five groups as follows: (A) controls; (B) high dose HCTZ at 6.0 mg/rat/day; (C) low dose HCTZ at 3.0 mg/rat/day; (D) HCTZ identical to (C) but with addition of amiloride at 0.6 mg/rat/day; (E) HCTZ identical to (C) but with addition of tolmetin at 40 mg/rat/day. The immediate response to treatment was a significant increase in urinary sodium excretion from mean values (mEq/kg/day) of less than 11 to higher than 13, except group E with value of 12. There was marked increase in urinary potassium excretion, (mEq/kg/day) from mean control value of 15.5 to 21.5, 20.8, 18.5, 17.7 in groups B, C, D and E respectively. During the last three days of the study, mean urine osmolality (U_{osm}) in mOsm/kg H₂O and free water reabsorption (T_{CH₂O}) in ml/min/kg BW increased significantly:

Group	A	B	C	D	E
U _{osm}	170	510	380	450	490
T _{CH₂O}	-0.28	0.15	0.08	0.12	0.12

These indices were higher in groups B, D and E than in group C. Serum osmolality decreased only in groups B, C and D but not in the HCTZ-tolmetin group. We conclude that these agents may eventually prove to be satisfactory alternative therapies in nephrogenic diabetes insipidus.

●1571

ONTOGENY OF NaKATPase ACTIVITY IN THE THICK ASCENDING LIMB OF HENLE AND OF THE URINARY CONCENTRATING CAPACITY IN RATS.

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NaKATPase provides energy for the transcellular Na transport in the thick ascending limb of Henle (TAL). The hypertonic transport out of TAL is considered to be the primary driving force for the formation of hypertonic urine. To examine the role of Na-transport in TAL for the ontogeny of the urinary concentrating capacity we have compared the development of NaKATPase activity in TAL and the capacity to concentrate urine in 12-40 day old rats. The enzyme activity (pmol Pi/mm tubule/h) was not different in 12 and 16 day old rats, increased rapidly between 16 and 20 days (1078 ± 93 ---> 2189 ± 102) and at a slower rate between 20 and 40 days (---> 3767 ± 324). The relation between enzyme activity in the cortical and medullary TAL was found to be the same in 20- and 40-day old rats and most enzyme determinations were made in the medullary TAL. The developmental patterns for NaKATPase activity in TAL and urinary concentrating capacity were strikingly similar. The developmental increase in NaKATPase activity and concentrating capacity between 16 and 20 days of age was accompanied by an increase in serum corticosterone level and was abolished by adrenalectomy. Treatment with glucocorticoid hormones precociously induced NaKATPase activity and concentrating capacity in 13-16 day old rats but had no effect on NaKATPase activity in 17-20 day old rats. The increase in enzyme activity from 20 to 40 days of age was accompanied by an increase in SNGFR.

The results suggest that NaKATPase activity in TAL is an important determinant of the concentrating capacity during development. The developmental surge in NaKATPase activity and concentrating capacity between 16 and 20 days of age is probably set off by the rise in the serum corticosterone level.

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IMPAIRED RENAL ACIDIFICATION IN INFANTS WITH FETAL ALCOHOL SYNDROME. Farahnak K. Assadi and Mohsen Ziai (Sponsored by Ira M. Rosenthal). Departments

of Pediatrics, University of Illinois Health Sciences Center at Chicago and University of Georgetown, School of Medicine, Washington, D.C.

Urinary acidification was studied in six unrelated infants with fetal alcohol syndrome. Eight healthy age-matched infants were served as controls. Creatinine clearance, fractional sodium excretion (FENa), plasma concentrations of sodium, renin and aldosterone were normal in all patients. Baseline fractional potassium excretion (FEK) was lower in patients (23±1.3%) than in controls (28±1.8%), (P=.0001). After ammonium chloride loading, urine pH fell from 6.0±0.2 to 5.5±0.1 in patients (P<.05) and from 5.9±0.1 to 4.7±0.1 in controls (P<.01). Net acid excretion (NAE) was lower in patients (24.5±1.7 μEq/min) compared to controls (27.8±2.1 μEq/min), (P=.008). Following sodium bicarbonate loading, fractional bicarbonate excretion was significantly higher (P<.00005) and FEK significantly lower (P=.002) in patients than in controls with comparable plasma pH and bicarbonate levels. Patients had a lower value of (U-B) pCO₂ than controls (P=NS). Treatment with chlorothiazide lowered plasma potassium and raised plasma bicarbonate to normal levels (P<.05). Concomitantly, FENa, FEK, and urinary NAE increased significantly (P<.01). We conclude that patients with fetal alcohol syndrome have a defect in their ability to excrete potassium and hydrogen ion that cannot be attributed to abnormal renin or aldosterone secretion.