1570 BILIRUBIN: EFFECT ON UREA AND WATER FLOW, A.S. Brem, M.A. Pacholski, and W. Cashore. Brown University, Department of Pediatrics, Providence, RI

Urinary concentrating and diluting defects have been described in hyperbilirubinemic Gunn rats. Renal medullary Na and urea concentrations are decreased in these animals (JCI 55:319-329,1975) suggesting a possible association between solute reabsorption and the urinary defects. While Na transport may be adversely influenced by bilirubin (BR) (Ped Res 16:319A, 1982), the effects of BR on transepithelial fluxes of urea and water have not been studied. Therefore, urea and water flux measurements were made in responsive epithelia (bladders) isolated from the Dominican toad (Bufo marinus). Tissues were acutely exposed to amphibian HCO_3^- Ringers, pH 8.1 containing BR (0.1 mM) and 0.05% bovine serum albumin (BSA) or BSA alone. Urea permeability (K trans) was calculated from the mucosal to serosal flux of ^{14}C labeled urea in short circuited bladders. Water movement was gravimetrically determined by the Bentley bag technique. Tissues were stimulated with vasopressin (VP) 40 mU/ml for urea and 20 mU/ml for water studies.

Urea K trans X 10^{-7} cm^2/sec ± SEM

	BR serosal bath				BR mucosal bath			
	Basal	n	VP	n	Basal	n	VP	n
cont.	6.7 ± 1.8	8	76.3 ± 4.6	12	2.6 ± 0.3	7	70.4 ± 5.1	10
exp.	6.6 ± 2.0	8	72.2 ± 4.2	12	2.2 ± 0.4	7	65.8 ± 5.2	10

The hydroosmotic response to VP was likewise unaffected by BR in the serosal bath; control 46.5 ± 2.7 mg/min vs. exp. 45.5 ± 3.3 mg/min (n=9). Although VP induced active Na transport is inhibited by BR, BR appears to have no effect on VP induced cell membrane permeability changes that allow for passive transepithelial movement of urea and water.

†1571 INCREASED RENAL BLOOD FLOW (RBF) AFTER TRANSIENT RENAL ISCHEMIA. Marc C. Browning (Spon. by William B. Lorentz). Bowman Gray School of Medicine, Department of Pediatrics, Winston-Salem, N.C.

This study examines the effects of 25 minutes of unilateral ischemia on RBF and on renal handling of PAH at high (H) and low (L) serum concentrations in the 40 minutes following reflow in anesthetized acutely saline expanded rabbits. RBF was monitored continuously by electromagnetic flow probes; serum (S) and urine (UV) were collected for clearance rates of PAH (Cpah) and inulin (Cin) from both the ischemic (I) and nonischemic (N) kidney. Infusion of PAH and inulin was begun after reflow. 40 minutes later kidneys were removed for determination of cortex-to-serum ratios of PAH (C/Spah) and inulin (C/Sin). Results are tabulated:

		RBF(Post/pre)	Cin	Spah(ug/ml)	Cpah	C/Spah	C/Sin	UV(ml)
L	N	1.04	2.6	17.8	14.1	7.4	1.8	2.0
n=5	I	1.45	1.9	17.8	11.3	8.5	1.4	12.6
H	N	1.16	5.0	531	11.2	2.9	1.4	9.2
n=6	I	1.36	2.0	531	5.9	3.4	1.0	12.5

25 minutes of transient renal ischemia produced increased RBF in 11/11 animals in the immediate post ischemic period (mean pre ischemic RBF 33 ml/min, mean 0-10 minute post ischemic RBF 54 ml/min, $p < .01$). The increased RBF was accompanied by an increase in UV but not in Cin and Cpah. In this model, the post ischemic reduction of Cin and Cpah cannot be attributed to decreased RBF.

†1572 SODIUM BENZOATE (BZ) ARRESTS PROGRESSION OF RENAL FAILURE IN INFANTILE PRIMARY OXALURIA (OXU). Barbara A. Fivush, Robert H. McLean, and Saul W. Brusilow. Children's Hosp., Wash., DC and Johns Hopkins Univ., Dept. of Ped., Balt. MD

Infantile OXU is characterized by oxalate (OX) nephrocalcinosis and rapid progression to end stage renal disease. BZ (which may reduce OX production by diverting its precursors, glycine and glyoxylate, to hippurate synthesis) has not been considered to be useful because short term clinical trials revealed no permanent decrease in OX excretion (BMJ 1:175, '58, AJM 29:820, '60). However, we hypothesize that because of the accumulated body OX burden, high excretion rates may persists even if OX production decreases. The value of BZ may better be judged by longterm outcome. An 8 week old female infant with OXU presented with severe OX nephrocalcinosis, and a serum creatinine (Cr) of 2.5 mg/dl. At 3 m of age her Cr rose to 4.8 and BZ (300 mg/kg/d) was started and continued to the present (25 m) at which time her Cr is 4.8. No OX bone deposition occurred after 8 m of age. Plasma hippurate levels of 4-14 mM produced no adverse affects. Mean plasma BZ level was <0.1 mM. We suggest that BZ reduces OX production, tissue deposition and destruction. Thus BZ may be useful in OXU including such patients who are transplant recipients.

1573 HYDROCHLOROTHIAZIDE-AMILORIDE IN NEPHROGENIC DIABETES INSIPIDUS. Uri Alon, and James C. M. Chan, Medical College of Virginia, Richmond, VA.

The effects of treatment with hydrochlorothiazide (50-75 mg/day p.o.) combined with amiloride (10-15 mg/day p.o.) were compared to hydrochlorothiazide (HCTZ) treatment alone in two brothers, aged 12 and 19 years, with nephrogenic diabetes insipidus. Whereas, both modalities of treatment resulted in reduction in voiding frequency and urine volume, decrease in daily fluid intake and increase in urine osmolality, the two-drug combination was found to be superior to HCTZ alone by preventing urinary potassium losses, hypokalemia and alkalosis. During admission of 3 weeks, it was also found that amiloride has an additive effect to the thiazide in terms of increasing initial urinary sodium excretion, reducing urine volume and free water clearance and lowering serum sodium and osmolality.

	Control	HCTZ	HCTZ & Amiloride
Serum osmolality	304.5 ± 3.5	292.0 ± 1.0	281.5 ± 2.5
Urine osmolality	103.0 ± 1.0	183.0 ± 1.0	180.0 ± 2.0
Free water clearance	3.8 ± 1.4	1.17 ± 0.09	0.92 ± 0.09

As evaluated by the above variables, in an additional study in the younger brother, HCTZ-amiloride showed a slight advantage over HCTZ-tolmetin.

Treatment of the two patients for 10 months with HCTZ-amiloride showed no adverse effects and consistent reduction in fluid intake and urine volume. It is concluded that the HCTZ-amiloride regimen is a satisfactory alternative treatment of nephrogenic diabetes insipidus.

†1574 RENAL TUBULAR ACIDOSIS TYPE 4 IN NEONATAL UNILATERAL KIDNEY DISEASES: Uri Alon, Michael B. Kodroff, Bruce H. Broecker, Barry V. Kirkpatrick, and James C. M. Chan, Medical College of Virginia, Richmond, VA.

Three neonates, two with unilateral renal vein thrombosis and one with unilateral dysplastic kidney, developed type 4 renal tubular acidosis, manifested by non-azotemic hyperkalemic metabolic acidosis with alkaline urine pH and reduced potassium excretion. Normal plasma sodium, aldosterone and renin activity together with normal fractional excretion of sodium, support the diagnosis of renal tubular acidosis type 4, subtype 5. To further define the acidification defect, all underwent arginine-hydrochloride loading studies. Despite urine pH <5.8, net acid excretion was inadequate relative to the corresponding plasma bicarbonate concentration.

Treatment with oral bicarbonate, 3-6 mEq/kg/day, resulted in sustained normalization of blood acid-base status and accelerated linear growth in the first two infants, in whom spontaneous recovery occurred by ages eight and 15 months, without further need for alkali therapy. Radiologic evaluation revealed shrinkage of the affected kidney with contralateral compensatory hypertrophy in both patients. In the third infant, persistent acidosis and growth failure obtained from medical non-compliance; removal of the dysplastic kidney at seven months of age was followed by normalized hydrogen and potassium excretion as well as blood acid-base status. We conclude that neonatal unilateral kidney diseases can give rise to renal tubular acidosis type 4, subtype 5. Early diagnosis and treatment provide an excellent prognosis.

1575 EFFECT OF PREDNISONE ON GROWTH AND ZINC METABOLISM IN RATS: Mary Jacob, James C. M. Chan and J. Cecil Smith, Medical College Virginia, Richmond, VA; Cal St Univ, Long Beach, CA; USDA, Beltsville, MD.

To test the hypothesis that prednisone administration interferes with zinc metabolism and impairs growth, 41 male, weanling Charles River rats weighing 43-60 g were randomly assigned to four groups. Three groups of 12 rats received prednisone daily for five weeks at dosages of 0.5, 2.0 and 8.0 mg/kg per day, respectively. The control group were pair-fed with the third treatment group receiving the maximum dose of prednisone. In the fifth week, all animals received ^{65}Zn at 0.5 uCi/100 g body weight by stomach tube. Retention was measured in whole body gamma counters. The rate of weight gain decreased in the prednisone-treated animals. While food intakes between the three groups of treated rats were no different, the food efficiency ratio of 0.10 ± 0.03 of the third group was significantly lower ($P < .001$) compared to the pair-fed controls (0.36 ± 0.03) as well as the other treatment groups (0.25 to 0.29). The whole body ^{65}Zn retention in the pair-fed control animals at 24 and 216 hrs was 90% and 60%, respectively, compared to retention of 60% and 10% in the maximally treated rats. Prednisone treatment depressed the capacity of the liver, kidney, muscle, bone and testes to accumulate ^{65}Zn. Urinary excretion of zinc and nitrogen increased in proportion to the doses of prednisone. We conclude that in growing rats, prednisone treatment impaired weight gain, reduced food efficiency and decreased ^{65}Zn retention.