●1582 CORRELATION BETWEEN POLYCYSTIC KIDNEY DISEASE AND GLUCOCORTICOID PROFILES. John F. S. Crocker, Stan R. Blecher, Susanna C. McCarthy, Morris L. Givner, Dalhousie University and Victoria General Hospital, Departments of Pediatrics, Anatomy and Pathology, Halifax, Nova Scotia

Hydrocortisone actetate when injected into newborn mice induces a pathological picture similar to human Infantile Polycystic Kidney Disease (IPKD). We recently showed that susceptibility to this teratogen is under genetic control and we proposed, for the naturally occurring IPKD, a two strike hypothesis of genetic susceptibility and an abnormal profile of glucocorticoids. Mice during the first 14 days of life have a "stress non-responsive" period with very low levels of corticosterone. C57BL/6J-cpk, a mutant of C57BL/6J strain of mice, develop, as homozygotes (cpk/cpk), a disease similar to human IPKD and die at about 3 weeks of age. Blood samples were obtained at 10 days of age from (a) control C57BL/6J mice; (b) homozygote cpk/cpk mice with IPKD and (c) unaffected siblings of affected animals. Phenotypic diagnosis of IPKD was confirmed histologically. Corticosterone levels were measured by RIA under blind control. Control animals (n=9) had corticosterone levels (undetectable (<12.5 ng/ml) n=8; low (12.5-30 ng/ml) n=1) within the expected normal for mice. cpk/cpk mice (n=11) had levels (86±19.4 ng/ml) far exceeding the normal range for this age. Of the 8 unaffected sibs studied, 4 were in normal range, (undetectable n=1; low n=3) and 4 (presumably heterozygotes) were in the cpk/cpk range. These data support our previous hypothesis that glucocorticoids play a role in the induction of IPKD when genetic susceptibility is also present.

1583 THE EFFECTS OF ANTIPYRETICS IN A MOUSE MODEL OF REYE'S SYNDROME. John F. S. Crocker, Ken R. Rozee, Spencer H. S. Lee, Kenneth W. Renton, Sharon Digout, Dalhousie University, Departments of Pediatrics, Microbiology and Pharmacology, Halifax, Nova Scotia

Aspirin has been implicated as an etiologic agent in Reye's syndrome (R.S.) in older children (>4 yrs.). However, in previous experiments, clinical doses of aspirin were unable to initiate any of the features of R.S. when given with Influenza B or varicella virus. We have previously described an animal model of R.S. using young mice exposed to an industrial surfactant and then infected with a mouse adapted Influenza B virus (Lee). We used this model in two age groups of mice, 10 days of age, and weanling mice (4 weeks). Aspirin (ASA), Tylenol (T), or a placebo were given for 3 consecutive days to mice at 50 mg/kg after infecting the animals intranasally with Influenza B virus. ASA and T alone, without surfactant, were also given with Influenza B virus. Survival curves for 10 day olds were statistically similar to virus control with T or ASA. A significant (p=0.01) shift of the early portion survival curve resulted when ASA was given to 10 day old mice which has been preinjected with surfactant and virus, similar results were seen in weanling mice. T had no effect on survival curves. Weanling mice also changed survival curves with ASA and not with T in the early stages of the disease, although, later the survival curves became similar. We conclude that aspirin has the potential of increasing the severity of disease in this R.S. model but by itself without the other factors cannot initiate the disease.

1584 USE OF DEFERROXAMINE (D) IN A PATIENT WITH IRON (Fe) OVERLOAD MAINTAINED ON CHRONIC HEMODIALYSIS (HD). Shermine Dabbagh, Aaron L. Friedman, Russell Chesney. Univ. of Wisconsin Hospitals, Dept. of Pediatrics, Madison WI.

Anemia is characteristic of chronic renal failure with resultant transfusion dependency, especially in growing children maintained on chronic HD. Most of these patients develop Fe overload. Chelation therapy has been used in uremic adults on HD to treat Fe overload, but its use in children has not been detailed. We report a 15-year-old white male who has been on chronic HD for the past 8 years. He has chronic normocytic, normochromic anemia of uremia. To maintain the hematocrit (Hct) above 20% and hemoglobin (Hgb) above 6 gm%, he has received 400 cc of packed red blood cells every 4-5 weeks for the past 6 years. Because of elevated serum ferritin and concern about Fe overload, chelation therapy with D was begun. A dose of 24 mg/kg is infused I.V. during the first hour of HD three times per week. The patient continues with the same transfusion requirements, and no adverse effects of D have been noted. The data indicate that chelation therapy during hemodialysis can be used to treat Fe overload in children to prevent hemosiderosis.

	Serum Fe µg/dl	Serum Fe BC µg/dl	Serum Ferritin ng/ml	Hct/Hgb %/gm%	Mean CV fl	Mean CHC gm/dl RBC
Pre-Treatment	78	186	3540	19/6.6	88	35
3 mo Post-Rx	236	300	2500	23/6.9	89	31
Normal	53-119	250-400	10-150	39/13.4	82-101	31.5-36

Chest X-ray, EKG and liver function tests were normal.

CV: corpuscular volume; CHC: corpuscular hemoglobin concentration

1585 THE AMINOACIDURIA OF VITAMIN D DEFICIENCY IS EXPRESSED BY CHANGES AT THE BRUSH BORDER MEMBRANE. Shermine Dabbagh, Russell W. Chesney, Naomi Gusowski. U. of Wisconsin Hospitals, Dept. of Pediatrics, Madison WI.

With vitamin D deficiency, excessive phosphaturia and aminoaciduria are common, but the pathophysiology of these abnormal losses is uncertain. To better understand the pathophysiologic mechanism of aminoaciduria, we placed weanling rats on various vitamin D-deficient diets for 4-7 weeks. The diets were: 1) very low calcium (0.02% Ca) diet (VLCD); 2) low-Ca (0.5%) diet (LCD); 3) normal-Ca (1.2%), low-phosphate (0.1%) diet (LPD). Another VLCD group received 500 pmoles of $1,25(OH)_2D$ intraperitoneally for 2 days before sacrifice (VLCD-1,25). Urinary excretion and isolated brush border membrane vesicle studies were performed, examining glucose and the amino acid taurine (T).

	Control	VLCD	LCD	LPD	VLCD-1,25
Plasma Ca	9.0±0.9	4.5±0.3*	4.3±0.3*	7.8±1.3	6.9±0.8*
Urine T	17.7±2.2	63.3±21.3*	78.3±26.6*	94.3±33.2*	89.8±20.9*
T uptake	23.9±9.0	20.3±1.5*	18.6±7.7*	16.4±0.8*	16.8±2.5*

Plasma Ca: mg/dl; urine T: µm/mg Cr; T uptake: pmole/mg/60 sec

All * parameters were different from control at $p < .05$. Kinetic analysis revealed a significantly ($p < .01$) reduced Vmax of T uptake on all experimental diets. The Km of uptake was not changed by vitamin D deficiency. These data indicate that the aminoaciduria of vitamin D deficiency is expressed at the brush border surface and that vitamin D deficiency is more important than plasma Ca level. This defect in T absorption is not altered by short-term vitamin D administration. BBMV uptake of glucose also was unchanged by vitamin D deficiency.

1586 DIBUTYRL CYCLIC AMP (dbcAMP) DOES NOT ALTER AMINO ACID ACCUMULATION BY BRUSH BORDER MEMBRANE VESICLES (BBMV). Shermine Dabbagh, Russell W. Chesney, Naomi Gusowski. University of Wisconsin Hospitals, Dept. of Pediatrics Madison, Wisconsin.

Aminoaciduria is found in 20% of hyperparathyroid patients and in virtually all patients with vitamin D-deficiency rickets or renal osteodystrophy in whom parathyroid hormone (PTH) is secondarily elevated. An ascribed mechanism of this aminoaciduria is measured PTH secretion with resultant activation of adenylate cyclase. To test the hypothesis that cyclic AMP blocks amino acid reabsorption, we examined the uptake of the β-amino acid taurine in the presence of the membrane-soluble cyclic nucleotide dbcAMP. At 10^{-3}M, dbcAMP did not block the accumulation of taurine in cortex slices from immature animals and actually increased taurine accumulation in tissue from adult animals. Accumulation by isolated BBMV from normal Sprague-Dawley rats was unaltered by dbcAMP over the concentration range 10^{-3} to 10^{-7}M, a concentration found by Hammerman et al (Biochim Biophys Acta 755:10, 1983) to block phosphate uptake in canine BBMV. Pre-incubation from 0 to 40 min and temperature alteration (4° to 23°C) did not alter these results. At very high levels (10^{-2}M or greater), dbcAMP did reduce taurine accumulation, but these concentrations are unphysiologic.

These data indicate that dbcAMP does not reduce amino acid accumulation at either the apical or basolateral surface and make it unlikely that the aminoaciduria of vitamin D deficiency is related to adenylate cyclase activation.

†1587 CONTRIBUTION OF THE FETAL KIDNEY TO PRESERVATION OF FLUID VOLUME DURING HYPOVOLEMIA. Salha S. Daniel, Raymond I. Stark, Pamela J. Tropper and L. Stanley James. Columbia Univ., Coll. P & S, Babies Hosp., Div. Perin., Depts. Ped. & Anes., N. Y.

Vasopressin in fetal plasma (VP_p) has been shown to increase following mannitol infusion to the mother (Leake, R.D. et al, Pediatr. Res.13:841, 1979). It was suggested that this increase was related to the hyperosmolality and/or hypovolemia induced by transfer of water from fetus to mother. In order to examine the response of the fetal kidney to these changes, we studied six chronically instrumented fetal lambs 120-131 days gestation following infusion of mannitol to the mother. Mannitol infusion caused an increase in osmolality of maternal plasma from 298±3.1 to 311±2.0 mOsm/kg. In addition this treatment caused an increase in fetal VP_p from 1.9 to 3.2 pg/ml and osmolality (OsM_p) from 292±2.9 to 299±2.1 mOsm/kg (Mean ±S.E.). Following infusion there was also a fall in fetal urine output from 0.15±0.019 to 0.10±0.009 ml/kg min and a rise in urine osmolality from 140±8.6 to 183±13.2 mOsm/kg ($p<0.01$). These changes led to a significant decrease in solute free water clearance from 0.08±0.009 to 0.05±0.004 ml/kg min but not in osmolar clearance.

These studies indicate that: 1) Mannitol to the mother induces a rise in fetal OSM_p, 2) the rise must be due to transfer of water to the mother rather than fetal diuresis and 3) the fetal kidney contributes to the preservation of fluid volume in response to hypovolemia. Furthermore these results raise the possibility that diuretics given during pregnancy may cause dehydration in the fetus.