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GROWTH FAILURE (GF) IN CHILDREN WITH MODERATE RENAL INSUFFICIENCY (MRI). H. Trachtman, O. Adamson, K. Phadke, A. Tejani. (Spon. by S. Fikrig). DMC, SUNY, Dept. of Peds, Brooklyn, NY.

Despite large numbers of children with chronic renal failure, there is insufficient information about GF prior to end stage renal disease. It has been stated that a GFR (ml/min/1.73M²) of 20-25 is the threshold below which growth retardation begins.

We report the linear growth in 11 prepubertal children with stable MRI for at least 1 year (34.4±24.4 mos., mean ±SD). Height was measured with a wall stadiometer. MRI was defined as a GFR between 20-40. The GFR was assessed using the endogenous creatinine clearance or a length estimation. There were 7 male and 4 female patients, mean age 9.3 years at onset. Six children had congenital and 5 had acquired causes of MRI. The GFR was initially 32.5±6.4 and declined to 26.7±6.5 at the end of follow-up. The mean serum Ca⁺⁺ was 9.4, PO₄⁼4.4 mg/dL and HCO₃⁻ 23.8 mEq/L. The PTH level was elevated in all 7 children with the determination.

During the observation period, 9/11 children suffered GF. Their mean cumulative loss of stature for age was 0.65±0.44 SD. The height SD fell at a mean yearly rate of 0.25±11. This is nearly 65% of the mean annual loss of length for age in dialysis patients, as reported by the EDTA Registry. We conclude that 1) stable MRI is associated with progressive loss of linear growth for age; and 2) the degree of GF approaches that observed in children on maintenance hemodialysis. Hyperparathyroidism and chronic metabolic acidosis may be contributing factors to this GF.

1661 CLINICAL TRIAL OF MEDICAL VS. SURGICAL TREATMENT OF VESICO-URETERAL REFLUX (VUR). Report of the USA Collaborative Study of Reflux in Children.*

VUR accounts for 15% of children and young adults with ESRD and it is a common cause of severe hypertension in the same population. Since 1980, we have conducted an international, prospective, randomized trial of early anti-reflux surgery (S) vs. medical therapy (M), namely, continuous antibiotic chemoprophylaxis. The study population consists of children up to 10 years of age with primary VUR, grade IV/V (International Classification). The end points of the trial are: 1) renal growth, as measured by planimetry, 2) progression of renal scarring or development of new scars, 3) individual kidney GFR, as measured by DMSA renal scans, 4) rate of resolution of VUR in patients treated medically, 5) incidence of UTI, 6) incidence of hypertension. To date, 300 pts. have been enrolled. Preliminary analysis of the 116 USA pts. has yielded the following information: 42% of pts have at least 1 renal scar at entry; new or progressive scars were seen in 36% of M pts vs 50% of S pts when entry urograms were compared to those done 6 mo. later (p > .1). By 18 mo. of follow-up, grade IV/V VUR was still present in 83% of the pts in the M group. The incidence of acute pyelonephritis was 1 per 0.007 pt-months at risk in the S group, and 0.013 for M pts (p > .1). Only 1 pt has developed BP > 95th percentile for age and sex during 18 mo. follow-up. Six pts allocated to M have undergone anti-reflux surgery because of recurrent UTIs and 1 pt allocated to S has required reoperation for persistent VUR. Thus, no dramatic differences in course between M and S are apparent at this early analysis.

* To be presented by Robert Weiss (spon. by Adrian Spitzer), Albert Einstein College of Medicine, Department of Pediatrics, Bronx, N.Y.

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MANAGEMENT OF ACUTE AND CHRONIC HEMOLYTIC UREMIC SYNDROME-RELATED HYPERTENSION BY CAPTOPRIL. Elizabeth Jackson, Thomas Welch, (Sponsored by C.D. West) Children's Hospital Research Foundation, Cincinnati, Ohio.

Hypertension in HUS may occur acutely or as a chronic sequela. The hypertension appears to be mediated in part by renin. For this reason captopril, an angiotensin converting enzyme inhibitor, is appropriate and experience with its use in a few individual patients has been reported. We present the successful management of hypertension by captopril in 4 patients with HUS. Pertinent data are summarized:

Pt #	Age	Pre-Cap.		Post-Cap		Init. Cr	D/C Cr
		B.P.	Dose	B.P.	Dose		
1	2-1/2 yrs.	143/96	1.25mg/kg/d	100/60		2.0	.8
2	5 mos.	150/104	3.1 mg/kg/d	125/74		3.6	.9
3	5-1/2 yrs.	160/110	3 mg/kg/d	110/70		.6	.7†
4	15-1/2 yrs.	190/110	1.25mg/kg/d	132/80		on dialysis	

(† after 18 mos. on captopril)

In patients 1 and 2 captopril alone was used during the acute disease. In patients 3 and 4 captopril with a diuretic was effective for management of chronic hypertension present more than a year following the acute illness.

Captopril may produce hyperkalemia via aldosterone inhibition. Serum potassium was modestly elevated in patients 1 and 2 but resolved after discharge despite continued captopril therapy. Renal function as determined by creatinine did not deteriorate upon institution of captopril.

In summary, captopril is effective in both acute and chronic hypertension related to HUS.

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CARNITINE LOSSES IN CHILDREN ON HEMODIALYSIS (HD) AND CONTINUOUS AMBULATORY PERITONEAL DIALYSIS (CAPD). Gaston Zilleruelo, Michael Freundlich, Milan Novak, Jose Foradada, Carolyn Abitbol, Brenda Montane, Jose Strauss. Department of Pediatrics, University of Miami, Miami, Florida.

Hyperlipidemia (HL), particularly elevated triglycerides (TG) is frequently seen in uremic patients undergoing dialysis. Carnitine plays an important role in the utilization of fatty acids and, being a small molecule, its possible losses in dialysis effluent may be a contributing factor to HL. We studied simultaneous concentrations of free carnitine (FC) and total carnitine (TC) in plasma (pre and post HD) and dialysis effluent in 9 HD patients (x age: 18 years) and 5 CAPD patients (x age 10 years). Serum TG were determined in all patients. Results (x ± SD) are summarized in the table (†p < 0.01 compared to controls).

Dialysis Modality		Plasma		Dialysis TC losses	TG (mg/dl)
		FC	TC		
HD	Pre	35±12	61±14	2,316±636	192±73†
	Post	13±6†	25±11†		
CAPD		43±7	76±18	567±595	410±280†
Controls		43±10	55±12		60±25

These results demonstrate: 1) significant removal of TC during dialysis (greater on HD than CAPD), but maintenance of normal plasma TC levels; 2) significant decrease of plasma FC and TC immediately following HD and 3) HL with significant elevation of TG in both groups. It is suggested that cumulative TC losses during dialysis may aggravate HL in these patients.

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PLASMA INFUSIONS (PI) IN THE MANAGEMENT OF HEMOLYTIC UREMIC SYNDROME (HUS). Gaston Zilleruelo, John J. Byrnes, Michael Freundlich, Carolyn Abitbol, Brenda Montane and Jose Strauss. Departments of Pediatrics and Medicine, University of Miami, Miami, Florida.

In spite of early dialysis and supportive therapy, children with severe HUS have a high incidence of sequelae with chronic renal failure (CRF) and/or hypertension. Previous experience at this center has shown 66% of children with HUS developing CRF. Since a plasma factor deficiency has been postulated in the pathogenesis of this syndrome, we studied the acute and long term effects of PI in HUS. Six children (3 boys) 2-5 years of age with HUS were treated with peritoneal dialysis and PI. Mean dose of PI was 25 ml/Kg/day given for 2-7 days. All children had oligoanuria >24 hours (x duration 15 days; range 2-30 days) and thrombocytopenia (lowest platelet count x 17,500; range 8,000-40,000). Mean serum creatinine before dialysis was 6.2 mg/dl. Transient hypertension was present in all the patients and two had evidence of multi-organ involvement. After the initial dose of PI, platelet count rose to >100,000 in x 4 days and oligoanuria resolved in x 10 days. Total duration of dialysis period was x 12 days (range 3-30 days). At last follow up (x 13 months) all six children have serum creatinine <0.8 mg/dl (estimated GFR >75 ml/min/1.73 m²) and only two have mild hypertension and proteinuria. These results suggest that judicious administration of plasma has a beneficial effect in HUS by accelerating recovery from the acute phase and improving its final outcome.

NEUROLOGY

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SALICYLATE INHIBITS CITRULLINE SYNTHESIS IN MITOCHONDRIA: IMPLICATIONS FOR REYE'S SYNDROME. Richard I. Kelley, Caroline A. Brown, June R. Aprille. Tufts University, Dept. of Biology, Medford, MA 02155.

In Reye's Syndrome (RS) there is a general decrease in the specific activities of mitochondrial enzymes, including two of the urea cycle, carbamyl phosphate synthetase and ornithine carbamyltransferase. These two enzymes catalyze the synthesis of citrulline (CIT) from ornithine, NH₃, and CO₂; the functional impairment of this reaction sequence probably contributes to hyperammonemia in RS. Salicylate (SA) has been implicated as a synergistic factor in the pathogenesis of RS. In this study we investigated whether SA inhibits CIT synthesis in isolated rat liver mitochondria. CIT synthesis was assayed at 37°C by measuring ¹⁴C₂ fixation in the presence of ornithine and NH₃ (ABB 178:19,1977). SA inhibited CIT formation (μmol/hr/mg mito protein) as follows:

SA concentration, mM:	0	0.25	0.5	1.0
Citrulline synthesis:	2.69±.05	2.17±.10	1.66±.10	0.51±.13

Genetic acid, salicylic acid and acetaminophen had no effect at 5 mM. CIT synthesis is dependent on matrix ATP: a mechanism of inhibition was suggested by further experiments showing that SA uncouples oxidative phosphorylation and decreases the rate of ATP synthesis. Matrix ATP/ADP ratios were decreased by SA as follows: 1.15±.04 (0 SA); 0.90±.21 (0.25 mM SA); 0.63±.09 (0.5 mM SA); 0.11±.04 (1 mM SA). Conclusion: SA is a potent inhibitor of CIT synthesis at physiological concentrations, probably as a result of its uncoupling action which lowers matrix ATP. The implication for RS is that SA might inhibit urea cycle function beyond the already compromised level. (NIH 14936)