175 SULFATE AND TAURINE METABOLISM IN EXPERIMENTAL UREMIA.

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The plasma levels of inorganic sulfate(SO_4)and most sulfur containing amino acids are known to be elevated in uremia(U). Taurine(Tau)is important for the regulation of neuromuscular functions, especially in the heart, where it comprises 75% of all amino acids. In order to investigate the role of SO_4 and Tau in U bilateral nephrectomy(NX) was performed in 38 rats. SO_4 and Tau concentrations in plasma and various organs were determined 12,24 and 48 hrs after NX and compared to sham operated and normal rats. In NX rats mean SO_4 rose linearly in plasma(0.9 to 7.8 mmol/l) and less in liver(0.6 to 3.2 mmol/g wet wt.). The increase was only x 2.0 in skeletal muscle and x 1.5 in brain. A close correlation was found between plasma SO_4 and creatinine(r=0.92). Tau levels increased in plasma from 0.2 to 0.5 µmol/ml and in liver from 2.0 to 7.2 µmol/g wet wt., but decreased in the heart from 26.0 to 21.0 µmol/g wet wt.($p<0.01$) and remained constant in skeletal muscle and brain.
In conclusion, intracellular changes of SO_4 and Tau are not reflected by plasma levels. The apparent efflux of Tau from the heart of NX rats might be related to the pathogenesis of uremic heart disease.

PHARMACOLOGIC AGENTS

176 INTRAVENOUS METHYLPREDNISOLONE IN THE TREATMENT OF STEROID RESPONSIVE NEPHROTIC SYNDROME. Kennedy, T.L. Rasoulpour, M. & McLean, R.H., Division of Pediatric Nephrology, University of Connecticut Health Center, Farmington Connecticut, 06032, U.S.A.

Six children in relapse with steriod responsive nephrotic syndrome received 3 doses of intravenous methylprednisolone (30mg/kg) on alternate days. The 6 children received a total of 9 courses of methylprednisolone and there were no adverse effects. Each course was followed immediately by prednisone therapy (2mg/kg) on alternate days. Five were frequent relapsers and the sixth had many recurrences over 15 years. All were males with a mean age of 4.5 years at onset and 9.1 years at the time of "pulse" therapy. All had normal renal function. Renal biopsies showed mild mesangial proliferation in 3, focal sclerosis in 1 and minimal change in 1. Four subsequently achieved sustained remissions after chlorambucil therapy and the remaining 2 continued to have occasional relapses. Following 8 courses, a remission occurred in 5 to 15 days (mean 7 days) and in the ninth a remission occurred after 46 days. During 11 previous relapses the interval to remission using oral prednisone was 5 to 21 days (mean of 11 days). Prior to "pulse" therapy the mean interval between relapses was 131 days (range 30 to 260 days); following "pulse" therapy, the mean interval was 130 days (range 23 to 420 days). We conclude that intravenous methylprednisolone "pulse" therapy in steroid responsive nephrotic syndrome of childhood can induce a remission which is similar with respect to the time of onset and the duration of the remission achieved with oral prednisone therapy.

177 CHLORMETHINE (C) IN NEPHROSIS (N). LENOIR G., KLEINKNECHT C., GUESRY P., BROYER M. Hôpital des Enfants-Malades. PARIS. FRANCE.

C. was used in 18 Steroïd-Resistant (SR) N and in 27 Steroïd-Sensitive (SS)N. Two regimens were used : in the former a total dose of 0.8tol/mg/kg was given alone using 12 IV injections over one month. In the latter a total dose of 0.8 mg/kg was given over two periods of 4 days separated by one month, and was associated with Prednisone (2 mg/kg/day) and anti-emetic agents. In SRN, only one patient remitted, whereas 2 had a transient (2 weeks) and one a partial remission. The others were un changed. SSN were all steroïd dependent and 13/27 had severe steroïd toxicity signs. C. was given 0.5 to 11 years after onset. A remission was obtained in all but two patients treated with the first regimen. Remission lasted less than one year in 10, 1 to 2 years in 5. In the remainder, follow-up was less than 2 years, except for 4 children : one had a relapse 4 years later, and 3 had sustained remission 2,2 1/2 and 13 years after therapy. Of the 16 patients who relapsed, 6 received other nitrogen mustards and 10 were controlled using non toxic doses of alternate-day Prednisone therapy. Side effects were leucopenia (20%) including pancytopenia in 3 children and gastrointestinal disorders (50%). Only one patient was studied in adulthood and had a normal sperm-count. In conclusion : C. was ineffective in SRN, and resulted mainly in short remissions in SSN. In SSN however, C. when associated with Prednisone seemsbeneficial in decreasing the dose of Prednisone required to maintain remission.

178 A CONTROLLED THERAPEUTIC TRIAL OF CYCLOPHOSPHAMIDE PLUS PREDNISONE VERSUS PREDNISONE ALONE IN CHILDREN WITH FOCAL SEGMENTAL GLOMERULOSCLEROSIS (FSGS). A preliminary report of the International Study of Kidney Disease in Children.

41 children with nephrotic syndrome having FSGS histologically were randomly allocated to one of two therapeutic regimens. Both groups received Prednisone 40 mg/m^2 on alternate days for 12 months either alone (group A) or together with Cyclophosphamide 2.5 mg/kg daily for the first 90 days of the year (group B).

Heavy proteinuria initially present in all children disappeared in 5/16 (31.3% in group A and 9/23 (39.1%) in group B. (X^2 0.03 p:NS). Serum albumin concentrations returned to normal in all 12 proteinuria-free patients for whom there was data - and also in 4/25 patients in both groups (2 in each) whose proteinuria persisted.

Deterioration of renal function occurred in 4/16 (25%) in group A and 12/25 (48%) in group B (X^2 1.31 p:NS). In 16 children with deteriorating function, data on proteinuria were available in 14 - all but one had persisting proteinuria. Other data show a tendency for functional deterioration to be commoner in older females with a longer duration of disease prior to entry in the study.

We conclude that while the disease runs a variable course there is no evidence from this study that either therapeutic regimen was superior to the other. The natural history of the condition in the absence of therapy is not known.

179 HIGH DOSE INTRAVENOUS METHYLPREDNISOLONE BOLUS THERAPY ("PULSES") IN SEVERE PROLIFERATIVE GLOMERULONEPHRITIS. Rose, GM, Morris, KB, Cole, BR, Beale, MG and Robson, AM. Wash. Univ. Sch. of Medicine, St. Louis Children's Hosp., Dept. of Peds. St. Louis, MO, USA

Twenty-nine patients with biopsy proven severe proliferative glomerulonephritis were treated with 6 alternate day "pulses" of 30 mg/kg each. Pre- and post-treatment inulin clearances (ml/min/1.73m^2) and maximum GFR achieved after pulses were (mean±SEM):

	N	Pre-	Post-	Maximum	
MPGN	9	30.5 ± 3.6	50.8 ± 8.3*	91.1 ± 11.7*	*p<.05 vs pre
HSP	7	39.5 ± 9.5	68.2 ± 8.3*	96.6 ± 10.7*	
Lupus	7	50.7 ± 7.0	70.6 ± 6.4*	82.0 ± 7.7*	
Other	6	18.2 ± 2.5	38.6 ± 7.5*	73.7 ± 10.9*	

C_{PAH} increased with pulse therapy in all groups, increasing from 307 ± 62.2 to 644 ± 81.3 ml/min/1.73m^2 in HSP patients (p<.02). Protein excretion decreased from pre-treatment 3.7 ± 1.0 to 1.4 ± 0.4 g/day post-treatment. Side effects of pulse therapy were few, hypertension being seen only in patients with pre-existing hypertension. Improvements in GFR following pulses were maintained in 25 patients treated subsequently with oral Prednisone-initial dose 2 mg/kg with subsequent stepwise reductions. Of the four patients failing to maintain improvement after pulses, three were treated late in the course of their disease.

These observations support our preliminary findings (J.Peds, 88,307,1976) that the use of steroids in pulse doses relatively early in the course of patients with severe glomerulonephritis is beneficial and improves their prognosis.

180 METHYLPREDNISOLONE "PULSE" THERAPY (MPT) IN CHILDHOOD SYSTEMIC LUPUS ERYTHEMATOSUS (SLE). Salcedo, J.R. and Turner, M. Depts. of Pediatrics, Division of Nephrology. Children's Hospital and Walter Reed Army Med. Ctr. George Washington University and USHUS.

Pulse therapy has been reported to be useful for the treatment in SLE Nephritis. Histopathologic correlation and response to therapy has yet to be determined. We are reporting 11 patients ages 13 ± 3 years who were treated with MPT (1 gram/day/ 3 days). The mean follow up range was between 6 months to three years. The patients were divided into three groups. Group I (5 pts.) had Diffuse Proliferative Glomerulonephritis (DPGN); Group II (4 pts.) had severe SLE systemic manifestations no DPGN; Group III (2 pts.) had Rapidly Progressive DPGN. Serum creatinines in groups I and II were normal, while in Group III creatinine values were 2.9 and 3.3 mg/dl, but had been normal within the last 3 months. All patients demonstrated prompt resolution of non-renal systemic manifestation. In Group III, patients' serum creatinine levels continued to rise despite treatment, but stablized or decreased by day 10. Hypertension (HBP) was observed in one patient in Group I, and exacerbation of preexisting HBP in both patients in Group III. In addition one patient in Group I developed diabetes; this was the only significant morbidity associated with this regimen. Based on the above observations, we conclude that the high dose of MPT is as safe as the accepted steroid regimen for SLE. Prompt clinical improvement, lack of infectious complications, or other steroid side effects suggests superiority of the MPT regimen. Long term side effects and patient outcome are not known.