181 PULSE NITROGEN MUSTARD TREATMENT OF CHILDHOOD IDIOPATHIC NEPHROTIC SYNDROME (INS.).

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As an alternative to long-term administration of oral cytotoxic agents, pulse intravenous nitrogen mustard (HN_2) has been used in 5 patients with steroid-resistant INS (all had "early resistance") and one patient with steroid responsive INS. The dose of HN_2 was 0.1 mg/kg/day x 4 days. All patients had minimal-lesion histology. The patient with steroid-responsive INS had a frequently relapsing course (4.8 relapses/year) despite treatment with cyclophosphamide (2 courses) and chlorambucil. Since HN_2, she has had no further relapses. The current status of 5 patients with steroid-resistant INS is: 3 have persistent mild proteinuria, normal excretory function and absence of overt nephrotic syndrome; 2 have persistent INS despite HN_2 but subsequently remitted after cyclophosphamide and both have since had a steroid-responsive, relapsing course. No toxicity attributable to HN_2 was noted. This preliminary experience suggests that HN_2 may ameliorate INS in some patients with steroid-resistance. HN_2 may also be a useful adjunct in the management of some patients with steroid-responsive, frequently-relapsing INS, in whom oral cytotoxic therapy may not be warranted. A controlled therapeutic trial to better assess the usefulness of HN_2 is planned.

182 PROTECTIVE EFFECT OF POLY I:C AGAINST SISOMICIN NEPHROTOXICITY IN RABBITS.

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The protective effect of Poly I:C during sisomicin nephrotoxicity in rabbits was determined by measurement of the urinary enzymes alkaline phosphatase(AF),lactic dehydrogenase(LDH)and N-acetyl-β-glycosaminidase(NAG). 18 rabbits were divided in 3 Groups. Separate 24 hours urines were assayed for controls(AF=110±20SD, LDH=25±4SD,NAG=30±6SD).Group 1,received a subcutaneous dose of sisomicin,200mg/kg,Group 2,a subcutaneous dose of Poly I:C,5mg/kg followed 24 hours later by sisomicin and Group 3,only Poly I:C. 24 hours urines were collected for the next 5 days and assayed for enzymes.Fractional sodium excretion($\%fE_{Na}$)was calculated on the 1st and 6th day.Urinalysis was done daily.All rabbits were killed on the 6th day and the kidneys were examined by light microscopy.Group 1,presented a sharp rise in the urinary enzymes(AF =825±95SD,LDH=164±18SD,NAG=650±76SD),Group 2,a gradual rise in the urinary enzymes with the peak on the 5th day(AF=655±92SD,LDH =112±14SD,NAG=480±54SD)and Group 3,only a slight elevation(AF= 156±24SD,LDH=37±6SD,NAG=60±4SD).Only in Group 1,the $\%fE_{Na}$ was 7.5 -9.6% on the 5th day(controls:0.62-0.85%),the urinalysis showed hyaline casts and red cells and the kidneys' light microscopy revealed the proximal tubular cells swollen with fine vacuolation of the cytoplasm.The results support the view that Poly I:C,a toxic substance itself,protects the kidney cells from damage,most probably,by induction of interferon production.

183 THE ROLE OF VOLUME DEPLETION IN FUROSEMIDE ENHANCED AMINOGLYCOSIDE NEPHROTOXICITY.

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Furosemide (F) enhances the nephrotoxicity of gentamicin and a related aminoglycoside, netilmicin (NET) (Kid Int 12:538, 1977; Ped Res 13:366, 1979). To determine whether enhancement is primarily due to volume depletion, dogs were given im injections q8h for 10 days of the following: (F) alone 2 mg/kg, Grp 1; (NET) alone 15 mg/kg, Grp 2; (NET) 15 mg/kg + (F) 2 mg/kg, Grp 3. Group 4 received (NET) 15 mg/kg + (F) 2 mg/kg + gavage (75 mEq NaCl+40 mEq KCl/l in a daily volume equal to 5% of body weight). Serum creatinine (Scr) values in Group 3 exceeded values of all other groups. Scr values did not differ between Groups 2 and 4. Necropsied renal tissue revealed moderate to severe diffuse acute tubular necrosis in Group 3; Groups 2 and 4 had only mild areas of tubular necrosis.

Serum creatinine (mg/dl)

Grp		Day 0	3	7	10
1	(F)	.93(.03)	1.16(.23)	1.25(.25)	1.26(.21)
2	(NET)	.87(.03)	.75(.06)	.84(.04)	.91(.02)
3	(NET)+(F)	.87(.03)	1.14(.09)	1.73(.37)*	3.02(1.0)§
4	(NET)+(F)+Gav	.87(.02)	.81(.04)	.94(.08)	1.02(.07)

*p < .01 (Grp 3 vs Grps 2,4); §p < .01 (Grp 3 vs Grps 1,2,4)

The studies suggest that (F) enhancement of (NET) nephrotoxicity is primarily due to volume depletion.

184 POSSIBLE ENZYMATIC INHIBITION BY VALPROATE (VA). A PRELIMINARY REPORT.

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Phenobarbital had been reported to reduce the survival of the renal allografts, by producing enzyme induction and by reducing the immunosoppressive action of the steroids. The aim of this study was to evaluate whether VA has the same effect or not. Two transplanted children with epilepsy and another epileptic, but otherwise normal child, were submitted to antipyrine-test before and, at least, 2 weeks after VA treatment. Informed consent was obtained from the parents. Antipyrine was assessed by means of HPLC technique and some kinetic parameters were calculated. While the apparent distribution volume of antipyrine remained unchanged in all 3 patients, the half-life clearly increased (+58%) and the clearance was reduced (-48%). These results, if confirmed subsequently,could suggest inhibition of hepatic microsomal enzymes by VA. This drug seems to be a useful alternative in epileptics with renal transplant. However a possible increase of side-effects of immunosoppressive drugs should be considered.

185 APPARENT CEREBRAL ATROPHY ON COMPUTED TOMOGRAPHY IN NEPHROTIC CHILDREN WITH STEROID THERAPY

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To know the influence of steroid on CNS in nephrotic S.,CSF-space/Intracranial space ratio(abb.C/T-R)was calculated by computor processing of CT at the level of the 3rd and lateral ventricles in 14 cases of nephrotic S.(MC 10;PGN 3;SHS 1;chr.sclerosing 1)

Mode of Tx	Daily		Alternate-day		Total N.
Prednisolone	60mg/SA 20-30mg/SA*		2.5-1.1 mg/kg/once		
CT at	4 weeks	2.5 months	2-5 ms / 3 weeks		
Number	8	1	4	1	14
Abnorm.C/T R.(%)	7**(87.5%)	1	3(75%)	1	12(85.7%)

*Pred. equivalent dose of para & β methasone **Mean C/I-R=5.6±2.1

Twelve of 14 cases treated with steroid revealed abnormaly high C/I-R than controls(non nephrotic,non steroid Tx,mean C/I-R=1.6± 0.8 SD.). Nine of 12 cases with abnormaly high C/I-R. showed normal C/I-R after the withdrawal of steroid,reduction or during the end of maintenance therapy by alternate-day regimen.

Abnormal neurological and psychiatric symptoms in the above 16 cases were 2 manic;1 depressive state;muscle weakness in 4;tremor of the finger 1,although no correlation with the grade of C/I-R abnormalities. C/I-R was the highest in a case with para or β methasone therapy for 2.5 months. C/I-R showed no relationship between the age or sex of the patients.

The above data suggest that massive dose of steroid might have apparent cerebral atrophic effect although it will be reversible.

186 GONADAL FUNCTION IN MALES TREATED WITH LIMITED CYCLOPHOSPHAMIDE FOR STEROID SENSITIVE NEPHROTIC SYNDROME.

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Gonadal damage is known to occur following treatment with high dose and/or prolonged courses of cyclophosphamide (CP). However, the effect of limited treatment has not been well established. 53 boys with steroid sensitive nephrotic syndrome received a standardised 8 week course of 3mg/Kg body weight per day of CP at the Hospital for Sick Children, London, during 1966-1974. 23 boys now over the age of 18 years were recalled for assessment of gonadal function. 4 were known to have fathered children, 4 declined to participate in the study and 1 was untraceable. Mean age at the time of treatment was 10.7 years and mean interval to follow up 10.3 years. Semen analysis in 11 postpubertal males who received only one course of CP showed that sperm densities were lower than in controls of the same age (Patients 60 ± 9; Controls 103 ± 17; mean sperm densities ± S.E.; million/ml). Evidence of sperm dysfunction was observed in 8 of these patients, and also in 2 out of 3 patients who received 2 standardised courses of CP. Libido and sexual performance was assessed as normal in all but 2 patients in whom it was considered to be diminished. Antisperm antibodies were not detected in the sera of patients. The data suggest that gonadal dysfunction may occur in males who receive even limited treatment with CP.