133 ANTICOAGULANT THERAPY VERSUS NO SPECIFIC TREATMENT IN THE HEMOLYTIC UREMIC SYNDROME

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In June 1976 a controlled randomized study was started on the usefulness of anticoagulant therapy in childhood hemolytic uremic syndrome.All infants and children with HUS,entering our department,are allocated to one of two different therapeutical schedules:the one consists of supportive therapy only (-ANT),the other comprises in addition the administration of heparin and dipyridamole (+ANT).Before dismissal,all patients undergo a percutaneous renal biopsy which is examined by light microscopy and immunofluorescence.Thirty-six patients have entered the study so far. Both groups are made of 18 infants and children and are almost similar as far as age distribution is concerned.The (+ANT)-group comprises an equal number of severe and mild cases whereas 12 children of the (-ANT)-group are considered to have had a mild form of the disease.Two children in the (+ANT)-group died, one of them three hours after admission, and one child in the (-ANT)-group,the overall mortality being 8.3%.Three patients in the (-ANT)-group had had an unusually prolonged course with severe hypertension,lasting for more than one year in one of them. All other patients made a reasonably quick recovery.A first analysis of the 34 kidney biopsies shows differences between both subgroups. These differences,although suggesting a beneficial effect of the anticoagulants,are,however,not statistically significant.Data on the long term evolution of kidney function are preliminary. Creatinine clearance values at 6, 12, 24 and 36 months are not statistically different between both groups.

NEPHROSIS

134 EFFECTS OF URINARY TRACT INFECTION (UTI) ON IDIOPATHIC NEPHROTIC SYNDROME (INS).

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NS episodes (NSE) are occasionally associated with UTI. However, the effect of UTI on NS is not clearly understood. We compared the clinico-laboratory findings and progress in steroid therapy (ST) of 22 NSE which, at onset were not on ST and had UTI with those of 22 other NSE without UTI. These occurred in 11 of 41 patients during an average follow-up of 5½ years. The two groups included 21 steroid sensitive (SS) and one resistant NSE. Diagnosis and ST were based on ISKDC protocol. Antibiotics were administered for UTI. The↑BP (>2SD) proteinuria mg/m²/hr and other laboratory findings (mean ± 1SD) were:

Group (N)	↑BP N(%)	Protein-uria	Serum Album	Serum Chol.	Serum Cr.	Crcl ml/min	BUN mg/dl	ESR mm/hr
UTI	10	221	1.7	486	0.88	76	24	59
(22)	(45)	(125)	(0.5)	(182)	(0.36)	(57)	(16)	(26)
No UTI	2	110	2.1	331	0.65	118	18	42
(22)	(9)	(70)	(0.6)	(111)	(0.23)	(11)	(8)	(23)
P Value	<0.005	<0.02	<0.05	<0.002	<0.01	<0.002	>0.05	<0.02

In addition, the mean duration of proteinuria (17 days) in the UTI group was longer than those without UTI ($P<0.01$). NSE associated with UTI is characterized by ↑BP, ↑serum creatinine, higher ESR and serum cholesterol, lower GFR and serum albumin and more severe prolonged proteinuria. Recognition of these adverse effects may enhance management of NS.

135 AN INVERSE RELATIONSHIP BETWEEN IMMUNOGLOBULIN G AND ALPHA-2 MACROGLOBULIN IN MINIMAL-LESION IDIOPATHIC NEPHROTIC SYNDROME.

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Patients with minimal-lesion nephrotic syndrome (MLNS) in relapse have hypogammaglobulinemia that is not solely explained by urinary losses, suggesting a defect in synthesis. Alpha-2 macroglobulin (alpha-2M) is elevated in MLNS (during relapse). Alpha-2M and IgG were measured by radial immunodiffusion in 18 patients with MLNS, during relapse and remission. During relapse mean (± 1 SD) alpha-2M was 896 ± 213 mg/dl; mean IgG was 218 ± 128 mg/dl. During remission mean alpha-2M was 422 ± 143 mg/dl; IgG was 493 ± 85 mg/dl. During relapse patients with the highest alpha 2-M had the lowest levels of serum IgG. 24 paired measurements were further analyzed and yielded an inverse log linear relationship. Although the mechanism for elevation of alpha-2M is unknown, we hypothesize that alpha-2M (which is known to have immunodepressant properties) specifically depresses IgG synthesis in MLNS, predisposing such patients to serious infection. Further studies of B-cell function in MLNS are in progress. The increase in alpha-2M may also account for altered T-lymphocyte function in MLNS.

136 THE IMMUNE RESPONSE TO TYPHOID VACCINE OF PATIENTS WITH IDIOPATHIC MINIMAL LESION NEPHROSIS.

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The etiology and pathogenesis of minimal lesion nephrosis (MLN) is uncertain. An abnormality of the regulatory function of T cells has been suggested to account for the decreased levels of IgG and increased levels of IgM. To learn more of the function of the immune system on these patients, 26 children with MLN and 12 children with renal disease other than MLN were immunized with dilute typhoid vaccine and the humoral antibody response to both protein (H or flagellar antigen) and polysaccharide (O or somatic) antigens was determined. The antibodies against H and O antigens were determined by quantitative agglutination test. Additionally, the O antibody titers were quantitated by the passive hemagglutination test. None of the 26 patients with MLN produced antibodies in titers of 320 or above against the H antigen, in contrast to 50% of the control subjects. The difference is statistically highly significant at a value of $p<0.01$. No such differences were noted in the antibody responses to polysaccharide O antigen. Determination of the immunoclass by means of 2-mercaptoethanol reduction indicates that the major portion of both H and O antibodies was of the IgM class. Therefore, it may be concluded that patients with MLN responded less well than control subjects to the typhoid protein H antigen but equally well to corresponding O antigen of S. typhi. These observations support the assumption of an immunologic abnormality of the disease.

137 HIGH DENSITY LIPOPROTEIN CHOLESTEROL LEVELS IN CHILDREN WITH THE NEPHROTIC SYNDROME - A POSSIBLE RISK FACTOR FOR CARDIOVASCULAR DISEASE?

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Fasting high density lipoprotein cholesterol (HDLC, Bernstein method) and total cholesterol (TC) were measured in 36 children aged 1.9 - 18.5 years with a history of nephrotic syndrome and a GFR > 70ml/min/1.73m². The nephrotic syndrome was steroid sensitive in 23, due to focal glomerulosclerosis (FSGS) in 11,and other nephritis in 2. 21 samples were collected in relapse (serum albumin < 30G/L), 5 in partial remission (proteinuria with serum albumin >30G/L) and 18 in complete remission. 15 healthy children matched for age and sex served as controls. Mean TC was higher in relapse (12.6mmol/L ± 4.3 SD) than in complete remission (7.4 ± 3.0 SD, $p<0.001$) or in controls (5.2 ± 1.0 SD, $p<0.001$). TC correlated negatively with serum albumin (r=-0.62). Mean HDLC was higher in relapse (2.64 ± 1.31 SD, $p<0.001$)and in complete remission (2.66 ± 1.08 SD, $p<0.001$) than in controls (1.37 ± 0.37 SD). HDLC correlated positively with serum albumin (r=0.60) in children in relapse. Only 2 children, both with FSGS, had HDLC/TC ratios below normal, and in only 1 was HDLC below normal. Prednisolone caused no significant alteration in HDLC or TC. If low HDLC predisposes to cardiovascular disease, few children with nephrotic syndrome would appear to be at risk.

138 MINIMAL CHANGE NEPHROTIC SYNDROME (MCNS) PRESENTING AS ACUTE GLOMERULONEPHRITIS (AGN).

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The classical form of MCNS is characterized by normocomplementemia, minimal glomerular pathology, responsiveness to steroid or N_2-mustard therapy and tendency to relapse. At onset, MCNS may have pre-renal azotemia,but nephritic features usually imply a different diagnosis. We report 2 cases of AGN whose subsequent courses were typical of MCNS. Both presented at 4 yrs. with acute onset of edema, hematuria and proteinuria. Initial data:

	B.P. (mm Hg)	Proteinuria (g/d)	BUN (mg/dl)	Creat. (mg/dl)	K (mEq/l)	S. Alb. (g/dl)	C3 (mg/dl)	Chol. (mg/dl)
N.L.	135/90	6	79	1.6	6.3	1.9	170	380
M.G.	125/95	4	96	1.5	6.7	1.4	180	320

ANA, Streptozyme tests neg. Urinalysis: 25 RBC/hpf and granular casts. Biopsy of NL: mildly increased mesangial matrix. All abnormalities resolved on prednisone (20 mg/M² tid X 5 wks). Renal function has remained normal for 2 years except for 2 relapses of nephrotic syndrome (NS) responding to prednisone. Biopsy of MG: moderate hypercellularity of glomeruli with polymorphs and increased matrix, but normal GBM and no immune deposits. Nephritic features resolved on prednisone (20 mg/M² tid X 38 d); proteinuria resolved on cyclophosphamide (3mg/kg X 6 wks). Renal function has remained normal for 3 years except for 1 relapse of prednisone-sensitive NS. MCNS may therefore present in a manner indistinguishable from AGN and then have the subsequent course of MCNS.