145 THE ROLE OF HBe ANTIGEN IN THE PATHOGENESIS OF HB ASSOCIATED MEMBRANOUS GLOMERULONEPHRITIS

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The purpose of the present study is to investigate the role of HBe antigen in the pathogenesis of membranous glomerulonephritis (MGN) in Japanese children. Of 364 children who underwent renal biopsy from 1976 through 1978 in our institution, 11(10 male, 1 female, ages 1 - 14 years) were found to be HBs antigen carriers and comprise the subject of the present study. All of them exhibited some abnormality on a routine urinalysis at one time during the course. Serum HB associated antigens were studied in all. A routine light, fluorescent and electron microscopic study was performed on 14 biopsied specimens from the 11children. In addition, direct immunofluorescence for HBsAg, HBeAg & HBcAg was done in the majority of the specimens.

The results are summerized in the table. The 14 specimens were divided into 2 groups depending upon clinical manifestations at the time of renal biopsy (Group A: 9 specimens from 9 children with nephrotic syndrome or heavy proteinuria, Group B: 5 specimens from 4 children with minimal hematuria). All of the Group A specimens showed MGN stage II or III and the Group B showed either minimal changes or MGN stage IV. In all of the 5 Group A specimens studied HBeAg immune complex was present along the glomerular capillary wall, but not present in any of the 4 Group B specimens. However, HBsAg was demonstrable in only one of the 11specimens tested. At the time of renal biopsy, circulating HBeAg was studied in 8 children (Group A: 4, Group B: 4). It is of interest that 2 of the 4 Group B children were found to have HBe antigenemia.

The above data suggests there is a highly significant relationship between glomerular HBeAg immune complex and the development of MGN. We believe that most cases of HB associated nephropathy seen in the Japanese children are HBeAg mediated MGN.

Group	No. of the specimens	Serum			Renal pathology						
		HBeAg	HBeAb	HBcAb	HBsAg	HBeAg	HBcAg	IgG	B1C	LM.	EM.
A	9	4/4*	0/4	6/6	1/7	5/5	0/5	7/7	7/7	MGN	II-III
B	5	2/4	1/4	4/4	0/4	0/4	0/4	2/4	0/4	MGN	IV or minimal changes

*: 4 out of 4 tested were positive

146 MESANGIAL CHANGES IN STEROID-SENSITIVE MINIMAL CHANGE NEPHROTIC SYNDROME (MCNS). A CLINICOPATHOLOGIC AND MORPHOMETRIC STUDY.

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The kidney biopsies of 25 children with MCNS were evaluated retrospectively to determine whether there is any correlation between the histological subgroups and the frequency of relapses. Biopsy material was examined by conventional LM, semithin sections, EM and morphometry. The frequently relapsing group (FR) comprised 15 and the non- or infrequent relapsing group 10 patients (IR). FR had been followed for longer periods before biopsy (mean 4 yrs.) than IR (1.4 yrs.). Mild mesangial hypercellularity and focal tubular atrophy were more common in FR (5/15) than in IR (1/10). In morphometric studies of semithin sections the number of mesangial nuclei per 1000 um^2 mesangial area was significantly increased in FR compared to IR (mean 9.40±0.28 S.E. vs. 8.04±0.23 S.E.; $p<0.005$). By electron microscopy no difference was found concerning the presence of unspecific electron-dense deposits, podocyte changes or glomerular basement membrane lesions. Morphometric measurement of mesangial alterations appears to be a promising method for exploring clinicopathological correlations in steroid-sensitive MCNS.

147 LONG-TERM FOLLOW-UP STUDY OF IDIOPATHIC NEPHROTIC SYNDROME(INS) IN CHILDHOOD

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Purpose: Study on relationship between long-term prognosis and renal histopathological findings of INS.
Methods: Seventy-nine patients with INS performed renal biopsy during 1958 to 1978, were followed up. Sixty-five out of 79 patients were followed up for ten or more years. Our histopathological classification is much the same as that by ISKDC. The disease status or response to treatment was recorded at 6 months, 1, 2, 5, 10 and 15 years, respectively, after the initial administration of corticosteroids.
Results: The patients with minimal chage or mesangial proliferative glomerulonephritis had a favorable outcome, even those with hematuria. No relapse was found among patients over 20 years of age. Long-term outcome in other renal histopathological groups, especially in MPGN, was poor.
Conclusions: The long-term prognosis of INS in childhood is closely related to the type and severity of renal lesions, and the histopathological findings of renal tissue provides an essential diagnostic and prognostic information for the care of individuals.

148 LONG-TERM GROWTH OF CHILDREN WITH IDIOPATHIC NEPHROTIC SYNDROME (NS)

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Body growth in NS has been studied mainly during steroid medication(ST) and rarely up to adult stature. In 156 children with NS body height(BH), growth velocity(GV) and skeletal maturation were followed from the onset of disease for >2 yrs and in 37 up to adult height. GV was transiently depressed <3rd centile(c) in 39 of 41 ST sensitive prepubertal pts treated by ST for >1 yr (mean prednisone dose 22g/m^2). After stopping ST for >1 yr catch-up growth (GV > 97th c) occured in all 23 children in this group. The growth depressing effect of ST was dose-dependent and more pronounced during puberty than before. Adult BH was reduced by >1SD from the original BH in only 1/18 ST sensitive male but in 8/11 female pts and only after a total prednisone dose >10g/m^2. Of 27 ST resistent children 20 presented with BH < 50th c at apparent onset of NS; only 5 cases (all severely hypoalbuminaemic) showed a decrease of GV to < 3rd c and of BH by >1 c curve after stopping ST and in absence of renal failure. In conclusion, growth potential of children with NS is usually conserved except for ST sensitive females treated by high ST and some pts with severe ST resistant NS. These data may have therapeutic implications mainly in males with ST dependent NS.

149 FOOD MANIPULATION AND MINIMAL CHANGE NEPHROTIC SYNDROME (MCNS).

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It has been proposed that MCNS is due to a variety of causes including hypersensitivity to inhalants, drugs, insects' sting, and/or foods. To test the latter, a study was undertaken in patients with MCNS (defined clinically and/or by biopsy) resistant to or dependent on corticosteroids or with frequent relapses (as defined by ISKDC). A response to dietary manipulation (improvement or worsening) was defined as the presence of acute and marked changes in 24 hr proteinuria (within 5 days, lasting>48 hr, increased≥4 fold or decreased to≤1/4). Most patients had simultaneous changes in weight, edema, urine output and serum albumin. Prior to the study period, all medications were discontinued; subsequently, no corticosteroids or immunesuppressors were administered until discharge from the protocol. 24 patients (age range 2-13 years) were studied over a 5 year period (1974-1979). 12 patients (50%) completed the study and had a response most likely as the result of dietary manipulation. 8 patients had no significant changes and 4 had incomplete studies. In conclusion: (1) observed changes probably were not due to spontaneous remission or relapse; (2) some patients did improve with dietary manipulation and no medications; (3) results obtained suggest need for further study to identify MCNS patients who would improve with dietary manipulation; (4) further study also is required to attempt quantitation of changes and objective conclusions.

150 PRELIMINARY OBSERVATIONS ON IMMUNOLOGIC CHANGES IN IDIOPATHIC NEPHROSIS OF CHILDHOOD (INC).

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Patients with INC had immunologic studies in 3 stages of their illness: I-heavy proteinuria pre-treatment or within 2 weeks of adrenal corticoids or cyclophosphamide; II-after 2 weeks of therapy with continued proteinuria; III-in remission off therapy. Measurements included: serum CH50 and immunoglobulins; lymphocyte transformation (LT) and E rosettes and leukocyte migration inhibition (MIT) using fetal kidney cortex as antigen (normal: 0.9 + 0.14).

DISEASE	NO.	MIT: NO. OF CASES (%) - (>0.76)	+ (0.62-0.76)	++ (<0.62)
INC				
I	22	5(23)	10(45)	7(32)
II	25	9(36)	8(32)	8(32)
III	26	16(61)	9(35)	1(4)
Normal	15	11(73)	4(27)	0

Three of 12 INC patients had low CH50 in I; serum IgG and IgA were low in I, returning to normal by III, but IgM was elevated in all three stages. LT and E rosettes were normal in 80% (all stages). Conclusions: (1) cell mediated immunity (CMI) to renal antigens was evident in INC and subsided with disease activity; (2) low IgG and IgA in I may reflect urinary loss or a defect in T lymphocytes leading to predominant IgM synthesis in response to antigen challenge; (3) whether or not INC is due to CMI or immune deficiency awaits further study.