1522 EVIDENCE OF CHRONIC RENAL DAMAGE IN PATIENTS WITH STEROID DEPENDENT MINIMAL CHANGE DISEASE (MCD) NEPHROTIC SYNDROME Sudesh P. Makker, Carlos Abramowsky, Masamichi Aikawa, Case Western Reserve Univ. School of Medicine, Rainbow Babies & Childrens Hospital, Cleveland, Ohio.

Renal biopsies of 11 patients with frequently relapsing, steroid-dependent but responsive nephrotic syndrome were evaluated prior to therapy with chlorambucil. There were 7 males and 4 females. Age at onset ranged from 2 to 10 yrs. (mean 4.5) and the duration of disease from 5 mos. to 12 yrs. (mean 3.6 yrs.). Glomerular histology was consistent with MCD and no deposits were seen on immunofluorescence and electron microscopy. However, histological changes of chronic damage were seen in 7/11 patients and included: focal tubular atrophy and thickened tubular basement membrane in 4/11, periglomerular fibrosis 2/11, interstitial fibrosis 4/11, interstitial inflammation 4/11, focal interstitial calcinosis 2/11 and thickened blood vessel wall in 3/11. All patients achieved complete, prolonged remissions with chlorambucil. Three subsequently relapsed but remained steroid responsive. Histological changes of chronicity showed no correlation to age at onset, sex, duration of disease, frequency and/or number of relapses, serum lipid levels, the selectivity of proteinuria and the in-vitro lymphoblast inhibitory factor in plasma. These results show that in some patients with steroid dependent MCD prominent histological evidence of chronic renal damage can occur. Whether these changes induce steroid dependency, are due to prolonged proteinuria, and would progress without therapy to chronic renal failure remains a possibility.

● 1523 INHIBITION OF LYMPHOCYTE BLASTOGENESIS BY SERUM B-LIPOPROTEIN FROM MINIMAL CHANGE NEPHROTIC SYNDROME (MCNS)PATIENTS. Thomas McLeod, Churchill McKinney, Gastón Zilleruelo, Douglas Sandberg, and José Strauss. Univ. of Miami Sch. of Med., Depts. of Peds. and Microb., Miami, FL.

Serum B-lipoproteins recently were reported to inhibit lymphocyte blastogenesis (Menchaca et al. Lancet 1:1085, 1980; McLeod et al. Ped. Res. 14:1012, 1980). This study further characterizes the inhibitory factors. Lymphocytes from normal donors were cultured in serum of 3 MCNS children in relapse or in normal serum (control) for 48 hours with phytohemagglutinin (PHA) and 3 H-thymidine added for the last 6 hours. Heparin-Mn-precipitate(H-Mn-p) from MCNS serum showed 36% inhibition of PHA response. Sepharose 4b chromatography showed a large peak by O.D. at 280 nm (Mol. wt. 2 million). This fraction inhibited blastogenesis in proportion to amount added. Immunoelectrophoresis (IEP) revealed a B-lipoprotein and 2 non-lipid containing proteins. All the fractions obtained by density gradient separation at 100,000 x g for 18 hrs showed inhibition and contained lipids by IEP, but the least dense (d=1000-1005) showed only one precipitin line. Normal serum showed no inhibition. H-Mn-p from normal serum showed no peak and no effect on PHA response at any concentration tested. Based upon observations that an inhibitory factor of lymphocyte blastogenesis 1) was precipitable with heparin-Mn, 2) eluted from gel filtration at high molecular weight, 3) appeared in a low density fraction, and 4) was associated with presence of B-lipoproteins, it seems that either lipoproteins or lipoprotein-bound compounds are responsible for that inhibition.

1524 SYSTEMIC DISEASE IN EPIMEMBRANOUS NEPHROPATHY (EN) OF CHILDHOOD. Melinda McVicar, Manju Chandra, and Myron Susin, Cornell Univ. Med. College, New York, N.Y., North Shore Univ. Hosp., Manhasset, N.Y., Depts of Peds and Pathology (Spon. by Joseph Kochen)

Approximately 2% of nephrotic children and 20% of nephrotic adults have EN. Recent reports have shown a high incidence of etiologically associated conditions for EN. At a renal referral center, 5 children had EN in a series of 422 renal biopsies over a period of 7 yrs. There were 3 boys and 2 girls ages 2-15 yrs at onset. The mean follow up is 6 yrs with a range of 1 to 11 yrs. The initial finding in each was massive proteinuria with nephrotic syndrome (NS) except for 1 child who had isolated hematuria at age 2 yrs associated with a family history of renal failure. This boy developed NS 3 yrs later, at which time renal biopsy showed EN, tubular fluorescence with IgG and C'3 and circulating antitubular antibodies. The two females demonstrated evidence of systemic lupus erythematosus at the time of onset of renal disease. One boy had asymptomatic hepatitis with positive Hb-s antigen and antibody (rising titer). The other boy had negative hepatitis antigen and negative anti-DNA antibody. He progressed to renal insufficiency within 2 yrs and has had a successful kidney transplant with normal GFR for 4 years. Three others had normal GFR and one had progressive renal insufficiency at the time of follow up. Our findings confirm the high incidence of primary systemic disease (3/5 in our series) in children with EN and the very low incidence of this form of renal disease in children.

● 1525 CELL FUNCTIONS IN UREMIA IMPROVED BY DIALYSIS AND AMINO ACID INFUSIONS Jack Metcoff, Paul Costiloe, James Pederson, Billy Matter, Seshachalam Dutta & Owen Rennert. University of Oklahoma Health Sciences Center & Veterans Administration Hospital, Oklahoma City, Oklahoma

Chronic uremia is often associated with impaired utilization of glucose, presumably intracellularly, since it is not dependent on insulin or insulin redeptors. Using the circulating polymophonuclear leukocyte (PMNL) as a cell model, 9 nondialyzed & 26 stable, maintenance hemodialyzed adults with chronic uremia (residual C_{cr} < 5ml/min) had significantly reduced levels of glycolytic enzyme activities pyruvate kinase (PK) & glucose -6-PO_4 dehydrogenese (G6PDH), ATP, & adenylate kinase (AK), protein (^{3}H Leu) & RNA (^{3}H-URI) synthesis, compared to 32 normal control subjects (blood donors). Following in vitro incubation of isolated PMNL in Krebs-Henseleit medium with 5mM glucose, cell levels of the glycolytic metabolites G6P, F6P, & F-1-6-P were reduced, while DHAP, 3-PGA & PEP were increased, indicating a perturbation in glycolytic flux (GF), although lactate production was not impaired. Hemodialysis improved AK activity & protein synthesis (PS), but G6PDH & ATP decreased. Lactate production by incubated PMNL fell. The postdialysis changes reverted to predialysis values within 1 week. Stable maintenance hemodialysis patients got 500ml amino acid infusions (AAI) (Aminosyn 10%) at the end of each 3x/week dialysis. After 12 infusions (1 month), predialysis ATP levels & PS reached normal levels. GF lactate production was unaffected but triose phosphate levels increased. To the extent that PMNLs reflect cell metabolism, the data is consistent with a cellular defect in glycolysis & protein synthesis in chronic uremics. Dialysis, coupled with AAI, improves cell functions.

1526 HUMORAL (H) CONTROL OF COMPENSATORY RENAL GROWTH (CRG). E.S. Moore, C. Akrami, M. Ocampo, F. Francisco, B.A. Kaiser, M. Loghman-Adham. Dept. of Pediatrics, Michael Reese Medical Center, Chicago.

In vivo study of H control of CRG was done in ewes and their twin fetal lambs (FL) at 100-140 d gestation. In 9 controls, fetus A (FA) was removed by cesarean section and fetus B (FB) was then removed either 30, 60, 90, or 180 min later. Both kidneys in each fetus were removed and total DNA/RNA content or the rate of ^{14}C-choline incorporation (^{14}C-chol) into renal phospholipids was measured. Mean ^{14}C-chol in FB was greater than that for FA ($p<.01$) at each time interval and increased with time in both FA and FB; however, the difference between FB and FA did not change with time. In experimental group I (G-I), left uninephrectomy (LUN) was performed in the ewe immediately after removal of FA (n=4). In group II (G-II), FB was removed 90 min after LUN in the ewe (n=5). In G-I, mean total DNA/RNA in both kidneys in FB was significantly higher than that for both kidneys in FA ($p<.05$). In G-II, mean rate of ^{14}C-chol in both kidneys in FB was significantly greater than that for the controls ($p<.001$). In vitro study of H factors was done in 6 adult Sprague-Dawley rats. Renal cortical slices incubated with serum from rats 60-90 min after LUN had a 26% greater ^{14}C-chol compared to controls. These data demonstrate in vivo and in vitro evidence for a transplacental humoral factor modulating renal growth in utero.

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● 1527 COAGULATION AND THE NEPHROTIC SYNDROME. Manoj Narayanan, Norma Alkjaersig, Anthony P.Fletcher, Alan M. Robson. Dept.Peds and Med., Washington University School of Medicine and St.Louis Children's Hospital, St.Louis,MO.

The coagulation and fibrinolytic systems were studied in children with nephrotic syndrome using methods including plasma fibrinogen chromatography (Kid.Int.1976,10,319). Patients with minimal change disease (MCNS) were studied sequentially i) relapse on no treatment (n=34), ii) relapse receiving steroids (n=12), iii) early remission on steroids (n=14), iv) late remission on steroids (n=17) and v) late remission, no treatment (n=10). Other nephrotics, including those with focal glomerulosclerosis (FGS) were studied too and compared to normal subjects. Irrespective of underlying cause, untreated nephrotic subjects had significantly elevated plasma levels of fibrinogen, high molecular weight fibrin-fibrinogen complexes and fibrinogen first derivatives. α_2 macroglobulin levels were elevated too whereas, factor XIII, α_1-antitrypsin, plasminogen and, surprisingly, antithrombin III levels were not different from normal. Values reverted toward normal when MCNS patients began to respond to steroid treatment (group iii) and were normal in groups iv and v. Abnormalities persisted in FGS patients who remained nephrotic. Thus coagulation changes occur prior to the administration of steroids and appear to be nonspecific being found in nephrotic syndrome irrespective of etiology. Our study provides a rationale for the recently advocated longterm use of oral anticoagulants in FGS patients (J.Ped.Neph.,1980,1,18) to prevent development of glomerulosclerosis and chronic renal failure.