1615 THE RENAL FUNCTIONAL RESPONSE TO AN ACUTE ORAL PROTEIN LOAD (OPL) IN CHILDREN. Kenneth V. Lieberman, Jill S. Stoller (Spon. by A.Y. Sweet). Mt. Sinai School of Med., Dept. of Ped., NY, NY.

GFR is variable. It is effected by dietary protein. We studied the effect on GFR of an OPL in 6 controls and in 14 patients with various nephropathies. After oral hydration, urine and blood samples were obtained for a baseline creat clearance. Subjects then received an acute OPL of 1-1.5 g/kg BW (max. - 80g) as cooked red meat. GFRs were determined at 1 hour intervals post meal. Test GFR was taken as the max. post meal GFR, typically at 2 hours.

GFRs-ml/min/1.73M^2	Baseline GFR	Test GFR
Normals (n=6, 4-17 yrs)	129±29	210±51
A.C.:reflux nephropathy	105	124
J.O.:MesProlif GN,no sclerosis	137	226
F.C.:S/P unilat nephx @ 10 mos.	89	126
D.F.:SLE with MPGN S-Cr 1.5	66	66
F.D.:CRF,S/P PUV S-Cr 2.3	38	38
L.C.:3 mos S/P AGN	87	121
L.C.:14 mos S/P AGN	101	158

The test GFR defines the filtration capacity(FC). Although normal baseline GFR is similar to that reported in normal adults (123±13), the test GFR is greater (adults - 157±13), indicating a greater renal functional reserve (RFR:test GFR-baseline GFR) in children - 81 vs 34(in adults). F.C., now 14 yrs old, has a FC less than normal children, yet still greater than that of acutely nephrectomized adults (83±4); possibly a measure of compensatory remnant kidney hypertrophy. Despite normal S-Cr and baseline GFR, A.C. has a low FC correlating with parenchymal scarring on IVP. D.F. and F.D. show that with chronic renal failure all available function is utilized at baseline with no RFR. Serial OPLs in L.C. show slow return of RFR following the insult of AGN.

As the above examples demonstrate, the determination of FC and RFR may be a useful tool in the evaluation of children with renal disease as well as helpful in the understanding of normal functional development and the pathophysiology of renal disease.

1616 B-LYMPHOCYTE DIFFERENTIATION IN NEPHROTIC SYNDROME (NS) Melinda McVicar, Manju Chandra and Savita Pahwa, Cornell University Medical College-North Shore University Hospital, Dept. Ped., Manhasset, NY

Abnormal T-lymphocyte modulation of B-lymphocyte (B-Ly) response has been suggested as a cause for decreased IgG synthesis in NS. The purpose of our study was to assess B-Ly differentiation and Ig synthesis driven by stimuli which were T-cell independent (Epstein Barr Virus-EBV), T-cell dependent (Pokeweed Mitogen-PWM) and partially T-cell dependent (S.aureus, Cowan 1 strain-SAC). Twenty determinations were performed in 13 nephrotic children (8 with minimal change NS). Immunoglobulin secreting cells (ISC) generated in the patients' peripheral blood lymphocyte cultures after exposure to EBV, PWM or SAC were quantified in reverse hemolytic plaque assays. The results, expressed as mean ± SEM number of ISC/10^6 lymphocytes, demonstrated a marked overall decrease of B-Ly differentiation in nephrotic patients compared to normal controls ($p < .005$).

	EBV	PWM	SAC
NS	30,520 ± 4,300	53,670 ± 11,050	67,890 ± 16,340
C	53,230 ± 7,210	120,670 ± 6,280	139,030 ± 11,550

Three of the children were retested after 2 mos, 3 mos and 14 mos remission. Respective ISC expressed as percent of normal were: EBV 56% 34%, 46%; PWM 31%, 12%, 104%; SAC 46%, 34%, 121%. We conclude: 1) NS is associated with diminished Ig synthesis. 2) Both T-cell independent and T-cell dependent B-Ly differentiation is markedly decreased. 3) These abnormalities may persist after remission.

†1617 PREVENTION BY DMSO OF GLOMERULAR INJURY IN NZB/WF$_1$ LUPUS MICE. L.S. Milner, J.P. de Chadarevian, P.R. Goodyer, J.S.C. Fong, and B.S. Kaplan. Departments of Nephrology and Pathology, The Montreal Children's Hospital, Montreal, Quebec, Canada.

Dimethyl sulfoxide (DMSO) was given to NZB/WF$_1$ lupus mice from 10 weeks of age to see if proteinuria could be prevented in this model of glomerular injury.

Twenty mice were randomized into saline (0.1 ml/day) and DMSO treatment groups (DMSO 4 mg/gm/day). Significant differences in urine protein excretion between controls and treated groups were evident at 5 months (DMSO: 5.5 ± 0.46 mg/24 hrs; Controls: 7.35 ± 0.59 mg/24 hrs; $p < 0.05$) and at 6.5 months of age (DMSO: 6.75 ± 0.73 mg/24 hrs; Controls: 15 ± 2.15 mg/24 hrs; $p < 0.01$). By 7 and 7.5 months, the protein excretion was not significantly different (DMSO: 18 ± 8.3 mg/24 hrs; Controls: 41 ± 8.7 mg/24 hrs; $p > 0.05$); 7.5 months: DMSO: 20 ± 7.4 mg/24 hrs; Controls: 29 ± 5.7 mg/24 hrs; $p > 0.05$. However, the urine protein:creatinine ratio was significantly reduced in DMSO treated mice compared to controls at 6.5 months (DMSO: 13.4 ± 1.32; Controls: 24.4 ± 4.2; $p < 0.05$), at 7 months (DMSO: 46.7 ± 23; Controls: 101 ± 28; $p < 0.05$), and at 7.5 months of age (DMSO: 37 ± 13; Controls: 88 ± 31; $p < 0.05$). The mean serum creatinine values were significantly lower at 7.5 months of age in DMSO treated mice (0.41 ± 0.08 mg/dl) compared to controls (0.91 ± 0.56 mg/dl; $p < 0.05$). By 7.5 months of age, 5/6 treated mice had relatively normal renal histology on light microscopy, while 6/8 untreated had focal proliferative glomerulonephritis, crescents and glomerular obsolescence ($p < 0.02$).

These findings demonstrate that DMSO has a protective effect on the progression of glomerular injury in this model.

●1618 CELLULAR MALNUTRITION IN UREMIA. Jack Metcoff, James Pederson, Francisco Llach, Jim Gable. University of Oklahoma, Health Sciences Center and Veterans Administration Hospital, Oklahoma City, OK.

Some of the cellular abnormalities of severe protein-calorie malnutrition in children (PCM), e.g., reduced energy-related enzyme activities, energy and protein synthesis levels and intracellular amino acid deficits, are also thought to occur in chronic uremics. Improvement of these abnormal cell bioactivities, characterizing cellular malnutrition, should stabilize and possibly retard progressive cellular deterioration in uremics. We have used the circulating granulocyte as a cell model to study energy-related enzyme activities (pyruvate kinase (PK), phosphofructokinase (PFK), adenylate kinase (AK), energy charge (Ech=ATP+0.5ADP/(ATP +ADP+AMP)), protein synthesis (^{3}H-leucine incorp.) and amino acid pools in 52 adult uremics (9 not dialyzed (ND), 40 hemodialyzed (HD) and 13 peritoneally dialyzed (CAPD)) and 61 normal control (C) subjects. Gross clinical estimators of chronic malnutrition (Wt/Ht ratio, skinfolds, arm muscle area, plasma albumin and total lymphocyte count) were within normal limits for the dialyzed uremics. In the ND uremics, all clinical and cell measures were abnormal. In the HD uremics, cell PK, AK, ATP, Ech and PS were significantly ($p < .05$) better than ND but less than C. A significant reduction in branched-chain amino acids (BCAA=valine, leucine, isoleucine) and methionine (MET) were noted in both ND and HD patients. In the CAPD patients, after 18 +9 (SD) months of dialysis PK, PS, BCAAs and MET levels were normalized. Ech was 90% of normal and >HD, but ATP and AK were not improved. We conclude that cellular malnutrition occurs in apparently stabilized adult uremics without clinical signs of malnutrition. CAPD seems to improve many cell bioactivities, and therefore, cellular malnutrition in uremics.

1619 EFFECT OF AGE AND SEX ON THE RESPONSE OF GLOMERULI TO ANTI-GLOMERULAR BASEMENT MEMBRANE ANTIBODY IN RATS. H. Miyazawa, A. Yared, D.J. Salant and I. Ichikawa. Harvard Med. Sch., Children's Hosp., Dept. of Peds. & Boston U., Boston City Hosp., Dept. of Med., Boston.

The incidence and clinical course of immunologically mediated renal injuries are known to vary with age and sex. We studied the effect of these two factors on the in vivo binding of anti-glomerular basement membrane antibody (aGBM) in 6 week old (Y, n=18 rats) and 10 month old (A, n=15 rats) Munich-Wistar rats, both males (M, n=18 rats) and females (F, n=15 rats). Following intravenous administration of ^{125}I-labelled aGBM in a dose of 3-20 µg/g BW, the degree of aGBM binding by glomeruli was examined. The amount of aGBM bound per single glomerulus (aGBM/gl) was closely correlated with plasma aGBM level in YM (r=0.95), AM (r=0.85) and AF (r=0.96). At a comparable plasma aGBM level, aGBM/gl was significantly lower in Y than A ($P < 0.001$ in both M and F). This difference persisted even when aGBM/gl was corrected by an index of GBM surface area ($P < 0.001$ in both M and F). Amount of aGBM bound per gram of glomerular protein, however, did not differ significantly between Y and A, due to wide variability in glomerular protein content. Functional response to aGBM binding, as assessed by percent reduction in whole kidney GFR at comparable plasma aGBM level, tended to be more pronounced in Y than A. Results from M and F were comparable for these parameters. These data indicate that, of the two epidemiological factors tested, age, but not sex, has an important influence on the glomerular response to this type of immunological insult.

●1620 EARLY EFFECTS OF STREPTOZOTOCIN DIABETES (SD) ON RAT GLOMERULAR FILTRATION RATE (GFR) AND PROSTAGLANDIN E_2 SYNTHESIS (PGE_2). Donald I. Moel, Richard A. Colm, Robert L. Safirstein (spon. by L. Pachman) Northwestern University Medical School, Children's Mem. Hosp., Department of Pediatrics, Chicago, Illinois.

In SD the development of moderate hyperglycemia is closely associated with increases in GFR that may be mediated by altered production of or reactivity to vasoactive substances. In the present studies renal cortical and medullary PGE_2 synthesis and whole kidney GFR (C_{IN}) were examined 8 days after induction of SD (45 mg/kg i.v.) in young rats (139±1.7 g) treated with either daily aspirin (ASA) 300 mg/kg/day or ASA vehicle. PGE_2 synthesis from ^{14}C-arachidonic acid was determined in cortical and medullary microsomes by thin layer chromatography. Mean values (± 1SE) for body weight (BW), blood pressure (bp), plasma glucose (P_{glu}, mg/dl), C_{IN} (ml/min/g KW), and PGE_2 synthesis (ng/mg/30 min) are shown below: *$p<0.05$, compared to group above; †$p<0.05$, compared to control (C).

	n	BW,g	bp,mmHg	P_{glu}	C_{IN}	PGE_2 Synthesis cortex	PGE_2 Synthesis medulla
C	5	176±4	114±5	151± 3	.85±.03	32.9± 3.0	206± 8.1
C/ASA	8	174±5	114±4	137± 9	.78±.04	20.1± 2.8†	123± 9.2†
SD	6	161±3†	122±6	373±19†	1.23±.10†	52.8± 4.7†	326±18.3†
SD/ASA	5	160±5†	130±4†	328±22†	.92±.08*	31.6±13.8*	177±17.9*

Weight gain in SD and SD/ASA rats was less than in C and C/ASA. After 8 days of SD PGE_2 synthesis and GFR were increased compared to control values. Eight days of PG inhibition reduced PGE_2 synthesis by 40% and GFR by 25% in SD/ASA compared to SD rats. ASA given to control rats reduced PGE_2 synthesis but had no effect on GFR. These data suggest that hyperfiltration observed in moderately hyperglycemic SD rats may be mediated by elevated rates of prostaglandin synthesis. Whether chronic alterations in prostaglandin synthesis influence the onset and progression of glomerular histologic changes remain unknown.