●1621 APICAL MEMBRANE LIPID FLUIDITY (LF) INFLUENCES PHOSPHATE (Pi) TRANSPORT IN FETAL KIDNEY.

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Plasma Pi in early life is high and renal Pi excretion low relative to that in adults. Renal tubular Pi transport kinetics and membrane LF was investigated in apical membrane vesicles (BBMV) in 6 fetal (F) lambs and pregnant ewes (E). Results:

	KmPi[1]	VmaxPi[2]	DPH[3]	2-AS[3]	Protein/Lipid[4]
F	950	1738	0.276	0.126	1.05
	±112	±126	±.006	±.002	±0.06
E	942	1004[a]	.285[b]	.134[b]	2.26[b]
	±151	±172	±.003	±.002	±0.31

[1]uMol; [2]pMol/mg BBMV prot/10s; [3]fluorophors 1, 6-diphenyl 1,3,5 hexatriene and DL-2(9-anthroyl) stearic acid fluorescence; [4]w/w [a]p<.025;[b] p<.05

KmPi was similar in BBMV in the F and E but Vmax Pi was greater in F. Alkaline phosphatase enrichment, lipid saturation index and [cholesterol/phospholipid], [sphingomyelin/phosphatidylcholine] ratios were not different, however, protein/lipid ratios was higher in E. The results demonstrate greater renal tubular Pi transport capacity in F compared to E and increased VmaxPi in F is due, in part, to greater membrane LF. Relative increased VmaxPi in F may be due to difference in carrier function rather than to an increase in carrier concentration. This may involve more rapid cycling of Pi carrier from lumen to cytoplasmic surfaces in F.

1622 K+ STIMULATED PHOSPHATE (Pi) CO-TRANSPORT IN FETAL LAMB (FL) KIDNEY.

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In the adult kidney, carrier mediated Pi co-transport is highly Na+ specific. Studies in our laboratory showed that Pi uptake (PiU) in renal brush border membrane vesicles (BBMV) from FL kidneys is also stimulated by Na+. In contrast to the adult, we report here that carrier mediated PiU in FL renal BBMV is also energized by a K+ gradient ($[K+]_o > [K]_i$). BBMV from 5 FL kidneys were prepared by $CaCl_2$ precipitation and verified by marker enzyme assays, electron microscopy, and PiU into osmoticaly active vesicles. Peak 60s PiU with a 100mM Na+ and K+ gradient was 1968±65 and 1010±133 pMol/mg BBMV protein, respectively (p<.01). PiU for each was greater than diffusion PiU (p<.001 each). The effect of trans-stimulation was studied by preloading BBMV with 5mM Pi. Initial 12s PiU in preloaded BBMV was 1007±181 pMol/mg BBMV protein and was 4-fold higher than PiU in non-loaded BBMV (p<.001). The effect of extravesicular (O) pH was studied by measuring initial 15s PiU in BBMV with constant intravesicular pH 7.4 and varying O pH from 6.0, 7.4 and 8.0. PiU was 700±64, 1983±230 and 411±10 pMol/mg BBMV protein for OpH 6.0, 7.4 and 8.0 respectively. PiU at $pH_o = pH_i$ was higher than that for OpH 6.0 and OpH 8.0 (p<.01; p<.001). The results demonstrate K+-Pi symport in FL kidney. The co-transport system may represent shared affinity by K+ with Na+ for the cation site on the carrier or a different carrier system.

●1623 RENAL ALPHA (α) AND BETA (β) ADRENERGIC RESPONSE IN FETAL AND ADULT SHEEP: DEMONSTRATION OF BETA-2 (β_2) VASODILATION IN FETUSES.

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Effects of intrarenal boluses of epinephrine (E) (0.00625 to 0.2 ug/kg of B.W.) on renal blood flow (RBF) were studied in chronically catheterized fetal (F) lambs (125-137 days; term 145 days) and adult (A) sheep using a doppler flowmeter. Effects of E alone and during α, α_1, and β_2 adrenergic blockade were studied. Blood pressure was unchanged during E infusion. The E dose that reduced RBF (%ΔRBF) by 50% (ED_{50}) was 0.0014 ug/kg/ml RBF in F and 0.0001 ug/kg/ml RBF in A; this response was blocked by the α_1 antagonist prazosin. Following α blockade with phentolamine, E produced vasodilation (%Δ RBF-α) in F and A which was blocked by the β_2 antagonist butoxamine. When E was given during α blockade at a dose equal to ED_{50} for vasoconstriction, E produced a 33% rise in RBF in F and 10% in A (p<0.05).

Dose	Fetus (n=6)			Adult (n=4)		
ug/kg	ug/kg/RBF	%ΔRBF	%ΔRBF-α	ug/kg/RBF	%ΔRBF	%ΔRBF-α
0.0125	.00054	-23±6	22±4	.000029	-26±12	---
0.025	.0011	-34±3	28±6	.000058	-36±18	7±2
0.05	.0022	-76±9	42±4	.00012	-49±18	10±2
0.1	.0044	-75±14	50±5	.00023	-54±8	16±2
0.2	.0088	---	55±10	.00047	---	23±4

Present results demonstrate that: 1) the E dose required for vasoconstriction, which is α_1 mediated, is 10 times greater in F than A, 2) the lower α receptor response in F may be secondary to the greater β_2 receptor activity than in A.

1624 PAUCITY OF MINIMAL CHANGE (MC) LESION IN YOUNG CHILDREN WITH EARLY FREQUENTLY RELAPSING STEROID SENSITIVE (FRSS) NEPHROTIC SYNDROME (NS).

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The morphological lesion in young children with early FRSSNS is presumed to be MC; however, there are no prospective studies that validate this assertion. From 1980-84, we performed a percutaneous renal biopsy on all children with the NS, ages 2-8 yrs, as soon as they developed a FRSS course. Relapse is defined as recurrance of NS within 2 months of an 8 week prednisone course.

15 children (8 male, 7 female) were studied, mean age at time of biopsy 4.8 yrs (2.7-8 yrs). An average of 4 relapses per patient occurred during the initial 13 months - the mean interval from diagnosis of NS to renal biopsy. No children were azotemic, 3/15 had hematuria and 0/15 hypertension.

Only 4/15 patients exhibited the MC lesion. In 73% (11/15) of patients, the renal histology was other than MC. 2 patients had diffuse mesangial hypercellularity, 7 had mesangial IgM nephropathy and 2 patients had focal segmental glomerulosclerosis. No clinical feature discriminated between patients with MC and those with severe lesions. Of the 11 children with non-MC histology, 1 patient requires dialysis, 4 have persistent proteinuria despite cyclophosphamide (CY), 5 are in prolonged remission following CY therapy and 1 is lost to follow up. Our study concludes that as in the adult, a variety of morphological lesions are seen in young children with FRSSNS and that the occurrence of frequent relapses even in children as young as 3 yrs may herald the presence of a more ominous histological lesion.

●1625 RENAL NEUROADRENERGIC TRANSMISSION DURING FETAL LIFE.

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The renal vasoconstrictor response to graded (0.2 to 3.0 Hz, 20V, 1 msec) direct electrical renal nerve stimulation (RNS) was studied in 9 chronically catheterized fetal (F) lambs (130-142 days gestation; term 145 days) and 3 adult (A) sheep. Changes in renal blood flow (RBF) were monitored using a doppler flowmeter. During RNS, RBF (r=-0.98) decreased and renal vascular resistance (RVR) (r=0.98) increased in a dose-response relation in F and A. Following administration of phentolamine, a rise in RBF (+57% at 1.0 Hz) and a decrease in RVR (-32% at 1 Hz) were observed in F; these changes were not completely blocked with propranolol. At low frequency (0.4 Hz) of RNS, % changes in RBF and RVR were significantly higher in F than in A.

Frequency	% change in RBF		% change in RVR	
(Hz)	F	A	F	A
0.2	-6	-2*	6	2*
0.4	-11	-2*	10	2*
0.8	-15	-15	34	28
1.0	-21	-27	43	55
3.0	-46	-49	152	150

(*for p<0.05 when F compared to A) In summary these results demonstrate that during fetal life 1) renal hemodynamics seems to be more sensitive to low frequency RNS than in A; 2) renal vasoconstriction following RNS is dependent on α adrenoceptors; and 3) renal vasodilation produced by RNS during α-blockade is not fully dependent on activation of β-adrenoceptors.

1626 ANALYSIS OF FOCAL SEGMENTAL GLOMERULOSCLEROSIS IN CHILDREN-IMPORTANCE OF CLINICAL PRESENTATION

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Focal segmental glomerulosclerosis (FSGS) may present with nephrotic syndrome (NS) or asymptomatic proteinuria (AP). We examined whether 16 children with FSGS and NS (Group A) had a worse outcome than 10 children with FSGS and AP (Group B). Initial clinical comparisons revealed: age (A-9.0±0.4 vs B-10.3 ± 1.4 yrs),U protein excretion (A-267±51.6 vs B-123.1±30.7 $mg/m^2/hr$, P-0.05), U protein/U creatinine ratio (A-35.5±14.03 vs B-5.13±1.46 mg/mg,P-0.001), total serum protein (A-4.39±0.21 vs B-5.79±0.43gm/dl,P-0.01), serum albumin(A-1.85±0.19 vs B-3.34±0.3gm/dl,P-0.001) and serum cholesterol (A-390.7±24.6 vs B-267±36.5mg/dl,P-0.02). Diagnostic renal biopsies revealed more prominent mesangial proliferation in Group A, P-0.016, more tubular atrophy in Group B, P-0.007, and no difference in percent sclerotic glomeruli (A-21.8% vs B-24.2%). Patients were followed for A-39.6±13 vs B-37.6±6.0mos. 7 of 15 Group A patients have serum creatinine values (Scr)>1SD from mean for age and 3 of 15 have end stage renal disease. Only 2 of 10 Group B patients have (Scr)>1SD from mean for age and none have end stage renal disease.Scr in Group A were higher, 2.01±0.92mg/dl, than Group B, 0.71±0.08mg/dl, but were not statistically different, P<0.2. Nephrotic syndrome in FSGS appears to be a poor prognostic sign in children. These data support the concept that hyperfiltration of protein adversely affects renal function.