

brane, swelling of endothelial cytoplasm and deposition of granular and fibrillar electron-dense material with periodicity of fibrin between the basement membrane and endothelium and in the mesangium, most pronounced during the early course of disease. Tissue from 8 patients was studied by immunofluorescent technics after 6 to 42 days of illness. Fluorescein-conjugated rabbit anti-human IgG, IgM, IgA and B1A-1C sera produced no staining; antifibrinogen serum produced intense smooth staining along capillary walls and diffuse staining in cytoplasm of endothelial and mesangial cells. The thrombocytopenia responded to heparinization in 6 patients; in 3, heparinization was discontinued prematurely—in each, platelet counts fell and rose again coincident with cessation and reinstitution of heparin therapy.

These findings support the hypothesis that accelerated intravascular coagulation occurs in the hemolytic uremic syndrome. (SPR)

- 46 *Renal Metabolism with Renal Disease in Man.* JACK METCOFF, M. ORT\*, K. SCHARER\*, GABRIEL RUIZ\*, L. BRAUDO\*, T. YOSHIDA\* and J. LEWY\*, Depts. Pediatrics, Michael Reese Hosp. & Chicago Med. Sch., Chicago, Ill.

The proximal tubular uptake and utilization of  $\alpha$ -ketoglutarate ( $\alpha$ KG) has been linked to cortical blood flow,  $H^+$  secretion and anaerobic  $CO_2$  production. Oxidation of  $\alpha$ KG at the substrate level is the first step in energy-dependent gluconeogenesis by renal cortex. Thus, renal  $\alpha$ KG dissimilation and renal glucose production (RGP), might reflect locus and extent of altered cell function in the kidney. To explore this, Na  $\alpha$ KG was infused, with parental consent, in 10 children with renal disease (9 acute glomerulonephritis [AGN], 1 nephrotic) and 12 controls under standard loading, inulin and PAH clearance conditions. Renal extractions of PAH (EPAH) and  $\alpha$ KG as well as RGP were determined from frequent concurrent samples of renal vein and aortic blood in 3 patients with AGN, the nephrotic, and 6 controls, with 'normal' kidneys but congenital heart defects. The studies were repeated in the 3 AGN patients during healing. Renal uptake and utilization of  $\alpha$ KG and RGP were calculated for body size and estimated kidney weight. *In vitro* RGP by human kidney slices obtained at operation from 2 intact and 2 diseased kidneys also was assayed for comparison.

In AGN, significantly reduced renal uptake and utilization of the  $\alpha$ KG load with persistently high  $H^+$  excretion and decreased reabsorption of Na accompanied the low  $C_{IN}$ , EPAH and CPAH (CPAH/EPAH). All patterns approximated controls with healing. RGP usually was impaired, especially in the nephrotic child. RGP with  $\alpha$ KG *in vivo* was similar to *in vitro* values for 'normal' human kidney slices with glycerol, fructose, pyruvate,  $\alpha$ KG, succinate or malate as substrates. These results imply increased 'non-cortical' renal blood flow and impaired proximal tubule metabolism referable to  $\alpha$ KG in the kidney diseases studied. (APS)

- 47 *Renal Hypertrophy with Diminished Function in Acidotic Rats.* DONALD E. POTTER\*, TADASU SAKAI\* and MALCOLM A. HOLLIDAY. Univ. of Calif. Sch. of Med., San Francisco, Cal.

Renal hypertrophy is a known response to metabolic acidosis produced by ammonium chloride loading in rats (LOTSPEICH: Amer. J. Physiol. [1965]). The hypertrophic response and functional correlates in this model were studied and compared with those following uni-

nephrectomy in 4 groups of rats: 1. controls; 2.  $NH_4Cl$  loaded; 3. uninephrectomized controls; 4. uninephrectomized  $NH_4Cl$  loaded. Glomerular filtration rates (GFR), glucose tubular maxima (TmG), wet kidney weights (WKW), and kidney DNA were determined.

Groups	$WKW \times 100$	GFR	TmG	DNA
	BW	WKW	WKW	Kidney
$H_2O$	0.359	1.11	3.36	5.56
$NH_4Cl$	0.428	0.88	2.56	5.92
$H_2O$ -Neph	0.513	1.26	3.04	7.01
$NH_4Cl$ -Neph	0.673	0.75	2.23	7.12

Hypertrophy occurred with  $NH_4Cl$  loading and was additive to that following uninephrectomy. Elevation of DNA levels indicated hyperplasia as well as hypertrophy in both models. As a function of kidney weight however, both GFR and TmG decreased in the  $NH_4Cl$  fed animals. Microscopic examination revealed no architectural difference in the 2 types of hypertrophy. The data indicate that stimulated growth of the kidney is not necessarily associated with an increase in function as is normal growth. These data together with the data from other models of kidney growth provide a basis for searching for the structural or enzymatic determinant of kidney function as measured by sodium reabsorption and maximal glucose reabsorption. (SPR)

- 48 *Urinary Acid Excretion in the Intact Lamb Fetus.* FRED G. SMITH, JR., and RICHARD BASHORE\*, Univ. of California, Los Angeles, Cal.

The role of the fetal kidney in regulating acid-base elimination in the intact fetus has not been elucidated. This study was designed to investigate the response of the intact fetus to acute acid loading with hydrochloric acid. The lamb fetus is delivered by Caesarean section onto a warm table adjacent to the mother. The umbilical cord was protected and the fetal pulse rate, blood pressure and body temperature were monitored continuously. The fetal external jugular, carotid artery and both ureters were cannulated. The glomerular filtration rates, urine ammonia, titratable acidity (TA), phosphate, chloride and blood pH,  $pCO_2$  and chloride were measured during two 30 minute control periods. 0.3 molar hydrochloric acid was then infused into the fetus at a rate to maintain the fetal blood pH between 6.9 and 7.1. The results during the control (Basal) and test periods are shown below for 7 fetal preparations:

	Mean basal values $\mu eq/min$	Mean maximum values $\mu eq/min$
TA	1.10	3.81
$PO_4$	0.68	2.64
$NH_4$	0.31	1.70

The mean basal urine pH was 6.91 and the minimum was 5.97 following acid loading. These studies demonstrate that the fetal kidney is able to increase hydrogen ion excretion significantly in response to acid loading. (SPR)

- 49 *A Transport System in Mammalian Kidney with Preference For  $\beta$ -Amino Compounds.* HY GOLDMAN\* and CHALRES SCRIVER, McGill Univ.-Montreal Children's Hospital Research Institute, Montreal, Canada.

An absorptive transport system in human kidney common to the naturally occurring  $\beta$ -amino com-