sions. Endothelial proliferation and leukocytic infiltration was observed in percutaneous renal biopsies. As regularly observed in our previous studies of sporadic acute glomerulonephritis, approximately $\frac{1}{4}$ of these patients had nodular deposits of IgG and beta γ C globulin along the glomerular basement membranes by immunohistochemical analysis. 90 % of remaining patients showed interrupted linear deposition of beta γ C along glomerular membranes without IgG. Electron microscopic study revealed minimal development of the characteristic discrete electron dense deposits on the epithelial side of the glomerular basement membrane. Focal membrane thickening and basement membrane-like material among mesangial cells was observed. This study, sampling an entire spectrum of acute poststreptococcal glomerulonephritis, suggests that nephritogenic strains of streptococci may exert a toxic action rendering the glomerulus susceptible to injury by antigen-antibody complexes. (Supported by American Heart Association, USPHS, and Minn. Heart) (SPR)

- 42 *Focal Nephritis, a Form of Normocomplementemic Persistent Glomerulonephritis Responsive to Steroid.* C.D. WEST, A.J. McADAMS* and J.D. NORTHWAY*, Children's Hospital, University of Cincinnati, Cincinnati, Ohio

Since advent of renal biopsy, the definition of a type of persistent nephritis characterized by focal and segmental lesions has been possible. Heptinstall has recognized this lesion in adults in the absence of lupus, bacterial endocarditis, anaphylactoid purpura or periarthritis. We have observed 11 cases of focal nephritis in children not attributable to any of the above entities. All the patients have been normocomplementemic and have had a course characterized by a mild-to-severe nephrotic syndrome, usually with signs of nephritis. The data suggest that signs and symptoms develop rapidly after onset, without a long, silent, subclinical stage. In 9 of the cases, onset was preceded by an upper respiratory infection, but ASO titers were usually not elevated. The entity is important to recognize because of the beneficial effects of steroid therapy. In 3 of our patients not treated with steroid initially, the nephritic-nephrotic picture subsided, but all signs and symptoms recurred several months later, usually following a respiratory infection. After treatment in these 3 patients as well as in 7 of 8 treated shortly after onset, no recurrences have been noted in follow-ups ranging from 9 months to 4 years. The 11th patient never responded to therapy and eventually succumbed with a severe nephrotic syndrome. In the remaining 10 patients, signs of the nephrotic syndrome have slowly disappeared with therapy, and several show no evidence of renal disease except for focal glomerular scarring. The similar pathological picture, clinical course and therapeutic results in the 10 responsive patients suggest that focal nephritis in children is a disease entity. Its diagnosis rests on typical histopathological changes by renal biopsy in a normocomplementemic patient. (APS)

- 43 *Evaluation of Combined Therapy (Steroids and Cyclophosphamide) in the Steroid Resistant (SR) and Steroid Dependent (SD) Nephrotic Syndrome.* LUTHER B. TRAVIS* and WARREN F. DODGE, University of Texas Medical Branch, Galveston, Tex.

Over the past 5 years there has been a revival of interest in the combined use of steroids and immunosuppressive agents in the child with the idiopathic

nephrotic syndrome (INS) who is either SR or SD. The combined administration of steroids and cyclophosphamide is usually effective in inducing an initial response in the majority. Little information is available on the course of these patients after cyclophosphamide is discontinued.

Of 169 patients with INS, approximately 40 % were found to be either SR or SD. Thirty-five of these were evaluated and subjected to combined therapy. Eleven were SR and 24 were SD. Seventeen of the 35 are classified as having 'lipid' nephrosis, while 10 had proliferative and 8, membranous glomerulonephritis. Eighteen SD patients had a complete initial response while 6 SR patients exhibited a similar response. An additional 3 SR patients had a partial response. Approximately 50 % of the patients who initially had a complete response and who have been followed for at least 6 months after discontinuing cyclophosphamide, have, however, had further exacerbations and their ultimate course does not appear to have been materially altered.

This study would suggest that 1. SR and SD are not infrequent; 2. clinical and pathologic studies may define groups of patients who are either steroid sensitive, SR or SD, but may be of little help with individual patients; 3. combined therapy will usually induce an initial complete response; 4. approximately one-half of patients so treated will ultimately revert to some degree of unresponsiveness. (SPR)

- 44 *Experimental Studies on Pathogenesis of Nephrotic Hyperlipemia and Dysproteinemia.* WALTER HEYMANN, STEPHEN CHENTOW* and JOHN L. ZITEL*, Western Reserve University, Department of Pediatrics, Cleveland, Ohio.

Drainage of the abdominal chyleduct was carried out for 1-18 days in 11 rats, a continuous i.v. drip preventing dehydration. Marked hypoalbuminemia (with values < 1.0 gm %) developed in all and cholesterol and total lipid values in sera remained within normal limits. At the same time electrophoretic patterns obtained on sera of these rats showed the appearance of proteins with the mobility of α_2 globulins that were not obtained before. Marked decreases of γ globulins were also noted. In as much as these observations were made on animals without kidney disease, it would seem possible that the increase of α_2 globulins observed regularly in the nephrotic syndrome do not reflect any etiological or pathogenic manifestation of the disease process. These observations also do not support the contention that the nephrotic hyperlipemia is due to hypoalbuminemia. Sera of 5 children with non-nephrotic hypoalbuminemias also revealed normal cholesterol and total lipid values with increased α_2 globulins. (APS)

- 45 *Accelerated Intravascular Coagulation in the Hemolytic Uremic Syndrome.* CAROLYN F. PIEL*, KENNETH HADLEY* and RODERIC H. PHIBBS*, Univ. California-S.F. Medical Center, San Francisco, Cal. (introduced by M.M. Grumbach).

Renal tissue was obtained by percutaneous biopsy in 11 patients with hemolytic uremic syndrome from 9 to 365 days after onset of disease; by autopsy in 5 after 6 to 58 days of illness. By light microscopy, the early histologic lesion (up to 30 days) was characterized by glomerular capillary ectasia and intracapillary eosinophilic depositions (fibrin-like material). Regardless of duration or severity, electron microscopy revealed irregular swelling and fragmentation of basement mem-

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 α -ketoglutarate (α KG) has been linked to cortical blood flow, H^+ secretion and anaerobic CO_2 production. Oxidation of α KG at the substrate level is the first step in energy-dependent gluconeogenesis by renal cortex. Thus, renal α KG dissimilation and renal glucose production (RGP), might reflect locus and extent of altered cell function in the kidney. To explore this, Na α 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 α 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 α 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 α 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 α KG *in vivo* was similar to *in vitro* values for 'normal' human kidney slices with glycerol, fructose, pyruvate, α KG, succinate or malate as substrates. These results imply increased 'non-cortical' renal blood flow and impaired proximal tubule metabolism referable to α 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 β -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 β -amino com-