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 αketoglutarate (αKG) has been linked to cortical blood flow, H+ secretion and anaerobic CO_2 production. Oxidation of αKG at the substrate level is the first step in energy-dependent gluconeogenesis by renal cortex. Thus, renal αKG dissimilation and renal glucose production (RGP), might reflect locus and extent of altered cell function in the kidney. To explore this, Na αKG was infused, with parental consent, in 10 children with renal disease (9 acute glomerulonephritis [AGN], I nephrotic) and 12 controls under standard loading, inulin and PAH clearance conditions. Renal extractions of PAH (EPAH) and αKG 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 αKG 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 αKG load with persistently high H+ excretion and decreased reabsorption of Na accompanied the low CIN, EPAH and CPAH (CPAH/EPAH). All patterns approximated controls with healing. RGP usually was impaired, especially in the nephrotic child. RGP with αKG *in vivo* was similar to *in vitro* values for 'normal' human kidney slices with glycerol, fructose, pyruvate, αKG, succinate or malate as substrates. These results imply increased 'non-cortical' renal blood flow and impaired proximal tubule metabolism referrable to αKG 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 uninephrectomy 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 × 100 / BW	GFR / WKW	TmG / WKW	DNA / 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 μeq/min	Mean maximum values μeq/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 CHARLES 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-

pounds, β-alanine, β-aminoisobutyric acid and taurine has been proposed on the basis of evidence found in the aminoacidopathy, hyper-β-alaninemia (New. Engl. J. Med. *274:* 635 [1966]). The proposal has been investigated further in the rat. Absorptive renal transport (lumen to cell) was selected for by using probenicid (200 mg/kg) to block tubular secretion of D-(-)βAIB. By means of intraperitoneal injection, the plasma concentration of β-amino compounds was raised; urinary excretion of amino acids was analyzed by chromatographic methods. Mutual competitive inhibition of absorptive transport was observed between βala, βAIB and Tau. βala had the greatest inhibitory effect, and Tau the least. β-amino compounds had no significant effect on the excretion of α-amino acids when the latter were present at either high or normal plasma concentrations; conversely, α-amino acids did not inhibit β-amino absorption. A common transport system for β-amino compounds operative at high concentrations, and whose order of substrate affinity is βala > L-βAIB> Tau, is thus demonstrable in mammalian kidney. (Supported by M.R.C. Grant, MA-1894, and N.I.H. Grant, AM-05117). (SPR)

50 *Bilirubin Nephropathy in the Gunn Rat.* GERARD B. ODELL, JURGEN C. NATZSCHKA* and G.N. BRUCE STOREY*, Dept. Pediatrics, Johns Hopkins Univ. Sch. Med., Baltimore, Md.

Homozygous, jaundiced, Gunn rats (jj) were compared with heterozygous control rats (jJ) for their capacity to concentrate their urine after water deprivation. Animals of comparable weights (5 jj and 6 jJ) were pair fed 7 days and then subjected to a 36-hour fast and thirst. Urine was collected for the last 6 hours, and the mean flow rates were 50 and 149 μl/100 g/h in the jJ and jj animals, respectively. The corresponding urine milli-osmolalities were 1909 and 815. Total solute loads excreted were comparable but the jj animals lost 3 times as much Na in the urine, and had a 30 % greater loss of body weight. Glomerular filtration rates were similar in hydrated jj and jJ animals. The concentrations of Na, K, Cl, NH_3 and urea in the renal cortex were similar in the two groups of animals. The concentrations of K and NH_3 of the medulla were also similar, but the concentrations of Na, Cl and urea in the medulla of the jj animals were only 1/3 that found in the jJ animals.

	Medullary analyses in mM/l tissue H_2O		
	Na	Cl	Urea
jj	103± 5.4 (S.E.)	91± 6.6	117±16.5
jJ	278±31.0	256±30.0	322±18.0

Regional analysis of the kidney for bilirubin demonstrated a 100 fold greater concentration in the renal medulla than in the corresponding cortex in jj animals. These results suggest that bilirubin may interfere with sodium and urea reabsorption in the medullary portions of the kidney and therby prevents the formation of hypertonic urine during thirsting comparable to normal rats. (SPR)

51 *Factor XIII—Report of a Family with Factor XIII Deficiency and the Concentrations in normal Infants.* JOHN D. BOUHASIN and CIGDEM ALTAY*, St. Louis Univ. Sch. of Med. and Cardinal Glennon Mem. Hosp., St. Louis, Mo. (introduced by Arthur E. McElfresh).

Since 1960 when DUCKERT *et al.*, observed a familial bleeding disorder due to a deficiency of Factor XIII, 21 cases, involving 8 families have been reported.

We have diagnosed Factor XIII deficiency in a 6-year-old boy with mild bleeding manifestations and studied the concentration of Factor XIII in his family and in normal infants.

An assay technique has been devised utilizing the patient's plasma as deficient substrate, with normal pooled plasma as the standard. Dilutions of plasma from 1:300 to 1:1000 yield a straight line with a steep slope when plotted on log-log paper against clot liquifaction time in minutes; it is reproducible. In vivo survival studies after transfusing the patient show a half-life of 5–7 days in agreement with other reports. Factor XIII was assayed in 50 infants and children from birth to 20 months of age as follows: newborn (10)-average 63 %, range 50–76 %; 0–5 months (10)-average 115 %, range 100–160 %; 6–9 months (10)-average 90 %, range 80–110 %; 10–15 months (10)-average 90 %, range 72–118 %; and 16–20 months (10)-average 94 %, range 70–120 %. Our adult range was 90 to 136 %. After the newborn period, Factor XIII is present in normal adult concentrations. Our data suggest a more rapid rise to normal and no evidence of the fall at ages 6–9 months as reported by KÜNZER (Ann. Pediat. *204:* 232 [1965]).

Family Factor XIII levels were: father 75 %, mother 48 %, 2 sisters 57 % and 48 % and brother 42 %. This tends to confirm the autosomal recessive inheritance of Factor XIII deficiency. (SPR)

52 *Effect of Diabetic Plasma in von Willebrand's Disease.* WM. E. HATHAWAY and H. GLEN HOSTETTER*, Univ. Colo. Med. Ctr., Denver, Colo.

Although in vivo correction of antihemophilic factor (AHF) levels is easily achieved in von Willebrand's disease (vWd), correction of the bleeding time (BT) defect is difficult by usual transfusion therapy. In an effort to find more effective treatment for four children with severe vWd (low AHF levels, prolonged BT, defective platelet adhesiveness), transfusion studies were done. Plasma AHF levels, BT's (modified Ivy), and native blood platelet adhesiveness tests were done before and after transfusions of fresh and fresh-frozen platelet-free ACD plasma. The results showed that plasma obtained from donors with diabetes mellitus (juvenile onset) corrected the bleeding time and platelet adhesiveness test temporarily in all four patients when doses of 10–15 ml/kg were used. Comparable dosages of normal plasma were effective in correcting the BT in only one patient. AHF-rich fibrinogen, cryoprecipitates of normal plasma, and plasma from an exercised donor did not correct the BT. The effectiveness of the diabetic plasma was approximately directly proportional to the severity of the diabetes. Also, the immediate rise in AHF levels was greater following diabetic plasma infusion than after normal plasma.

Mixtures of vWd blood and fractions of plasma were tested for platelet adhesiveness (PA) by the in vitro method of HELLEM. Diabetic plasma and cryoprecipitate showed excellent correction of the defective PA; AHF-fibrinogen and normal plasma showed moderate correction, and diabetic and normal serum, normal cryoprecipitate, and dextrose showed poor PA.

These in vitro and in vivo studies suggest that the blood from certain diabetics contains an increased amount of the factor(s) responsible for correction of