of the mother for measurements of flow, osmolality and clearance. The glomerular filtration rate (GFR) was studied utilizing inulin ^{14}C administered by a single rapid injection. Following surgery fetal urine osmolality increased by 2–4 times that observed later in pregnancy when a steady state was established. During surgical stress urine flow was frequently less than 0.03 cm^3/min/kg body weight and urine osmolality was > 350 mOsm. The urine osmolality stabilized 3–6 days following surgery at a value markedly hypotonic to plasma (range 65–150 mOsm) and fetal urine flow increased to approximately 0.15 cm^3/min/kg—over 1,000 cm^3/day in a near-term fetus. Fifteen measurements of GFR in two fetuses gave a value of 1.05 ± 0.04 cm^3/min/kg (mean$\pm$SEM). Column chromatography on Sephadex G-10 confirmed that there was no hydrolysis of inulin by fetal tissues. Recovery of approximately 85% of inulin ^{14}C in the fetal urine over a 3-day period suggests that the fetal kidney is the primary means of inulin excretion *in utero*. The techniques permitting fetal renal function measurements in unstressed animals will be described.

42 *Immaturity and Enhanced Renal Clearances of Native Proteins.* LEONIDAS G. MORPHIS, PAUL M. TAYLOR and PHILIP FIREMAN, Dept. of Ped., Univ. of Pittsburgh Sch. Med. and Magee-Women's Hospital, Pittsburgh, Pa.

Renal clearances of 3 plasma proteins were studied in the mature and immature human neonate and adult to test the hypothesis that capillary permeability may be directly related to immaturity in the human, as it is in the sheep [J. Physiol. *201:* 567, 1969] and dog [Amer. J. Physiol. *213:* 441, 1967]. Urine was collected for 18–24 h, filtered, dialzyed and concentrated by lyophilization. Protein concentrations were measured in the serum and concentrated urine by the technique of radial immunodiffusion with specific antisera. Eighty to 90% of the 3 proteins studied were recovered from pooled human serum diluted to the approximate protein concentration of urine and subjected to the same procedures. Clearances (mean$\pm$SD) $\times 10^{-2}$ in ml/kg body wt/24 h and the number of subjects studied (in parentheses) follow:

	Transferrin	Albumin	α1-Antitrypsin
Molecular weight	90,000	69,000	45,000
Premature (9)	7.2 ± 4.1	1.6 ± 0.8	2.1 ± 0.7
Full-term (5)	1.3 ± 0.4	0.3 ± 0.1	0.3 ± 0.1
Adult (5–8)	0.2 ± 0.1	0.2 ± 0.1	0.1 ± 0.04

Thus, there was 1.5- to 7-fold greater clearance for full-term infants than for adults and 5- to 7-fold greater clearance for premature than for full-term infants. Protein clearances did not correlate with molecular weights.

The data suggest that the immature as compared to the mature human has greater glomerular capillary permeability, greater tubular excretion or decreased tubular reabsorption either singly or in combination.

43 *Intrarenal Blood Flow Distribution (IRBF) in the Puppy Using Xenon Washout and Microspheres.* PEDRO A. JOSE, ALEXANDER G. LOGAN, GILBERT M. EISNER, LAWRENCE M. SLOTKOFF, CHARLES E. HOLLERMAN and PHILIP L. CALCAGNO, Depts. of Ped. and Physiol., Georgetown Univ. Sch. of Med., Washington, DC.

Total renal blood flow measured by the ^{133}Xenon washout (Xe) rose from 1.5 ml/g/min at 6 wks. to 3.5 at 16 wks. of age in 30 canine puppies. IRBF analyzed from the Xe curve showed Component I (CI) increased from 1.7 ml/g/min at 6 wks. to 4.6 at 16 wks. and Component II (CII) increased from 0.9 at 6 wks. to 1.1 at 16 wks. The ratio CII/CI was 0.55 at 6 wks. and fell to 0.25 at 16 wks. ($p < 0.01$). The low cortical flow was also demonstrated by ^{169}Yb microsphere method. Anatomical vascular development using silicone rubber further showed an increase in cortical size with age. Cardiac output measured by indocyanine green in 8 anesthetized puppies over an age range of 6–16 wks. remained at 90 ml/kg/min while RBF in ml/g/min increased. The relatively low cortical flow at 6 wks. was associated with a PAH extraction ratio (E_{PAH}) of 0.44 and filtration fraction (FF) of 0.40. E_{PAH} increased to 0.75 at 12 wks. and FF decreased to 0.24 at 16 wks. These studies directly demonstrate for the first time underperfusion of the young puppy renal cortex as compared to the medulla. Renal functional maturation is accomplished in the canine by an increase in cortical blood flow during growth.

44 *Regulation of Glucose and Ammonia Production in the Isolated, Perfused Rat Kidney.* RICHARD D. PROPPER and ROBERT E. GREENBERG, Dept. of Ped., Stanford Univ. Sch. of Med., Stanford, Calif.

Renal gluconeogenesis *in vitro* is enhanced by increased [H+]. *In vivo*, both acute and chronic metabolic acidosis are associated with increased NH_4^+ excretion. Previous studies from our laboratory, using renal cortex slices, indicated that increased rates of ammonogenesis from glutamine are not dependent on corresponding changes in glucose production. The following studies have utilized perfusion of the isolated rat kidney to further investigate these interrelationships.

A modified, oxygen-saturated Krebs-Henseleit buffer, with added glutamine, was utilized as perfusate in an open system. The adequacy of this system was shown by the capacity to establish a [H+] gradient, and constancy of urine flow, glomerular filtration (C+) and rates of gluconeogenesis for a period of two hours.

Glucose production and urinary ammonia excretion were markedly increased when the pH of perfusate was 7.1 as compared to 7.7. However, total ammonia production (effluent+urinary) was decreased at the acid pH. Addition of α-ketoglutarate or pyruvate to the perfusate led to expected increases in gluconeogenesis while total ammonia production decreased. Addition of glucose to the perfusate had no effect on total ammonia production from glutamine.

These studies indicate the following: (1) urinary ammonia excretion is not directly correlated with total ammonia production; (2) enhanced ammonia production is not an obligate consequence of increased glucose formation; (3) rates of ammonogenesis are regulated by changes in concentration of Krebs cycle intermediates.

45 *A Relation Between α-Ketoglutarate Utilization and Excretion of Ammonia, Titratable Acid, Sodium Reabsorption and Renal Gluconeogenesis in Man.* J. METCOFF, J. E. LEWY, K. SCHARER, M. ORT, G. RUIZ and T. YOSHIDA, Michael Reese Hosp. and Med. Center, Dept. of Ped., Chicago, Ill.

In vivo utilization of the renotropic substrate alpha-ketoglutarate (α-Kg) is associated with a high RQ