(LVC), and LV contractile element velocity (VCE) were calculated. Mean values for VCE at isostress points during isovolumic contraction were not different from normal in 9 patients with moderate LVH (LV Mass 115±13 vs. normal 82±10 g/M²). In 5 patients with more severe LVH and LV Mass averaging 156±31 g/M², VCE was significantly depressed from normal during isovolumic systole indicating a depressed force-velocity relationship. In addition 4 of the 5 patients with severe LVH had depressions of LV stress at isocircumference points at end-systole when compared with normal children suggesting a depressed length-tension relationship. These date indicate that severe left ventricular hypertrophy in children may be accompanied by impaired muscle function when expressed in terms of basic muscle mechanics.

38 *Vector Analysis of Ventricular Function—an Approach to the Study of Myocardial Performance.* RENÉ A. ARCILLA and ROBERT L. REPLOGLE, The Univ. of Chicago Pritzker Sch. of Med., Dept. of Ped. and Surg., Chicago, Ill.

Evaluation of myocardial performance must take into consideration stroke work as related to ventricular force generation. A method has been developed whereby pressure, flow velocity and their derivatives could be X-Y correlated and represented as vector loops, with time dashes to facilitate direction and amplitude analyses of the various loop components. Of several X-Y combinations, the most informative loops were those derived from: (1) LV pressure vs. aortic flow velocity (P-F loop); (2) LV pressure vs. derivative (P-dP/dt loop); (3) pressure derivative vs. flow derivative (dP/dt-dF/dt loop). Planimetry and analysis of the outgoing and returning limbs of the P-F loops enable separation of LV stroke work into its major early and late systolic components. These could be correlated with the P-dP/dt loops which reflect the corresponding ventricular force generation, and with the dP/dt-dF/dt loops which relate to work efficiency. In 10 adult dogs with chronically implanted aortic flow probes, various inotropic drugs and adrenergic blockers produced consistent changes in the loops indicating augmented or decreased myocardial performance. Loops obtained from children immediately before and after cardiopulmonary bypass provided information relative to changes in myocardial performance.

39 *Digitalis Mechanisms: Effects on Sodium Flux.* G. GALL, P. USHER and R. KLEIN, Boston Univ. Sch. of Med., Boston, Mass.

Measurements were made of human erythrocyte ghost Na flux, Na+K dependent ATPase activity, and intracellular water and electrolyte concentrations in patients receiving cardiac glycosides and in normal subjects to investigate mechanisms of action of cardiac glycosides. The effects of *in vitro* exposure of normal cells to cardiac glycosides were also studied. The mean erythrocyte ghost Na efflux rate constant in adequately digitalized patients was elevated to 1.19±0.027 (SEM). Normal mean efflux rate was 0.62±0.017 and the difference was significant, $p < 0.01$. The increased efflux was due to increased active transport since the passive outward leak of Na was unaffected. Since erythrocyte intracellular Na concentration was normal in these patients the passive influx rate of Na was also increased. The *in vitro* exposure of normal ghosts to ouabain 10^{-9} to 10^{-10} M. produced similar increases in Na flux. Erythrocyte water and Na+K dependent ATPase activity were both increased in digitalized patients. Patients with digitalis toxicity had reduced active transport of Na, reduced Na+K dependent ATPase activity, and increased intracellular Na concentration. Similar changes in flux and ATPase were produced *in vitro* by ouabain 10^{-4} to 10^{-7} M. It is believed that these findings support KLAUS' suggestion that therapeutic doses of cardiac glycosides are associated with increased active transport of Na, decreased intracellular Na concentration and suggest increased cell water. Toxic effects of cardiac glycosides are associated with decreased active Na transport, decreased Na+K dependent ATPase and increased intracellular Na.

40 *Recordings of His Bundle and Other Conduction Potentials in Children.* SIDNEY J. BRODSKY, M. MIROWSKI, L. JEROME KROVETZ, RICHARD D. ROWE and ANTHONY N. DAMATO, Dept. of Ped., Johns Hopkins Univ. Sch. of Med. and USPHS Hosp., Staten Island, NY.

A technique for recording His bundle potentials in man has recently been described and utilized in the study of the AV conduction system in normal and pathological states. These previous *adult* studies have dealt with defining the His bundle potential as well as making a more precise assessment of the nature of AV block possible in a way hitherto not attainable.

Thirty-five children between 3 months and 13 years of age with various congenital cardiac defects were studied. All had normal sinus rhythm and normal AV conduction and included both non-operative and post-operative patients. The His bundle potential was recorded in 34 of the 35 patients, the one exception being a post-operative tetralogy of Fallot. The HQ interval varied from 22 to 60 msec. In 26 of the 35 patients, a potential was recorded which probably represented the AV node. Furthermore, in 27 of the 31 children who did not have complete right bundle branch block, a right bundle branch potential was also recorded. Additionally, a left bundle branch was recorded in 5 patients.

In a two-week-old infant with congenital complete AV block, the presence of a left bundle branch potential in association with the absence of the His bundle or right bundle branch potentials suggests that the impulse originated in or near the left bundle branch.

The technique of intracardiac His bundle recording has been shown to be both feasible and practical in children of all ages. Further studies are in progress to define in more detail, the mechanisms of congenital disturbance of AV conduction.

41 *Fetal Renal Function in Unstressed Pregnancies.* EDWIN L. GRESHAM, JOHN H. G. RANKIN, EDGAR L. MAKOWSKI, GIACOMO MESCHIA and FREDERICK C. BATTAGLIA, Depts. of Ped., Physiol. and Obstet.-Gynecol., Univ. of Colorado Med. Center, Denver.

Previous studies of fetal renal function in animals under surgical stress have produced conflicting results. Since acute surgical stress may have contributed to some of the previous variability, a chronic sheep preparation has been developed which permits repeated studies of fetal renal function over several weeks. A hysterotomy was performed during the latter third of pregnancy; catheters were placed in the urinary bladder, femoral artery and vein of the fetus, and in the amniotic sac. Fetal urine was diverted to the outside

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±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±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