at several frequencies (F) from 1–15/sec, duration 5 msec, and 10–15 V. Slowing was a function of F, but was unaltered by changes of PO_2, PCO_2 or pH up to an F of 10/sec. At F 15 the bradycardia was often enhanced by hypercapnia. It is concluded that hypoxemia and lactic acidemia do not alter adrenergic (A) or cholinergic (C) transmission, but that hypercapnic acidosis may reduce A, and enhance C during maximal stimulation. This suggests a mechanism whereby autonomic control of the heart may be altered in neonatal asphyxia.

34 *The Role of the Adrenergic Nervous System in Regulating Systemic Arterial Pressure and Venous Return.* RICHARD M. SCHIEKEN, GEORGE J. PECKHAM, ARMAN BILGIC and WILLIAM J. RASHKIND, The Children's Hosp. of Philadelphia, Philadelphia, Pa.

Total cardiopulmonary bypass was achieved in closed chest dogs. Systemic venous return (SVR) was directed through a recording electromagnetic flowmeter. Systemic arterial (SAP) and central venous pressure (CVP) were also monitored continuously. Alpha adrenergic agents caused a mean increase in SAP of 74% without any change in SVR. Beta adrenergic agents produced a mean fall of 34% in SAP and a mean increase of 9% in SVR and a mean increase of 4% in CVP. Alpha adrenergic blockage simulated beta adrenergic effect with a mean fall in SAP of 52% and a mean increase of 8% in SVR and a mean increase of 3% in CVP. No significant changes occurred as a result of beta adrenergic blockade. These data demonstrate the dominent effect of the beta adrenergic nervous system in increasing systemic venous return by an increase in venomotor tone.

35 *Increased Oxygen Release in Hypoxemia and Heart Failure.* WILLIAM W. MILLER, FRANK A. OSKI, MARIA DELIVORIA-PAPADOPOULAS, Dept. of Pediatrics, Medical School of the University of Pennsylvania, Philadelphia.

Red cell 2,3-diphosphoglycerate (DGP), a primary regulator of oxygen-hemoglobin affinity, was measured in 55 infants and children with congenital cardiac diseases. The levels were compared with those from 20 normal patients and were analyzed with regard to patient age, arterial oxygen tension (P_aO_2), and the presence of heart failure. In 14 patients the oxygen dissociation from whole blood was also measured, and values for DPG were correlated with those for P 50, the PO_2 for 50% oxygen saturation.

Elevated levels of DPG were found in 17 of 18 infants and children with heart failure, regardless of age or P_aO_2.

Thirty-seven patients had subnormal P_aO_2, but no heart failure. Among those > 3 months of age, DPG was elevated in 26 of 28 with P_aO_2 = 16–56 mm Hg, and it was normal in 5 with P_aO_2 > 56 mm Hg. In these 33 older patients, the level of DPG was inversely related to P_aO_2 ($r = -0.656$). In four hypoxemic infants < 3 months, DPG was normal.

The close correlation found between elevated values for red cell 2,3-DPG and for whole blood P 50 ($r = 0.7142$) supports *in vitro* studies indicating that DPG is a primary regulator of oxygen release from human blood. The correlation between levels of DPG and of P_aO_2 in patients > 3 months supports *in vitro* studies demonstrating deoxyhemoglobin control of red cell DPG synthesis. Among newborn infants the elevated levels of DPG measured in those with heart failure and the normal concentrations found in those with hypoxemia indicate two different control mechanisms for synthesis of this important modulator of oxygen homeostasis.

36 *Effects of Chronic Hypoxemia on the Electrophysiological Properties of Right Atria Tissue in Children.* HENRY GELBAND, HARRY L. BUSH, GERARD A. KAISER, JAMES R. MALM, ROBERT J. MYERBURG and BRIAN F. HOFFMAN, Coll. of Physicians and Surgeons, Columbia Univ., NY. (introduced by O. R. Levine).

The purpose of this study was to determine the electrophysiological properties of normal right atrial tissue in children and to evaluate the role of chronic hypoxemia in the genesis of atrial arrhythmias. Using standard microelectrode techniques we studied the electrophysiological properties of preparations of right atrial tissue obtained during open heart surgery in two groups of patients. Group A consisted of 6 patients with uncomplicated ventricular septal defects. Group B comprised 6 patients with tetralogy of Fallot with arterial O_2 saturations of 80–84%. All patients underwent cardiovascular diagnostic studies and had normal right atrial pressures and no evidence of atrial shunting. In Group A mean resting potential (RP) was -86 ± 5.7 mV, action potential duration was 210 ± 8 msec at a cycle length of 1,000 msec and conduction velocity was 0.45 ± 0.05 M/sec. The relationship between the rate of rise of phase 0 of the action potential (AP) and the membrane potential at which the AP was elicited (membrane responsiveness) was 'S' shaped. Cells were unresponsive at a mean RP of -56 ± 1.6 mV and maximum rate of rise occurred at a mean RP of -86 ± 5.7 mV. An increase in extracellular [K+] above control caused a decrease in the RP which was linearly related to log [K+]. When [K+] was reduced below control levels, RP decreased slightly. There were no significant differences ($p = > 0.05$) between Group A and Group B for all properties measured. Results from Group A can be used for 'normal' reference values. Chronic hypoxemia does not seem to alter the electrophysiological properties of right atrial tissue. This is consistent with the clinical observation of the lack of atrial arrhythmias in cyanotic congenital heart disease when there is no pressure or volume overloading of the right atrium.

37 *Evaluation of Left Ventricular Contractile State in Children With a Chronic Left Heart Pressure Overload.* THOMAS P. GRAHAM, JAY M. JARMAKANI and RAMON V. CANENT, Duke Univ. Med. Center, Dept. of Ped., Durham, NC (introduced by Madison S. Spach).

Recent animal investigations have indicated that myocardial hypertrophy may be accompanied by a depression of muscle function as analyzed in terms of length-tension and force-velocity relationships. Myocardial function was evaluated in these terms in 14 children with left ventricular hypertrophy (LVH) secondary to aortic stenosis or coarctation of the aorta and 10 children with normal left hearts who were undergoing diagnostic cardiac catheterization. Serial left ventricular volumes were calculated from biplane cineanangiocardiograms exposed at 60/frames sec, and left ventricular pressure was recorded simultaneously using a catheter tip transducer. Left ventricular circumferential stress (LVS), LV circumference at the equator

(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