mean PO_2 dropped from 102 to 35 mm Hg, and mean Cl prot. increased 38 % (range 15 to 49 %) over control values. Cl prot. returned to control values on return to 21 % O_2 ventilation in 3 pups, and remained elevated in 2. Arterial pH was maintained at normal levels throughout the experiments. Transpulmonary artery wedge pressure was similar during periods of ventilation with 21 % and 10 % O_2. Thus a hemodynamic basis for the increase in Cl prot. associated with hypoxemia is unlikely. These data indicate that PCP, which is already increased as a handicap of immaturity in pups, is further increased by severe hypoxemia. Similar studies are in progress on adult dogs. (SPR)

4 *Effect of Alternations of Pulmonary Arterial and Alveolar Gas Tensions on the Pressure-volume Curve and Surface Tension of Dog Lungs.* EDMUND E. FARIDY* and VICTOR CHERNICK, Dept. of Peds. and Physiology, Univ. of Manitoba, Winnipeg, Canada.

The effect of acute alterations of pulmonary blood flow (Q_p), pulmonary arterial blood gas tensions (P_{VCO_2}; P_{VO_2}) and alveolar gas tensions on the mechanical properties of lungs has been studied in left lower lobes of open-chest dogs. Static deflation pressure-volume curves and the stability ratio (SR) of bubbles expressed from the lung were measured. In non-ventilated lobes, the absence of circulation for 4 hours did not produce a change in the percent of maximum air volume remaining at a transpulmonary pressure of 10 cm H_2O ($V\%_{10}$). In non-ventilated lobes, perfusion with hypercapnic hypoxic blood ($P_{VO_2} > 60$ mm; $P_{VO_2} < 45$ mm) caused a significant decrease in $V\%_{10}$. In lobes ventilated with 100 % nitrogen and perfused with hypercapnic hypoxic blood, $V\%_{10}$ decreased more than in the non-ventilated lobes. Change in $V\%_{10}$ could be reversed by perfusing with normal P_{VCO_2} and P_{VO_2} for 3 hours. In contrast, $V\%_{10}$ was unaltered in lobes perfused with blood having normal P_V gas tensions and ventilated with 100 % nitrogen, even when Q_P was decreased to 15 to 20 % of control values. However, $V\%_{10}$ decreased in lobes perfused with blood having normal gas tensions but ventilated with 10 % CO_2 in nitrogen. A decrease in $V\%_{10}$ correlated with a decrease in SR. These studies suggest that the presence of normal surfactant depends upon the intimate gaseous environment of the alveolar cell. Both hypercapnia and hypoxia are required for the production of increased retractive forces on lung deflation. Reversal to normal deflation characteristics is possible by reverting to normal gas tensions. (Supported by the Medical Research Council of Canada) (SPR)

5 *Effect of Magnesium on Pulmonary Vasomotor Response to Hypoxia.* GERD J. CROPP*, Univ. Colo. Med. Ctr., Denver, Col. (introduced by Frederick C. Battaglia).

Magnesium relaxes constricted smooth muscle in systemic arterioles and bronchioles, and alveolar hypoxia causes pulmonary vasospasm. Since pulmonary vasoconstriction strains the right ventricle and causes shunting of blood away from the lung in the neonatal period, prevention of hypoxic pulmonary vasospasm would be beneficial; drugs used up to date to overcome this vasospasm have had undesirable side effects. We therefore determined the effect of intravenous infusions of isotonic, buffered $MgCl_2$ in blocking hypoxic pulmonary vasospasm. Anesthetized dogs breathed 100 % O_2, followed by 7 % O_2, 10 % O_2 or 10 % O_2 6 % CO_2. Systemic and pulmonary arterial pressures, heart rate, cardiac output (CO), respiration, plasma Mg and arterial pO_2, pCO_2 and pH were measured during high and low O_2 breathing, before and following infusion of $MgCl_2$. All dogs showed a marked rise in pulmonary vascular resistance (PVR) during hypoxia at normal blood Mg levels. As Mg-concentrations increased the rise in PVR during hypoxia lessened. At levels above 10 mEq/l hypoxic pulmonary vasoconstriction was usually absent. [Mg] of less than 13 mEq/l did not decrease resting CO or the CO response to hypoxia and did not cause hypotension or hypoventilation. [Mg] above 15 mEq/l produced hypoventilation and areflexia. It is concluded that controlled elevation of blood Mg to 10–12 mEq/l will block hypoxic pulmonary vasoconstriction without causing deleterious changes in hemodynamics or pulmonary ventilation. (Sponsored by American Heart Association) (SPR)

6 *Ventilation/Perfusion Relationships in the Lungs of Children with Congenital Heart Disease.* MARTIN H. LEES*, R. CLIFTON WAY* and BENJAMIN B. ROSS*, University of Oregon Med. Sch., Portland, Ore. (introduced by Richard Goldbloom).

The large increases and reductions of pulmonary blood flow (Q_p) observed in congenital heart disease must challenge the lungs in their function of maintaining physiologic respiratory gas tensions in arterial blood. If ventilation (V_A) and Q_p are not well matched throughout the lung, alveolar-arterial respiratory gas tension differences result. We have examined the extent of uneven V_A/Q_p ratio distribution by the alveolar-arterial O_2 difference ($A\text{-}aDO_2$) breathing air and 100 % O_2 (10 subjects) and the steady-state air-breathing arterial-alveolar N_2 difference ($a\text{-}ADN_2$) (21 subjects). Arterial N_2 tension was assessed by gas chromatographic determination of urine N_2 tension (PuN_2). Normal subjects had air breathing $A\text{-}aDO_2$ of 10 ± 2.7 mm Hg and 16 ± 10 mm Hg breathing 100 % O_2. Those with pulmonary overperfusion had $A\text{-}aDO_2$ of 22.4 ± 8.6 mm Hg on room air and 135 ± 48 mm Hg on 100 % O_2 suggesting that intrapulmonary venous admixture rather than V_A/Q_p unevenness was the major cause of lowered arterial O_2 tension. Urine-alveolus N_2 difference ($U\text{-}ADN_2$) in normal subjects was 7.6 ± 4.3 mm Hg. $U\text{-}ADN_2$ was 3.3 ± 6.4 mm Hg in those with overperfused lungs suggesting very even V_A/Q_p ratio distribution. Children with underperfused lungs had $U\text{-}ADN_2$ of 14 ± 7.7 mm Hg indicating considerably increased V_A/Q_p ratio unevenness. We conclude that pulmonary overperfusion is associated with rather even matching of ventilation to perfusion throughout the lung. Diminished pulmonary blood flow (with low pulmonary arterial pressure) results in poor matching of ventilation to perfusion, probably because of selective perfusion of lower lung zones and overventilation of upper zones—an exaggeration of the normal effect of gravity. (SPR)

7 *Airway Obstruction in Cystic Fibrosis.* ROBERT B. MELLINS*, O. ROBERT LEVINE*, ALFRED P. FISHMAN* and CAROLYN R. DENNING*, Columbia-Presbyterian Med. Ctr., New York, N.Y. (introduced by Edward C. Curnen).

The ineffectiveness of cough in cystic fibrosis (CF) has been attributed to the viscosity of the bronchial secretions. In the present study, the contribution of abnormal lung mechanics to airway obstruction was investigated in 13 patients with CF, using 8 normal

subjects and 10 asthmatics as controls. Instantaneous changes in lung volume, air flow and esophageal pressure were measured and simultaneous flow-volume and flow-pressure curves recorded. Striking differences were noted between asthma and CF: 1. below 95 % of the total lung capacity, pressures in excess of those required to produce maximum expiratory flow rates depressed flow in CF but not in asthma; 2. forced expiration was associated with a transient reversal in the slope of the single breath nitrogen curve in CF and not in asthma. Cineradiographic evidence of collapse of bronchiectatic airways during forced expiration and cough with retention of contrast medium distal to the collapse was provided. It is concluded that in CF: 1. airway obstruction is less uniform and involves larger airways than in asthma; 2. increased expiratory pressure collapses larger airways. This study emphasizes the necessity of combining postural drainage with liquefaction of bronchial secretions in CF. (SPR)

8 *Influence of Intracardiac Shunting on Left Ventricular Muscle Mechanics in Tetralogy of Fallot.* MOUAZZA M. JARMAKANI*, MADISON S. SPACH, SAM B. EDWARDS*, RAMON V. CANENT, Jr.*, M. PAUL CAPP*, VISHNU JAIN* and ROGER C. BARR*, Duke University Medical Center, Durham, N.C.

The need continues for better quantitation of left ventricular function. Previous studies have indicated the nature of intracardiac shunting in tetralogy. Simultaneously recorded left ventricular pressure and biplane cines were analyzed to construct continuous left ventricular function curves in 'normales' and in tetralogy patients. The original measurements throughout 3–6 consecutive beats were analyzed by a digital computer with numerical and graphic outputs of: LV pressure, LV volume, rate of volume change (flow), LV mid-circumference and its instantaneous velocity, tension at the endocardial surface, work and power. The force-velocity-length and pressure-volume-flow relationships of the left ventricle were depicted in three dimensional plots during the active state (systole) of the LV muscle for normals and tetralogy patients. In normals, maximum flow and peak velocity of shortening occurred at high tension levels in mid-systole; whereas in tetralogy, peak flow and velocity occurred during 'isovolumic' contraction at lower tensions. The continuous' function curves' were markedly abnormal in tetralogy with peak rate of flow and of circumference shortening occurring prior to opening of the aortic valve. The results indicate that the left ventricle in tetralogy functions more efficiently than normal and unloads 15 to 40 percent of its stroke volume during isovolumic contraction. This results in lower than normal stroke work values. (SPR)

9 *Studies of Left Ventricular Function in Children by Increasing Peripheral Resistance with Angiotensin.* L. JEROME KROVETZ, THOMAS G. MCLOUGHLIN* and GEROLD L. SCHIEBLER, Univ. Florida Col. of Med., Gainesville, Fla.

While satisfactory catheterization techniques for detection of shunts and abnormal movements of heart valves are available, assessment of myocardial function remains difficult. In normal human subjects angiotensin, produces systemic vasoconstriction which results in increased left ventricular stroke work (LVSW). Ross and BRAUNWALD studied 18 patients using graded infusions of angiotensin and showed a good correlation of clinical severity and LV function curves. To learn the value of this technique in children, LV function was assessed using graded infusions of angiotensin (2 to 3.8 mcg/min) in ten normals (age range 5 to 15 years) and 21 patients with LV abnormalities (age range 2 months to 15 years). The best method of graphing this data is to plot LV end-diastolic pressure versus the ratio of calculated to predicted LVSW. Predicted LVSW (in newton-meters), based on 24 normal children, is given by the formula: $= 0.745 + 0.0133$ wt (kg) $- 0.00243$ ht (cm) $- 0.00384 \times$ heart rate. All nine patients with primary LV endocardial fibroelastosis had abnormal LV function curves. Four of eight patients with Hunter-Hurler syndrome had depressed LV function as did two of three patients with idiopathic myocardial hypertrophy. One 2-month-old male with cardiac glycogenosis had a markedly depressed LV function curve, LV stroke work decreasing with increasing LV end-diastolic pressure.

Of the 16 abnormal LV function curves, only 7 had resting elevated LV enddiastolic pressures. An additional 5 had low resting LVSW ranging from 17 to 43 % of predicted. Thus, abnormal LV function was detected only following angiotensin infusion in one-fourth of these patients. (SPR)

10 *Neurohumoral Mechanisms of Ventricular Tachycardia in Experimental Heart Block.* HERBERT D. RUTTENBERG*, ROGER A. HURWITZ* and IWAO KANDA*, UCLA Sch. of Med., Los Angeles, Cal. (introduced by Leonard M. Linde).

The purpose of this study was to investigate the pathways by which electrical stimulation of the hypothalamus produces paroxysmal ventricular tachycardia (PVT) in dogs with chronic complete atrioventricular (A-V) block. Left thoracotomy was performed in 20 dogs to pass wire loops around the stellate ganglion and ansa subcalvia (cardiac nerves). Two weeks later, right thoracotomy was performed for placement of wires around the right cardiac nerves for production of complete A-V block by transatrial injection of formalin into the A-V node. One week later, under chloralose anesthesia, monopolar electrodes were placed into the lateral hypothalamic areas for 20 sec stimulations of 20 V, 1 msec, 50 cps stimulations. Aortic pressures (AP), left ventricular pressures (LVP) and ECG were recorded. In all 20 dogs, stimulation in the posterolateral hypothalamus (fields of Forel) caused an immediate depressor response followed by an increase in AP (systolic, diastolic and pulse pressure) with moderate increase in ventricular rate (VR). In 8 of these dogs, the pressure rise was followed by PVT with an average latency of 23 sec, a change in VR from 56 (resting VR) to 140, and a change in site of pacemaker. Production of PVT was not prevented by bilateral ablation of cardiac nerves. The long latent period suggested a humoral pathway. Administration of epinephrine HCl 5 to 10 μg/kg body weight produced PVT in 10 of 13 dogs with a latent period of 25 sec. This humorally-induced PVT was not prevented by ablation of cardiac nerves or α-adrenergic receptor blockade but was blocked by β-adrenergic receptor blockade. These studies suggest that adrenergic humoral mediation is a major pathway for production of PVT in heart block. (SPR)

11 *The Effect of Human Growth Hormone (HGH) on Red Cell Glucose Metabolism.* FRANK A. OSKI and ALLEN ROOT*, Dept. of Pediatrics, Univ. of Pa. Sch. of Med., Philadelphia, Pa.

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