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EVALUATION OF DIGOXIN DOSAGE IN PREMATURE INFANTS. William W. Pinsky, Paul C. Gillette, Joes R. Jacobsen, James M. Adams, John A. Burdine, Dan G. McNamara

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The effective and safe dosage of digoxin for premature infants has not yet been established. We compared the digoxin serum level, change in left ventricular systolic time interval (LVSTI) and toxic manifestations in 2 groups of premature infants, administering a total digitalizing dose (TDD) of 30 µg/kg to Gp. I and a TDD of 20 µg/kg to Gp. II. The birthweight (BW) of the 26 pts. in Gp. I (720-3170 gms, mean 1553 ± SE 112 gms) and the gestational age (GA) (26-35 wks, mean 31.7 wks) were similar to the BW (980-2160 gms, mean 1475 ± SE 115) and GA (27-35 wks, mean 31.8 wks) of the 12 pts. in Gp. II. Digoxin was administered parenterally ½ TDD, then ¼ TDD 8 hrs. later and the remaining ¼ TDD 8 hrs. later, then 1/8 TDD every 12 hrs. for remainder of study. Radioimmunoassay of serum digoxin levels obtained 72 hrs. after the initial dose and just before the maintenance dose revealed a higher level in Gp. I: 1.4-7.5 µg/ml (mean 3.5 ± SE 0.39) than in Gp. II: 1.2-3.0 µg/ml (mean 1.73 ± SE 0.15),  $p < .001$ . In Gp. I the smaller more immature infants had the higher serum levels. In Gp. II the levels were similar, irrespective of BW and GA. Despite lower serum level of digoxin in Gp. II, the echocardiographically determined LVSTI was effectively reduced. Toxicity was noted in only 1 pt. who was in Gp. I, serum level 5.0 µg/ml. Serum digoxin half-life in 7 pts. from both groups was 56-88 hrs. (mean 72 ± SE 5.2 hrs). Since hemodynamic effect was achieved with the lower dose (20 µg/kg TDD), we recommend this dose for premature infants.

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COMPARISON OF METHODS OF CARDIOPLEGIA. William W. Pinsky, Paul C. Gillette, Robert M. Lewis, Craig J. Hartley, Edward P. Borner, Mark L. Entman,

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The purpose of our study was to compare the effectiveness of three techniques of coronary artery perfusion for protection of the canine myocardium during ischemic cardiac arrest (IA).

In each of three different methods, the perfusate, chilled to 4°C., consisted of 5% dextrose in water, 15 meq KCl, 5 meq NaHCO<sub>3</sub> and 10,000 units heparin/l. In method 1, during aortic cross-clamping, the solution was infused continuously at a rate sufficient to maintain myocardial temperature at 18°C. In method 2 the solution was given as a single bolus of 10 cc/kg. In method 3 the solution was administered also by a single bolus and to the solution was added 2 mM CaCl<sub>2</sub> and 25 mM MgCl<sub>2</sub>. In a control preparation (method 4), no perfusate was administered during IA. In the table are listed the number of immediate survivors of the experiment, the indices of subcellular and hemodynamic myocardial function (the latter expressed as % of control).

	HR	MAP	CO	Lvdf/dt	SURVIVORS	SR
1.	99	73	148	96	9/9	normal
2.	95	70	113	76	5/9	variable
3.	92	71	117	74	4/5	variable
4.	91	74	74	64	8/20	abnormal

HR=heart rate; MAP=mean arterial pressure; CO=cardiac output; Lvdf/dt=LV force of contraction; SR=sarcoplasmic reticulum. Continuous perfusion appears to provide better protection of the myocardium than the single bolus technique.

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PATENT DUCTUS ARTERIOSUS: BIOCHEMICAL STUDIES. Morton P. Printz and William F. Friedman. Univ. of Calif., San Diego, Sch. of Med., Div. of Peds. Card-

iology, Dept. of Peds. and Med., San Diego, CA. Whether patency or constriction of the ductus arteriosus is related more importantly to alterations in circulating levels of prostaglandins (PG's) or with alterations in PG synthetase activity within the ductus itself is conjectural. In the present study the latter possibility was examined by evaluating the ability of the ductus arteriosus and other fetal vascular tissues to synthesize from intermediate endoperoxide (PGH<sub>2</sub>) various terminal prostaglandins. Fetal lamb ductus arteriosus generated only the potent vasodilator PGI<sub>2</sub>. The aorta and pulmonary artery produced twice the PGI<sub>2</sub> of ductus arteriosus while vena cava produced half as much. None of these vessels produced the potent vasoconstrictor, thromboxane A<sub>2</sub> (TXA<sub>2</sub>). In contrast, adult lung, but not fetal lung, produced abundant quantities of TXA<sub>2</sub>. Thus, ductus arteriosus may be more profoundly affected by PG synthetase inhibition (used clinically in premature infants) than other arteries. Moreover, an interplay is suggested between lung-derived TXA<sub>2</sub> and PGI<sub>2</sub> production within the wall of the ductus per se that promotes ductal constriction. The altered circulatory pathways associated with birth foster constriction of the ductus by providing a change in the interaction between the potent vasoactive PG's. The data suggest an explanation for prolonged ductal patency in the face of lung immaturity, for the normal process of ductal closure, and for the ability clinically to manipulate PG metabolism to alter ductal caliber.

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AGE AND SEX AS DETERMINANTS OF THE PULMONARY VASCULAR (PV) RESPONSE TO CHRONIC HYPOXIA IN RATS. Marlene Rabinovitch, Kathleen Murray, Mark Aronovitz, Walter

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To determine the effect of age and sex on the rise in pulmonary artery (PA) pressure (P) and on morphologic changes in the PV bed in response to chronic hypoxia, 12 Sprague-Dawley infant rats (I-rats) and 11 adult rats (A-rats) were placed in hypobaria (air at 380 mmHg) for 1 month. The I-rats, 8 male (M) and 3 female (F) were 8 days old (mean weight=10 grams); the A-rats, 7M and 4F, 3 months old (mean weight=280 grams). After exposure, indwelling PA and aortic (Ao) catheters were inserted under pentobarbital anesthesia and the next day unanesthetized pressure measurements were recorded. The rats were sacrificed and their lungs analyzed (after injecting the PA tree with barium-gelatin and the parenchyma with formalin) by 3 structural features: 1) extension of muscle into small arteries (EMSA), 2) percentage wall thickness of peripheral arteries (%WT) and 3) alveolar artery ratio (A/A). A rise in mean PAP to 51±5.1 (compared with 16.6±1.1 in C-rats) observed in I-rats was similar in AM-rats, but mean PAP in AF-rats was lower (29.6±2.1,  $p < 0.03$ ); AOP was unchanged in all. Increased EMSA, %WT and A/A were found in I-rats and A-rats compared with C-rats ( $p < 0.005$ ); however AF-rats compared with AM-rats showed less increase in %WT ( $p < 0.05$ ). Thus, after chronic hypoxic exposure, adult female rats had developed milder PA hypertension associated with less medial hypertrophy.

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CONTINUOUS MONITORING OF PO<sub>2</sub> FOLLOWING CARDIAC SURGERY, R. Raker, L. Indyk, C. Kull, L.S. James, W. Gersony, Dept. Ped., Coll. P & S, Columbia Univ., N.Y.

The transcutaneous oxygen tension (P<sub>tc</sub>O<sub>2</sub>) was studied in 18 children (age - 6 mos. to 13 yrs; wt. - 5 kg. to 54 kg.) following open heart surgery. Four of the operations were done under deep hypothermia (T<sub>core</sub> = 15-20°C), 11 under mild hypothermia (24-28°C) and 3 at normothermia (>34°C).

The P<sub>tc</sub>O<sub>2</sub> was recorded continuously for a period of several hours while an arterial catheter was in place, beginning within 8 hours after completion of surgery. Core temperature was at least 35°C in all patients at the start of recording. An electrode temperature of either 44°C or 45°C was utilized. PaO<sub>2</sub> values from arterial blood samples were correlated with P<sub>tc</sub>O<sub>2</sub>. A plot of all paired values had a greater scatter than had been previously encountered with the use of the electrode in sick newborns ( $r = .53$  vs  $r = .94$ ). Virtually all of the P<sub>tc</sub>O<sub>2</sub> values were lower than PaO<sub>2</sub> with 20% of the P<sub>tc</sub>O<sub>2</sub> values considered unacceptable on the basis of large discrepancies at the low range of PO<sub>2</sub>. Correlation at 45°C electrode temperature was better than at 44°C ( $r = .62$  vs  $r = .41$ ). P<sub>tc</sub>O<sub>2</sub> values taken beyond 8 hours post-surgery correlated significantly better than those taken earlier ( $r = .78$  vs  $r = .24$ ). Despite differences in the individual quantitative correlations, abrupt changes in PO<sub>2</sub> reflecting changes in respiratory status were consistently detected rapidly. These studies indicate that recording of the P<sub>tc</sub>O<sub>2</sub> is potentially a valuable tool in the monitoring of post-operative cardiac patients.

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LEFT VENTRICULAR MUSCLE MASS BY ECHOCARDIOGRAM IN CHILDREN. P. Syamasundar Rao, Mohinder K. Thapar, Robert J. Haggard, William B. Strong. Medical

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In several recent studies, left ventricular muscle mass (LVMM) was derived from echocardiographic (ECHO) measurements in adults. No such studies were reported in children. The purpose of this study is to establish normal LVMM values in children and to determine if this measurement is sensitive to detect the increased LVMM in patients with sickle cell disease (SS). Echocardiograms were performed in 251 children ages 3-17 yrs. (White (W)-107, Black (B)-97, and SS-47). LVMM in diastole and systole was derived by subtracting the volume of ventricular cavity from the volume occupied by the ventricular wall, septum and cavity. The volumes were calculated by three methods: 1. The cubed-function (C) of the given left ventricular ECHO diameter and by the modified methods of 2. Teichholz (T) and 3. Ratshin (R). The values for the diastolic LVMM (gm/M<sup>2</sup>; mean ± SD) are tabulated:

	LVMM (C)	P	LVMM (T)	P	LVMM (R)	P
W	89 ± 18		121 ± 20		52 ± 25	
B	96 ± 17	<0.05	130 ± 20	<0.01	54 ± 24	>0.1
SS	170 ± 44	<0.001	202 ± 50	<0.001	131 ± 46	<0.001

The LVMM in systole, in each age and sex subgroup and percentile distribution, as well as its relationship to level of hemoglobin in SS (not shown in abstract) will be presented. The data suggest that each method can detect the increased LVMM in SS patients. The C and T methods should be used for quantitating LVMM in children because of low mean values with the wide scatter of normal LVMM derived by the method of R.