

than 120 days gestation; (3) reflex bradycardia was blocked by atropine but not influenced by propranolol; (4) in fetuses the regression coefficients of SP or PP vs. R-R increased with gestational age, but not when SP or PP was correlated with HR because of the lower initial HR in older fetuses; (5) lambs had significantly higher regression coefficients for all correlations than fetuses. We have not yet evaluated if baroreceptor responses depend on gestational age and initial HR in combination.

Cardiovascular responses to autonomic blockade in intact fetal and newborn lambs. EERO K. VAPAAVUORI, ELLIOT A. SHINEBOURNE, ROBERT L. WILLIAMS, MICHAEL A. HEYMANN, and ABRAHAM M. RUDOLPH. *Cardiovas. Res. Inst., Univ. of California, San Francisco, Calif.*

Sympathetic and parasympathetic activity have been studied in exteriorized fetal lambs but not in intact fetuses in utero. We placed vinyl catheters in a systemic artery and hindlimb vein in 20 fetuses from 92 days of gestation to term and also in 3 newborn lambs. The animals were allowed to recover from surgery for 2-3 days and then studied daily for several weeks. Maternal and fetal pH, PCO<sub>2</sub> and PO<sub>2</sub> were normal in all experiments. The blood pressure (BP) and heart rate (HR) responses to selective intravenous injection of propranolol (1 mg/kg), practolol (1-2 mg/kg), atropine (1.0 mg/kg), phentolamine (0.1 mg/kg), phenoxybenzamine (5 mg/kg) and tyramine (0.25 mg/kg) were recorded. The adequacy of autonomic blockade was confirmed by absence of response to acetylcholine (5-15 µg/kg), isoproterenol (0.1 µg/kg) or methoxamine (50 µg/kg). Changes in HR from resting levels without significant BP change were observed as follows: propranolol 5-25% decrease, practolol 8-22% decrease and atropine 0-64% increase. Response to beta-adrenergic blockade did not vary significantly with gestational age. Phentolamine and phenoxybenzamine decreased systolic BP 2-14 and diastolic BP 2-12 mm Hg in 19/21 animals and tyramine increased systolic BP 7-60 and diastolic BP 10-46 mm Hg in 7/7 animals. No significant difference in sympathetic responses were observed in fetal and newborn lambs, indicating HR and BP to be under similar autonomic control at all ages studied.

Catecholamine uptake and storage of the newborn rat heart during post-natal development. GERALD F. ATWOOD and NORMAN KIRSHNER (Intr. by Madison S. Spach). *Duke Univ. Med. Ctr., Durham, N. C.*

The ability of atria, removed from Sprague-Dawley rats at ages 1-21 days, to take up and store catecholamines was studied to correlate this activity with the previously observed physiologic immaturity of the cardiac sympathetic nervous system in the neonate. The cardiac tissue was incubated in Krebs-Henseleit bicarbonate buffer containing 10<sup>-5</sup> M iproniazid and 10<sup>-7</sup> M H<sup>3</sup>-norepinephrine (H<sup>3</sup>NE). Total uptake and subcellular distribution at 1, 4, 7, 14, and 21 days were determined at various time intervals between 5 and 30 minutes. Uptakes at 0°C. served as controls.

Uptake rates were expressed on a per gram wet weight basis. There was a small amount of uptake observed during the first post-natal day (0.515 nanograms/minute) which increased only slightly by 4 days of age (0.683 ng/min). The most significant change occurred between 4 and 7 days (115%). Uptakes at 7, 14, and 21 days were similar to adult values. Since reserpine effectively blocks uptake of catecholamines into the storage granule,

10<sup>-5</sup> M reserpine was added to the incubation media to determine the role of the granule in the previously observed uptake. Reserpine inhibited the 30 minute uptake 57% during the first day of life increasing to 70% inhibition by 7 days of age. The uptake observed in the microsomal (granular) fraction showed similar developmental patterns and effect of reserpine. These studies suggest a marked inability of the newborn rat heart to take up and store norepinephrine due to either decreased number of storage vesicles or an immature uptake mechanism in the granule.

Energy production in the developing heart. ROBERT WELLS, BURTON E. SOBEL, and WILLIAM F. FRIEDMAN. *Univ. of Calif., San Diego Sch. of Med., La Jolla, Calif.*

The influence of growth on myocardial energy metabolism is not clear. Mitochondria are the main source of production of ATP in cardiac muscle. Accordingly, mitochondria from the hearts of 9 fetal and 7 newborn lambs, and 9 adult sheep were isolated in KCl-albumin-EDTA media, studied polarographically, and compared biochemically. No age-related differences were found in P/O ratios, a measure of efficiency of ATP production, with either succinate or glutamate as substrate; or in ATPase activities, in the presence or absence of DNP. However, mitochondria from fetal and newborn animals had significantly increased maximum O<sub>2</sub> consumption/mg protein in the presence of ADP (state III respiration) (0.19 ± 0.01 S.D. and 0.17 ± 0.01 µatoms/min.) compared to the adult (0.10 ± 0.01, p < 0.001). Thus, increased respiratory control ratios, a measure of the dependence of respiratory rate on ADP, were increased in the fetus (12.9 ± 0.6) and newborn (15.6 ± 2.6) compared to the adult (9.5 ± 0.5 p < 0.001). O<sub>2</sub> consumption in mitochondria uncoupled by DNP, was highest in the fetus and newborn (0.30 ± 0.02 and 0.29 ± 0.02 µatoms/mg protein) compared to the adult (0.16 ± 0.01, p < 0.01). These augmented respiratory rates in mitochondria from the youngest hearts may reflect increased electron transport, a view consistent with the finding of 56% of 65% greater cytochrome oxidase activities in fetal and newborn heart mitochondria, respectively, when compared to the adult. Thus, age-dependent differences exist in cardiac energy metabolism that are of potential importance to our understanding of myocardial function in the perinatal period.

Alteration of fetal pulmonary vasculature by maternal hypoxia. STANLEY J. GOLDBERG, RICHARD A. LEVY, BIJAN E. SIASSI, and JOANNE BETTEN. *Univ. of Arizona, Tucson, Ariz., UCLA, and USC Schools of Med., Los Angeles, Calif.*

A syndrome of pulmonary vascular obstruction in the newborn human in which massive right to left shunting occurs through the ductus arteriosus has been recently described. In an effort to simulate the syndrome in an animal model, pregnant rats were maintained in atmospheres containing 13%, 40% and 20% oxygen. The remainder of the atmosphere was nitrogen. In all other respects, pregnant rats were treated the same. Pregnant rats were removed from their experimental atmospheres during delivery so that all newborns were delivered into room air. Newborn rats were sacrificed at birth, the fourth, fifth, tenth, twelfth, thirteenth and twenty-first days of life. The entire lung was sectioned and stained so that intima and media could be easily distinguished. The medial to diameter ratio of all arteries between 50-150 microns (total = 474) were measured according to the technique of Wagenvoort. The mean ratio of neonatal arteries of progeny of hypoxic mothers was significantly thicker for each size group than those born of control or hyperoxic mothers. Thickening