

TITLE: INTEGRATED CORONARY AND SYSTEMIC HEMODYNAMIC RESPONSE TO GRADED INSPIRATORY RESISTIVE LOADING IN CHRONICALLY INSTRUMENTED ANESTHETIZED DOGS**AUTHORS:** J. Peters, M.D., P. Ihle, M.D.**AFFILIATION:** Zentrum für Anaesthesiologie, Heinrich-Heine Universität, D-4000 Düsseldorf, FRG**Introduction:** We have shown previously (1) that negative pleural pressure applied at constant left ventricular (LV) preload and heart rate decreased stroke volume, consistent with an increased afterload. This suggests that negative intrathoracic pressure, such as during airway obstruction or weaning from mechanical ventilation, could also alter coronary hemodynamics.**Methods:** Six dogs were chronically instrumented to measure circumflex coronary and ascending aortic blood flows (transit time ultrasonic flow probes), as well as left ventricular, aortic (micromanometers), and esophageal (air filled balloon) pressures. 3 weeks later inspiratory resistances of varying degree ("none, moderate, high") were imposed in random order for 10 min each during spontaneous breathing under chloralose anesthesia. Effects were contrasted (ANOVA, $p < 0.05$) to those of controlled mechanical ventilation (base line) sufficient to suppress spontaneous respiration.**Results:** As inspiratory resistance increased, peak negative and mean esophageal pressures decreasedto $-5.4 \text{ mmHg} \pm 0.2 \text{ SE}$ and -2.2 ± 0.5 (no resistance), -18.6 ± 2.8 and -5.4 ± 0.7 (moderate resistance), and -38.4 ± 4 and -11.8 ± 1.5 (high resistance), respectively, while PaCO_2 increased ($+2.5 \text{ mmHg} \pm 0.9$, $+8.4 \pm 1.2$, $+22.9 \pm 2.7$). This was associated with a progressive significant increase in circumflex coronary flow by $20.5\% \pm 5.3$, 33.2 ± 6.5 , and 65.2 ± 13.6 , almost exclusively accounted for by a decrease in diastolic coronary resistance ($-17.5\% \pm 3.7$, -21.2 ± 3.6 , and -44 ± 5). Heart rate mean transmural aortic pressure product, an estimate of LV oxygen consumption, increased by $20.7\% \pm 3.2$, 32.3 ± 14.7 , and 59.5 ± 23.4 , respectively, mainly due to increases in heart rate ($+18.4\% \pm 3$, $+23.1 \pm 10$, $+51.1 \pm 14$). Direct measurements of LV oxygen consumption (coronary sinus catheterization) in three dogs also demonstrated an increase. Systemic blood flow increased with inspiratory resistive loading while aortic resistance decreased.**Conclusion:** Thus graded inspiratory resistive loading is accompanied by pronounced changes in both the coronary and systemic vascular bed including a decrease in coronary vascular resistance, an increase in heart rate, and an increase in LV myocardial oxygen consumption. We conclude that inspiratory resistive breathing imposes an increased burden not only on the ventilatory but also on the circulatory pump.**References:** 1. Am J Physiol. 257: H120-131, 1989

Supported by DFG Pe 301-1

A612**TITLE:** A RAT MODEL OF CHRONIC HYPOXIA**AUTHORS:** P. Rothstein, M.D., W.F. Cao, M.D.**AFFILIATION:** Departments of Anesthesiology and Pediatrics, College of Physicians and Surgeons, New York, NY 10032**INTRODUCTION:** The laboratory study of hypoxemia requires a reproducible experimental preparation. We describe cardiac and hematologic characteristics of a chronic, normobaric hypoxic rat model.**METHODS:** Female Sprague-Dawley rats were placed in a chamber that provided free access to food and water. A nitrogen-oxygen mixture was flowed into the chamber to produce an ambient $\text{PatmO}_2 = 59 \pm 2 \text{ mmHg}$. Gas in the chamber was recirculated through an absorber to remove CO_2 . The chamber was opened briefly each day to weigh animals and change bedding and water. At the end of 1 and 2 weeks animals were sacrificed and the following variables measured: right ventricle/left ventricle weight (RV/LV), left ventricle/body weight (LV/BW), right ventricle/body weight (RV/BW), and hematocrit (Hct). Control values were obtained from animals not exposed to hypoxia. In selected animals, arterial pressure (Part) and gas tensions, and right ventricular pressure (Prvent) were measured. Values are reported as mean \pm S.D.**RESULTS:**

	CONTROL (N=85)	1 WEEK (N=63)	2 WEEKS (N=38)
BW (gm)	244 \pm 7	212 \pm 10	235 \pm 13
RV/LV	0.27 \pm .02	0.38 \pm .04*	0.51 \pm .08*
LV/BW	0.21 \pm .02	0.21 \pm .01	0.21 \pm .02
RV/BW	0.06 \pm .01	0.08 \pm .01*	0.11 \pm .02*
HCT (%)	43 \pm 3	56 \pm 4*	66 \pm 3*
Part#	138/101		122/99
PaO ₂ #	91 \pm 7		30 \pm 2 [~]
Prvent#	26/4		76/16 [~]

@: value $\times 100$ #: all pressures in mmHg*: different than control, $p < .001$, ANOVA~: different than control, $p < .001$, t-test**DISCUSSION:** This model produces systemic hypoxemia with concomitant polycythemia and right ventricular hypertrophy. Animals lost weight during the first week of exposure, then regained weight. Left ventricular mass was found to be constant with respect to body weight, whereas the right ventricle hypertrophied, apparently in response to hypoxia-induced pulmonary hypertension and right ventricular hypertension. Our model avoids surgical intervention to create hypoxemia and the mechanical problems associated with hypobaric models of hypoxemia. The model is not limited to examination of the cardiovascular system and can be used for studies of the behavior of other organs in the presence of hypoxemia.