HEATING-COOLING EFFECTS ON AIRWAY RESISTANCE MEASUREMENTS IN RATS, J.S. Reynolds, D.G. Frazer, B.M. Stolarik, W.G. McKinney, W.T. Goldsmith, and J.S. Fedan. E&CTB, PPRB, HELD, NIOSH, Morgantown, WV 26505. U.S.A.

Effects of thermal artifacts due to heating/cooling of air on airway resistance-compliance (Raw•Cg) measurements for rats by a two chamber plethysmograph have been studied. A simple RC model of the airways of a rat was coupled with an additional first order model of thermal flow. This system of equations is solved by a routine employing a Kalman gain for noise modeling. Four Sprague-Dawley rats were exposed to an aerosolized solution (15 mg/m^3) of methacholine (300 mg/mL) for approximately six minutes. Measurements were taken pre- and post-exposure. Raw•Cg and a thermal time constant (θ) were found for inspiration and expiration. These were compared to Raw•Cg calculated by a technique employed by Buxco using a double chamber plethysmograph which measures phase shift at the zero crossings after inspiration. Results are given below. All values are in msec ± standard error. θ is smaller for

	Pre-Exposure		Post-Exposure	
Parameter	Raw•Cg	θ	Raw•Cg	θ
Inspiration	2.16 ± 0.26	13.35 ± 3.15	9.43 ± 2.65	18.84 ± 4.22
Expiration	1.98 ± 0.33	27.01 ± 8.92	5.71 ± 1.18	19.84 ± 4.90
Zero Crossing	3.90 ± 0.39		10.98 ± 1.80	

inspiration because air heats faster during inspiration than it cools during expiration. The zero crossing method overestimates Raw•Cg by not accounting for thermal effects. For baseline measurements, Raw•Cg is twice as large using the Buxco method, but as Raw•Cg increases relative to θ the error is less pronounced.

This abstract is funded by: NIOSH

BIO-CALORIMETER SYSTEM TO MEASURE THE METABOLIC RATE OF LABORATORY ANIMALS AFTER INHALATION EXPOSURE TO TOXIC MATERIALS. W. T. Goldsmith, W. G. McKinney, L. Huffman, J.S. Fedan, J. S. Reynolds, E. Goldsmith, J. Smith, and D. G. Frazer. E&CTB, PPRB, HELD, National Institute for Occupational Safety and Health, Morgantown, WV. U.S.

Metabolic rate of animals can be affected by a variety of toxic agents. Virtual instrument software was developed to capture and display data provided by a modified direct calorimeter. The calorimeter system was evaluated by examining four groups of rats (n=6) injected with thyroxine(T_4) or solvent alone. Half of each group was exposed to ozone (2 PPM for 3 hours) or air. Breathing rates in addition to metabolic rates were measured pre-exposure, immediately post-exposure and 18 hours post-exposure. Metabolic rates were computed following equilibration which occurred in ten to twenty minutes.

Injection - Exposure	Metabolic Rate (calories / m^2 / hr.)		
	Pre-Exposure	Post-Exposure	18 hr. Post-Exposure
Solvent - Air	63.43 ± 1.89	66.40 ± 3.03	62.65 ± 1.80
Solvent - Ozone	62.96 ± 2.76	50.63 ± 3.65	58.10 ± 2.85
T_4 - Air	96.41 ± 1.29	88.87 ± 3.41	96.71 ± 3.99
T_4 - Ozone	92.52 ± 3.32	72.37 ± 3.07	71.06 ± 2.49

The calorimeter system provides non-invasive, reproducible results which can be used to evaluate an animal's metabolic response to toxic materials. In addition, the system displays and saves the data in real time and is easily operated.

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PULMONARY RESPONSES TO EPISODIC OZONE EXPOSURE IN RATS: BREATHING PATTERN AND AIRWAY SUBSTANCE P. E. S. Schelegle, W. F. Walby, M. F. Alfaro, D. M. Hyde and C. G. Plopper. Department of Anatomy, Physiology, and Cell Biology and The Center for Comparative Respiratory Biology and Medicine, U. C. Davis, CA, USA 95616.

Initial exposure to oxidant air pollutants, such as ozone (O_3), results in severe cellular, physiologic and inflammatory changes from acute injury . However, there is little understanding of how the lungs respond to repeated episodes of exposure. To determine the impact of repeated episodes of exposure on breathing pattern, physiologic adaptation, and airway Substance P (SP) levels, adult male Harlan Sprague Dawley rats were exposed to 2 episodes (5 days each, 1PPM, 8 hrs/day) followed by 9 days of filtered air (FA). Breathing pattern and ventilatory response to 8% CO_2 was assessed daily. Rats were sacrificed on days 0, 1 and 5 of exposure and 9 days after each exposure episode. The trachea were analyzed for SP. **Episode 1**, Day 1: No change in breathing frequency (f_R), Tidal volume (V_t) decreased 48 and 53% (air and CO_2 challenge, respectively) compared to pre-exposure #1 baseline (V_t = 1.3/2.25 ml, f_R = 148/196 bpm, air/CO_2), SP decreased by 26% compared to FA controls (292 pg/mg protein). Day 5: All ventilatory parameters had returned to pre-exposure levels but SP decreased 56%. Day 9 Recovery: Breathing pattern and CO_2 response were similar between groups, SP levels recovered to 199. **Episode 2**, Day 1: V_t decreased 51 and 56% compared to pre-exposure #2 baseline (V_t = 1.53/2.44 ml, f_R = 134/195 bpm), f_R increased 37 and 24%, SP levels decreased by 49%. Day 5: Neither V_t or f_R had returned to pre-exposure values, Sp levels were decreased by 44%. V_t remained depressed through day 5 of recovery while SP levels recovered to 220 (pg/mg protein) by day 9. This data suggests that maintenance of SP levels is not required for full development of the acute O_3 response and subsequent adaptation with repeated episodic exposure.

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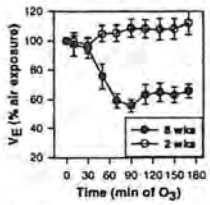
VENTILATORY RESPONSES TO OZONE (O_3) ARE REDUCED IN IMMA... RATS. S.A. Shore, J. Abraham, and G.G. Krishna Murthy. Physiology Progr... Harvard School of Public Health, Boston, MA.

During O_3 exposure, rats decrease their minute ventilation (V_E). Because the d... O_3 delivered to the lungs is the product of O_3 concentration, exposure time, and r... decrease in V_E is likely to be protective. To determine whether such changes are ... observed in immature animals, Sprague Dawley rats ... 2 wks or 8 wks, were exposed to O_3 (2ppm) in nose ... exposure plethysmographs. The rats breathed filtered ... for 45 min, then O_3 for 3 hours. In 8 wk rats, O_3 c... approximate 35% decrease in V_E (Fig, solid circles, ... begins at t=0). The change in V_E was primarily the r... a decrease in tidal volume (V_T). The timing of ventil... was also altered, such that inspiratory time (Ti) decr... and expiratory time (Te) increased. Much of the in... in Te was the result of an increased end expiratory p...



Baseline V_E normalized for body weight was greater in 2 wk than 8 wk rats (2.3 ... vs 0.68 ± 0.065 ml/min/g body weight), consistent with the high metabolic rates ... younger animals. This difference was primarily the result of a greater specific V_E ... though frequency was also higher. Not only was V_E higher in 2 wk old rats, but th... induced decrease in V_E did not occur (Fig, open symbols). Indeed in 2 wk old ra... caused virtually no change in any aspect of the pattern of breathing. The lack of a ventilatory response to O_3 in 2 wk old rats could be the result of incomplete matur... of the neural circuits that link activation of sensory afferents to changes in ventilat... The increased baseline V_E and the absence of any decrease in V_E during O_3 expos... 2wk old rats implies that their delivered dose of O_3 is much higher than in 8 wk ra...

This abstract is funded by: HL33009, HL56383, ES00002

Vagal C-Fiber Mediated Rapid Shallow Breathing Limits Ozo... Induced Reparative Epithelial Cell Proliferation of Distal Airways ... Conscious Rats. M. F. Alfaro, D. M. Hyde, L. Putney, M. Stovall and E... Schelegle. Dept. Anat., Physiol., and Cell Biol. School of Veterinary Medicine & C... for Comparitive Respir. Biol. and Med., Univ. of Calif., Davis, CA, USA.

We examined the role that vagal C-fiber mediated rapid shallow breathing plays in the disribution of airway injury induced by acute ozone inhalation. Seventeen W... rats weighing 250-300g were anaesthetized and both vagus nerves were isolated ... treated with either 1% capsaicin in mineral oil or mineral oil for 2 min. Followi... vagal perineural capsaisin treatment (VPCT) osmotic minipumps loaded with bro... deoxyuridine (BrdU) were placed s.c. between the scapula. After 20 hrs of recovery ... rats were placed in 8 liter glass exposure chambers and exposed to either FA or 1p... O3 for 8 hrs followed by 16 hrs post-exposure recovery. Tidal volume (VT), breath... frequency (f) and minute ventilation (VE) were measured continuously during ... exposure and during the first 4 hrs of recovery in the conscious unrestrained ... Sixteen hrs postexposure the rats were sacrificed and prepared for the morphometr... analysis of the regional distribution of BrdU incorporation into proliferating epithel... cells of proximal conducting airways and terminal bronchioles. The control rats expos... to O3 developed a marked rapid shallow breathing pattern, while the VPCT rats exposed to O3 showed no changes in f and only a mild delayed decrease in VT after 3 hours of exposure. Both FA groups showed no alterations in breathing pattren. The pattern and density of BrdU epithelial labeling of the large conducting airways was similar in control and VPCT rats exposed to O3. Whereas, there was greater BrdU epithelial labeling in the terminal bronchioles of VPCT rats compared to control rats exposed to O3. These studies demonstrated the protective role that vagal C-fiber mediated rapid shallow breathing plays in limiting the injury to the distal airways of conscious rats during acute O3 inhalation.

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MUSCARINIC RECEPTOR BLOCKADE INHIBITS OZONE-INDUCED INFLAMMATION. A.N. Freed, and S. McCulloch. The Johns Hopkins Medical Institutions, Baltimore, MD 21205, USA.

The purpose of this study was to evaluate the role of muscarinic receptors on the development of peripheral airway obstruction produced by an acute local exposure to ozone (O_3) in dogs. We hypothesized that an O_3 stimulated muscarinic-dependent pathway is eclipsed by a muscarinic-independent pathway during or after O_3 exposure. To test this hypothesis we compared untreated and ipratropium bromide (IPB) pretreated canine sublobar airways that were locally exposed via a bronchoscope for 6 h to either room temperature-humidified air or humidified 0.2 ppm O_3. Peripheral airway resistance (R_p) was monitored throughout the study and airway reactivity to hypocapnia was recorded before, and at 6 and 18 h after exposure. Although air had no effect, O_3 progressively increased R_p during the exposure, and R_p was further increased 18 h later. At that time, bronchoalveolar lavage revealed the development of significant neutrophilic inflammation. O_3 exposure did not affect airway smooth muscle reactivity at any time. IPB abolished the O_3-induced increase in R_p during exposure, but not the increase in R_p 18 h later. However, this late airway obstruction was significantly less than that seen in untreated O_3 exposed airways. Finally, IPB significantly reduced the O_3-induced airway inflammation. These data suggest that 1) O_3-induced airway obstruction and inflammation are mediated via muscarinic receptors, and 2) the obstruction that develops 18 h later results from muscarinic-dependent and muscarinic-independent pathways.

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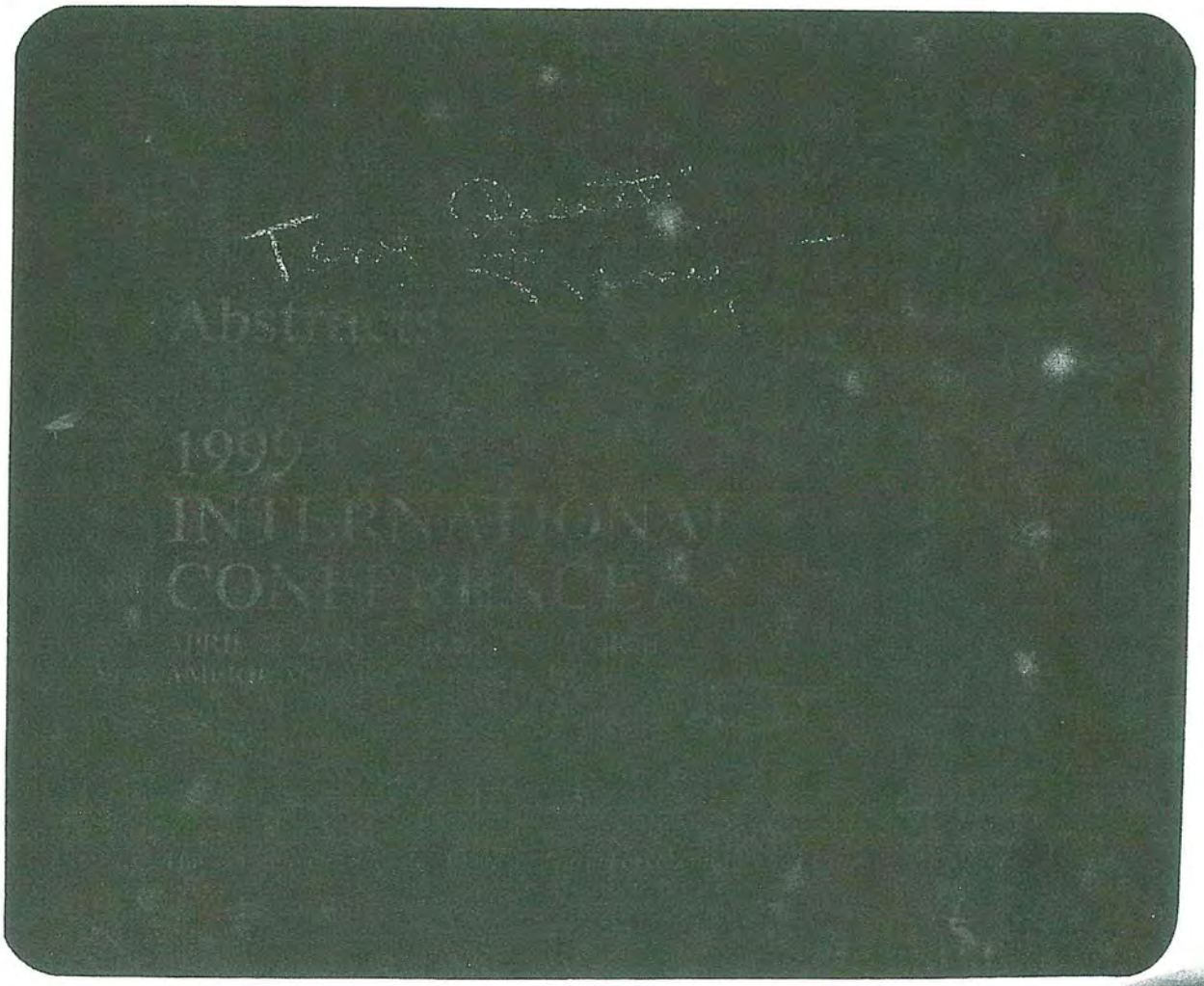

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