**The Effect of Exercise on Nasal Absorption of Ozone in Healthy Human Adults**

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The nose may help protect the lower respiratory tract from the effects of ambient ozone by scrubbing ozone from inspired air. Reductions in both nasal resistance and nitric oxide production with exercise may influence the efficiency of ozone uptake in the nose. Nasal ozone uptake was measured in ten healthy volunteers before and after 15 minutes of moderate, bicycle exercise. Ozone (0.2ppm) was pulled through both nostrils and out of the mouth at a constant flow while the subjects closed their epiglottis. Nasal uptake of ozone was determined by comparing the ozone concentration entering the nostrils to that exiting the mouth. Average pre-exercise uptake of ozone was 56% (+/- 7.8) and 37% (+/- 4.9) at 10 and 20 l/min, respectively. These averages did not significantly differ from those immediately post-exercise (55% and 37%). Nasal ozone uptake increased significantly ($p < 0.001$) with decreasing flow rate, but intersubject variability in uptake could not be predicted by nasal volume or cross-sectional areas (as measured by acoustic rhinometry), or endogenous nitric oxide production. However, the percent change in ozone uptake after exercise, within an individual, was correlated with both 1) percent change in nasal volume ($r = 0.70$ at 10 l/min) and 2) percent change in the rate of volumetric expansion between the nasal valve and turbinates ($r = 0.82$ at 10 l/min). These results may be useful for assessing human risk associated with ozone exposure

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**Nasal Effects of VOCs and Ozone**

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RATIONALE Volatile organic compounds (VOCs) may contribute to the nasal symptoms that are prominent in indoor air complaints. A mixture of 22 VOCs has been associated with nasal irritation and increased PMNs in nasal lavage (NAL). Unsaturated VOCs and ozone react to form particles, aldehydes and other irritating compounds. We hypothesized that exposure to 23 VOCs and ozone (VOCO) would cause more nasal irritation and inflammation than VOCs or clean air (CA). METHODS In a repeated measures design, 62 healthy women completed (to date) three 3-hour exposure conditions. Subjects were screened for atopy by questionnaire and RAST, and stratified as high and low chemical odor intolerance (CI) based on self-report. VOCs and ozone were maintained in the exposure chamber at 7 ppm and 40 ppb, respectively. The CA exposure was effectively masked with a pulse of VOC mixture (0.7ppm) at the onset of the exposure condition. Symptoms were rated before, during, and after exposure. NAL fluid, collected before and after exposure, was analyzed for PMNs, IL-6 and IL-8. RESULTS Measurements confirmed the formation of aldehydes and reactive particles during the VOCO condition. We found no significant differences in total symptoms or nasal symptoms between VOCO, VOC and CA conditions, nor did we find differences in markers of nasal inflammation between conditions. There were no increases in these measures for hi- vs. low-CI, or for atopic vs. non-atopic subjects. CONCLUSIONS Effective blinding to the exposure conditions, absent in prior studies showing positive results, may explain the negative symptom findings, but physiologic discrepancies with prior research lack clear explanations.

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**Ozone Alters the Differentiation of PGP 9.5 Positive Ciliated Epithelial Cells in the Airways of Infant Rhesus Monkeys**

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Epidemiological studies indicate that ozone (O3) exposure during childhood results in decrements of lung function. This is supported by recent experimental data showing that O3 exposure during postnatal lung development leads to airways remodeling including diminished epithelial innervation and a corresponding increase in the number of protein gene product 9.5 (PGP 9.5) positive epithelial cells. This study was designed to test the hypothesis that O3-induced increases in PGP 9.5 cells in postnatal rhesus monkeys is caused by retarded lung development. We compared airways from 6-month-old and 5-day-old monkeys using markers for PGP 9.5, a widespread neuronal marker, serotonin (5HT) for neuroendocrine cells (NECs), and beta tubulin to identify cilia. Left cranial lobes from 5-day-old monkeys housed in filtered air (FA) and 6-month-old monkeys exposed to FA or O3 for 11 episodes (5days at 0.5 ppm, 8 hrs/day) were inflation fixed with paraformaldehyde, dissected to expose the airway tree, processed for whole mount immunohistochemistry, and imaged by confocal microscopy. In 5-day-old monkeys, there were focal areas of PGP 9.5 positive/5HT negative ciliated epithelial cells organized in strips running parallel with the airway. The 6-month FA controls lacked the cells seen in the 5-day-old monkeys, however, they did have a typical population of non-ciliated NECs. In the 6-month O3 exposed monkeys, there were substantial localized strips of PGP 9.5 positive/5HT negative ciliated epithelial cells with intermingled NECs. We conclude that O3 retards the normal differentiation of PGP 9.5 positive ciliated epithelial cells in the airways of infant rhesus monkeys.

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**Sex-Specific Induction of Pulmonary Glutathione S-Transferase (GST) a CYP2F2 after Chronic Pre and Postnatal Exposure to Sidestream Tobac Smoke (TS)**

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The lung is capable of substantial metabolic bioactivation and detoxification chemicals by enzymes that shift in abundance during lung development. The effect a lifetime of exposure to TS on these enzymes by sex in the mouse lung is not kno We used aged and diluted TS to determine the effect of chronic exposure during lu development on pulmonary expression of GST and CYP2F2. Male and female m were exposed to either 1 mg/m3 TS or filtered air (FA) 5 d per wk starting at 6 d ges tional age and continuing until adulthood. Pulmonary morphology was evaluated us high resolution histopathology. Distribution and abundance of CYP2F2 and GST alp mu and pi enzymes was defined using immunohistochemistry. CYP2F2 was quantif using laser capture microdissection and Taqman RT-PCR. TS produced increases immune and neuroendocrine cells in both sexes. High levels of GSTs and CYP2 were found in the conducting airway epithelium. Expression of CYP2F2 was eleva in female, but not male, mice exposed to TS, particularly in terminal bronchiolar epit lium. GST pi was lowest in the FA female less than TS female=FA male less than male. The expression of the GST mu and alpha did not differ by sex but increased distribution and abundance in response to TS. We conclude that chronic TS expos during lung development alters steady state protein expression of xenobiotic metal lizing and detoxifying enzymes and that these effects differ by gender. This may res in a mismatch in metabolic activation/detoxification that renders females more susc tible than males to compounds that are activated by CYP2F2 and detoxified by GST

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**A Dynamic Nonlinear Model of Ozone-Induced FEV1 Response unc Changing Exposure Conditions**

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Ozone exposure results in FEV1 decrements which are a function of oz concentration (C), minute ventilation, time, and age. We have previously identif a two-compartment dynamic exposure-response model which accurately predic mean FEV1 change as a function of these variables for two-hour controlled oz exposures. The purpose of the present analysis was to determine whether a simi but improved, model could accurately describe FEV1 responses from an expan group of 15 existing studies including some of longer duration, some with chang activity patterns, and some which include measures made during recovery in cl air. Participants were healthy, white males, ages 18-35 yrs, exposed under vari conditions (C=0.0 to 0.4 ppm, activity level = rest to heavy exercise, exposur 1 to 7.6 hrs, recovery = 0.5 to 3.3 hr). A total of 3502 observations were provi by 547 participants. The data were successfully fit to the nonlinear mixed eff model using SAS proc NLMIXED with all coefficients observed to be statistic significant. Response decreased by 3.9% (95% CI= 1.8 to 6.1%) per yea increased age, and the time constant of the first compartment was 4.1 hr (95% C 3.6 to 4.6). The model described the 3502 responses accurately with the excep of some underprediction at the highest dose rates. We concluded that this model capable of accurately describing response to ozone across the range of condition these studies, and we hypothesize that it is capable of predicting FEV1 respc over time as a result of the dynamic ozone exposure conditions experienced in environment. This abstract of a proposed presentation does not necessarily re sent EPA policy.

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**Ambient Air Quality in the Vicinity of Large Swine Production Facilities**

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The industrialization of livestock production has led to concern over pu health impacts from air emissions. Hazardous emissions from Concentrated An Feeding Operations (CAFOs) include gases, bioaerosols, odors, and other semi atile organic compounds. While research has established that these emissions occupational hazards, there is less known about adverse effects on surroun communities. Methods: Iowa CAFOs were selected and the downwind ambier monitored at the nearest public use area. Along with meteorological conditi analytes measured included odor, hydrogen sulfide (H2S), ammonia, inhal particulate, volatile organic compounds, and bioaerosols including endot fungi, mesophilic bacteria, and gram-negative bacteria. Results: Downwind m toring distances ranged from 23 to 418m. Meteorologic conditions varied wide temperature (range: 12-33°C), relative humidity (range: 37-97%) and wind sp during sampling (range: 1-8 m/s). The maximum 1 hr time-weighted average concentration was 68 ppb, however, most sites ranged between 6-14 ppb. Endot ranged from 4-3371 EU/m3 and one-third of the sites exceeded 200 EU/m3. In able particulate ranged from below detection to 576 μg/m3 with most sites sho levels between 75-300 μg/m3. Odor levels generally tracked with H2S. Airb gram-negative enteric bacteria averaged 1.1x103 CFU/m3 while mesop bacteria averaged 2.0x103 CFU/m3. The mean concentration of culturable f was 5.2x103 CFU/m3. Conclusion: This study demonstrates that off-site conce tions of gases, particulates and bioaerosols occurring downwind from CAFOs a levels high enough to cause health concerns.

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