Immunostaining for P- and N-cadherins suggested changes in Sertoli cell - gonocyte interactions in the DBP-treated testis. Our data indicate that *in utero* exposure to a high dose of DBP affects cords formation and development of Sertoli cells that may alter meiosis in gonocytes. These data support the hypothesis linking impaired spermatogenesis in the adults with failure of fetal Sertoli cells to proliferate and mature.

927 MODULATION OF HOST DEFENSES BY AIR POLLUTANTS.

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Epidemiological evidence links air pollutants with increases in morbidity and mortality in susceptible populations. Among the health effects of long term and episodic air pollution, parameters associated with respiratory infections in susceptible populations, especially small children and the elderly, may be of primary importance. The mechanistic work detailing the modulation of infection by air pollutants is a developing and exciting field of research that brings together cutting edge biology and mechanistic toxicology. For example, the role of toll-like receptors (tlr) in response to infection and airborne particulates has been recognized. This symposium will address the epidemiological evidence suggesting that ambient air pollutants may modulate the occurrence and/or severity of respiratory infection. Subsequently, the current state of experimental models of host defense mechanisms and pathogenesis will be presented in relation to both bacterial and viral respiratory infection as modulated by individual pollutants and pollutant mixtures. Speakers will detail susceptibility to, and lung clearance of gram positive and negative bacteria, and viruses such as RSV. Focus will be placed on infection models modulated by ambient particulates, source emissions (coal fly ash and diesel exhaust), and metals. Target Audience: This Symposia encompasses the fields of microbial pathogenesis, immunology, air pollution, mixtures and mechanistic toxicology.

928 MECHANISMS OF HOST DEFENSE.

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The respiratory tract is maintained in a remarkably sterile condition by the combined anti-microbial activity of the mucociliary, phagocytic and immune systems. Epidemiological studies of smokers and others exposed to high levels of air pollutants have demonstrated that these individuals suffer from more frequent and severe respiratory infections. Experiments in animals have also shown that a wide range of airborne pollutants including cigarette smoke, oxidant gases, acid aerosols, metals, organic compounds, and combustion products can interfere with the normal defense processes of the lung to enhance susceptibility to respiratory infection. The mechanisms for these effects include decreases in mucociliary clearance and macrophage phagocytosis, as well as reduced specific immune responses such as antibody formation, and natural killer (NK) and T cell function. Although there is some evidence that similar effects occur in humans, the link to ambient air pollutants are not as strong because of incomplete individual exposure histories. Animal studies provide dosimetric information, which can be used to predict the relative health risk of simple and complex exposures, and also lend insight into the mechanisms of air pollution toxicity. This presentation will describe host defense processes in the respiratory tract and illustrate how these may be reduced by air pollutant exposure resulting in increased severity of lung disease. These data can then be applied to risk assessment through *in vitro* and *in vivo* comparisons of immune function in animals and humans. This abstract does not reflect EPA policy.

929 EPIDEMIOLOGY OF AMBIENT AIR POLLUTION AND PULMONARY INFECTION.

A. Pope. *Department of Economics, Brigham Young University, Provo, UT.* Sponsor: M. Reed.

Substantial epidemiological evidence suggests that air pollution common to many urban and industrial environments is a risk factor contributing to the exacerbation or development of pulmonary infection in susceptible populations including children and the elderly. Associations observed include an increased prevalence of respiratory symptoms consistent with chronic and acute pulmonary infection, and increased hospitalizations for bronchitis and pneumonia. These findings suggest that inhaling air pollutants may modulate host defenses and immunity. This presentation will review the current state of epidemiological associations of air pollutants, especially those of ambient air, with risk of pulmonary infection.

930 INCREASED LUNG PATHOGENESIS TO RESPIRATORY VIRAL INFECTION BY DIESEL ENGINE COMBUSTION COMPONENTS.

K. S. Harrod[1], J. A. Berger[1], J. D. McDonald[2] and M. D. Reed[2]. *[1]Asthma and Pulmonary Immunology Program, Lovelace Respiratory Research Institute, Albuquerque, NM and [2]Toxicology, Lovelace Respiratory Research Institute, Albuquerque, NM.*

Epidemiology studies clearly indicate a relationship between poor air quality and childhood illness, particularly respiratory infections. However, experimental evidence is lacking, leaving a poor understanding of the mechanisms by which air pollutants alter susceptibility to pulmonary infections and disease. Using an inhalation exposure system of diesel engine emissions (DEE), altered susceptibility to a common childhood pathogen, respiratory syncytial virus (RSV), was examined in an *in vivo* experimental model. At concentrations reflecting ambient exposures, RSV persistence was increased in the respiratory tract following exposure to inhaled DEE, and increased lung viral burdens were concordant with increased lung pathogenesis and disease. Following exposure to DEE, distinct lung epithelial cell populations exhibited altered remodeling and/or injury to RSV infection. Evidence shows that lung epithelial-specific mechanisms of host defense or immunomodulation were altered by prior exposure to DEE. Furthermore, adaptive and innate immune mechanisms were exacerbated by DEE following infection, suggesting a greater reliance on immune mechanisms for clearance of RSV from infected lungs. Collectively, these studies suggest a role for air pollutants from engine combustion sources in the increased susceptibility to respiratory infection and provide an experimental model for elucidation of mechanisms by which these pollutants contribute to respiratory disease in childhood.

931 EFFECT OF WORKPLACE PARTICULATES ON THE SUSCEPTIBILITY TO BACTERIAL INFECTION AND THE SUPPRESSION OF LUNG DEFENSE RESPONSES IN RATS.

J. M. Antonini. *Health Effects Laboratory Division, National Institutes of Occupational Safety and Health, Morgantown, WV.*

Inhalation of increased levels of air pollutants generated in the workplace and environment may augment pulmonary infection and increase morbidity and mortality. The effect of exposure to different workplace particulates on lung defense responses was investigated using a rat bacterial infectivity model. Male Sprague-Dawley rats were pretreated by intratracheal instillation with 1.0 mg/100 g body wt of residual oil fly ash (ROFA), stainless steel welding fumes particulate matter (SS), or silica (Si) prior to bacterial inoculation with 5×10^3 or 5×10^5 Listeria monocytogenes. Particle-induced effects on pulmonary clearance of the bacteria, lung macrophage function (phagocytosis, oxidant production, and bacterial killing), and the secretion of lung cytokines, important in immune responses, were assessed. Pretreatment with ROFA and SS significantly slowed the lung clearance of bacteria, increased animal morbidity, suppressed macrophage function, and altered IL-2, IL-6, and IL-10 production after infection. The suppression observed for ROFA was due to soluble metals, whereas a combination of soluble and insoluble metals was responsible for the effect seen with SS. Conversely, Si pretreatment enhanced lung bacterial clearance and significantly upregulated non-specific lung defense responses (macrophage phagocytosis, oxidant production, and neutrophil activation) despite the presence of significant lung inflammation and fibrosis. In conclusion, inhalation of different workplace particulates may induce varied lung defense responses to infection. Chronic exposure to metal particles in the workplace may alter macrophage function and increase the susceptibility to lung infection in exposed workers.

932 EXACERBATION OF PULMONARY PNEUMONIA BY INHALED AMBIENT PARTICULATE MATTER AND ASSOCIATED METALS.

J. T. Zelikoff, Y. Li, K. Schermerhorn, M. D. Cohen and R. B. Schlesinger. *Nelson Institute of Environmental, NYU School of Medicine, Tuxedo, NY.*

Epidemiological studies demonstrate that pneumonia contributes to the increased morbidity among individuals following exposure to ambient particulate matter (PM). This suggests that inhaled PM can act as an immunosuppressant. A 5 hr exposure of Streptococcus pneumoniae-infected rats to concentrated PM 2.5 μm from N.Y City air exacerbates infection and depresses antimicrobial pulmonary defense mechanisms. Infected rats exposed to PM 48 hr following bacterial instillation have increased: pulmonary bacterial burdens; bacterial-associated lung lesions; and, bacteremia compared to sham. Exposure to CAPS also decreased lavageable neutrophils, cytokines, and bronchus associated lung tissue. To identity the possible constituents responsible for the worsening pneumonia, studies were undertaken to

Society of Toxicology
43rd Annual Meeting
Baltimore, Maryland

THE TOXICOLOGIST

a supplement to
TOXICOLOGICAL SCIENCES

An Official Journal of the Society of Toxicology

Volume 78, Number S-1, March 2004

Preface

This issue of *The Toxicologist* is devoted to the abstracts of the presentations for the symposium, workshop, roundtable, platform and poster sessions of the 43rd Annual Meeting of the Society of Toxicology, held at the Baltimore Convention Center, Baltimore, Maryland, March 21-25, 2004.

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