Impact of Combustion Related Pollutants (CRPs) on the Development of Asthma

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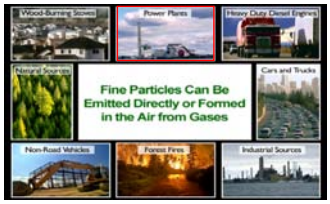
Science Questions

Epidemiology studies have shown convincingly that during episodes of air pollution, emergency room visits and medication use in asthmatics increase. Recent studies supported by EPA have also suggested that exposure to CRPs such as diesel exhaust, and secondary atmospheric products like ozone, can increase the actual incidence of asthma events in adults and in children. These reports have prompted us to ask:
What is the relationship between exposure to air pollutants and the incidence and severity of asthma?
On a comparative basis, which sources of combustion related pollutants (CRPs) enhance asthmatic disease the most?
What are the biological mechanisms by which air pollution components affect the incidence and severity of asthma

Research Goals

Asthmatics and children in particular appear to be more sensitive to air pollutants than healthy individuals and thus represent a susceptible sub-population that has added risk to CRP exposure. The goals of this program are to identify which CRPs, and the relevant concentrations and components of these that may affect the incidence or severity of asthma. Determination of the biological mechanisms for these effects will underlie extrapolation to the public scenario



Approaches/Methods

The approach tests the general hypothesis that environmental factors influence the induction and exacerbation of asthma, and that these factors can be controlled. This multidisciplinary program spans numerous scientific areas including exposure assessment, combustion engineering and chemistry, epidemiology, pulmonary medicine, laboratory animal science, mucosal immunology, airway physiology and molecular biology. Epidemiology and exposure assessment studies provide information on what type and concentrations of pollutants are in the air, what sources they come from, and whether they are associated with the incidence or severity of asthma in the population. Clinical experiments and panel studies provide more specific and detailed information on personal exposures and susceptibility factors which may drive the progression of disease during or after exposures. Animal studies screen a large number of exposure scenarios for hazard identification and quantitative risk assessment purposes, and are used to test different biological mechanisms of the effects.

Exposure Assessment

Collection of particulate matter and other air pollutants related to CRPs have been performed using specialized personal exposure monitors. Additionally, residential indoor, residential outdoor and community-based monitoring have been conducted involving children and adults asthmatics in panel studies. The result of this effort is a better understanding of what asthmatics are exposed to and some of the first coordinated efforts in investigating potential exposure factors of this susceptible subpopulation.

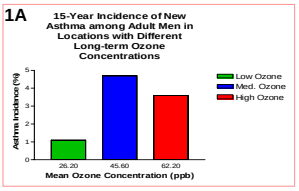
Personal monitoring

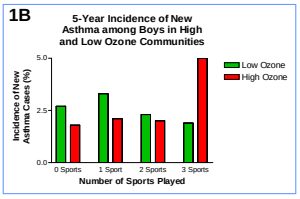
Residential monitoring

Community monitoring

Epidemiology and Panel Studies

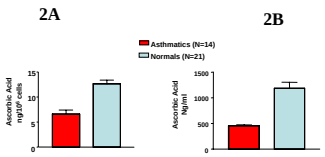
Long-term residence in areas of high ambient ozone concentration was associated with an increased incidence of new cases of asthma in adult men (Fig1a) and in boys who participated in at least 3 sports (Fig1b). Similar effects were not observed for girls or women.

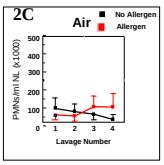


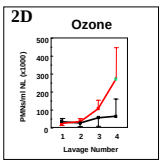


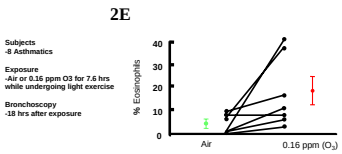
Clinical Studies

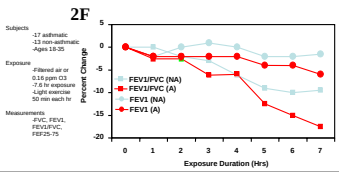
Asthmatics have less antioxidants (ascorbate) in their airway cells (Fig 2A) and lung fluid (Fig 2B) than healthy subjects, making them more susceptible to oxidant pollutants such as ozone. Asthmatics exposed to 0.16 ppm ozone also have a greater neutrophil cell influx in the nose following allergen challenge (Fig 2C & 2D). Asthmatics exposed to 0.16 ppm ozone have increased eosinophils in bronchoalveolar lavage fluid 18 hrs after exposure compared (Fig 2E), in contrast with non-asthmatics who do not have an eosinophil response to ozone. Asthmatics also experience larger ozone-induced decrements in lung function than healthy subjects (Fig 2F).





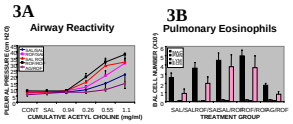




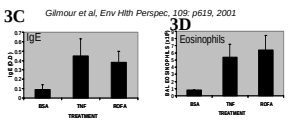


Animal Studies

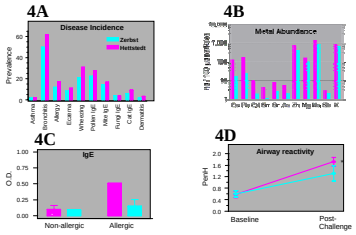
Rats exposed to residual oil fly ash increases airway reactivity (Fig 3a) and pulmonary eosinophils (Fig 3b) during allergic sensitization to house dust mite allergic. This allergic adjuvancy can be reproduced with the pro-inflammatory cytokine TNF-a (Fig 3c & 43), and ameliorated by neutralizing this signaling molecule (not shown).



Gilmour et al, Env Hlth Perspec, 109: p619, 2001



Rate of allergic disease is higher in the industrial town of Hettsted that Zerbst (Fig 4a) and this is associated with increased level of metals in PM 2.5 samples (Fig 4b). Mice treated with PM2.5 from Hettsetdt have higher IgE levels (Fig 4c) and airway reactivity (Fig 4d) following sensitization to ovalbumin than animals treated with the same amount of PM 2.5 from Zerbst.



Impact and Outcomes

The results of these studies directly feed into criteria documents and standard setting for various air pollutants (e.g. http://cfpub.epa.gov/ncea). In addition, the information is used by the Office of Air and Radiation and the Office of Transportation and Air Quality, for hazard identification and risk and benefits assessment purposes. Most recently the data has also served to develop new educational materials, and programs which support health messages for the Air Quality Index http://www.airnow.gov/health-prof/. Fundamental research on the development of asthma contributes to understanding host and environmental risk factors for regulatory and outreach programs.

Future Directions

Current approaches in population studies are examining the relationship between asthma prevalence and the proximity to roadways or presence of vehicle exhaust tracers. People respond differently to the same environmental exposures due in large part to genetic heterogeneity. Ongoing clinical investigations are tracing single nucleotide polymorphisms (SNPs) in healthy and asthmatic individuals to identify genetic factors that influence asthma susceptibility and pathogenesis in response to inhaled pollutants. Exposure studies are manipulating the chemistry of combustion atmospheres to find which components most affect asthmatic responses, and are then applying computational toxicology models to predict these effects in ambient air sheds. In addition, different strains and genetically altered animals are being used to identify response elements which are responsible for increased development or severity of allergic lung disease.

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