Science Abstracts on Diesel Exhaust

Children's Exposure to Diesel Exhaust on School Buses

J. Wargo, D. Brown, Environment & Human Health, Inc. (2002)

Abstract:
In the United States nearly 600,000 school buses transport 24 million students to school daily. Each year buses travel 4.3 billion miles as children take nearly 10 billion school bus rides. If rides average 30 minutes in each direction, students will spend 180 hours on buses each year. Collectively, U.S. children spend 3 billion hours on school buses.

A vast majority of U.S. school buses are powered by diesel fuel. Diesel exhaust is comprised of very fine particles of carbon and a mixture of toxic gases. Federal agencies have classified diesel exhaust as a probable human carcinogen. Benzene, an important component of the fuel and exhaust, is designated to be a known human carcinogen. Components of diesel exhaust are genotoxic, mutagenic, and can produce symptoms of allergy, including inflammation and irritation of airways. There is no known safe level of exposure to diesel exhaust for children, especially those with respiratory illness.

Diesel exhaust can adversely affect children with underlying respiratory illness such as asthma, bronchitis, and infections. Diesel emissions may enhance the effects of some allergens among sensitive individuals. Children's airways are not yet fully developed and have a smaller diameter than those of adults. If airways are inflamed or constricted by asthma, allergies or infections, diesel exhaust may make breathing more difficult.

Fine particulate concentrations (PM2.5) measured on buses in this study were often 5-10 times higher than average levels measured at the 13 fixed-site PM2.5 monitoring stations in Connecticut. Levels of fine particles were often higher under certain circumstances: when buses were idling with windows opened, when buses ran through their routes with windows closed, when buses moved through intense traffic, and especially when buses were queued to load or unload students while idling.

* * *

Inhalation of diesel exhaust and allergen alters human bronchial epithelium DNA methylation

Clifford, et al, Journal of Allergy and Clinical Immunology, January, 2017

Abstract: Allergic disease affects 30% to 40% of the world's population, and its development is determined by the interplay between environmental and inherited factors. Air pollution, primarily consisting of diesel exhaust emissions, has increased at a similar rate to allergic disease. Exposure to diesel exhaust may play a role in the development and progression of allergic disease, in particular allergic respiratory disease. One potential mechanism underlying the connection between air pollution and increased allergic disease incidence is DNA methylation, an epigenetic process with the capacity to integrate gene-environment interactions. We sought to investigate the effect of allergen and diesel exhaust exposure on bronchial epithelial DNA methylation. We performed a randomized crossover-controlled exposure study to allergen and diesel exhaust in humans, and measured single-site (CpG) resolution global DNA methylation in bronchial epithelial cells. Exposure to allergen alone, diesel exhaust alone, or allergen and diesel exhaust together (coexposure) led to significant changes in 7 CpG sites at 48 hours. However, when the same lung was exposed to allergen and diesel exhaust but separated by approximately 4 weeks, significant changes in more than 500 sites were observed. Furthermore, sites of differential methylation differed depending on which exposure was experienced first. Functional analysis of differentially methylated CpG sites found genes involved in transcription factor activity, protein metabolism, cell adhesion, and vascular development, among others. These findings suggest that specific exposures can prime the lung for changes in DNA methylation induced by a subsequent insult.

Exposure to allergen and diesel exhaust particles potentiates secondary allergen-specific memory responses, promoting asthma susceptibility

Brandt, et al, Journal of Allergy and Clinical Immunology August 2015

Abstract: Exposure to traffic pollution particulate matter, predominantly diesel exhaust particles (DEPs), increases the risk of asthma and asthma exacerbation; however, the underlying mechanisms remain poorly understood. We sought to examine the effect of DEP exposure on the generation and persistence of allergen-specific memory T cells in asthmatic patients and translate these findings by determining the effect of early DEP exposure on the prevalence of allergic asthma in children. The effect of DEPs on house dust mite (HDM)–specific memory responses was determined by using an asthma model. Data from children enrolled in the Cincinnati Childhood Allergy and Air Pollution Study birth cohort were analyzed to determine the effect of DEP exposure on asthma outcomes. DEP co-exposure with HDM resulted in persistent T_H2/T_H17 $CD127^+$ effector/memory cells in the lungs, spleen, and lymph nodes of adult and neonatal mice. After 7 weeks of rest, a single exposure to HDM resulted in airway hyper-responsiveness and increased T_H2 cytokine levels in mice that had been previously exposed to both HDM and DEPs versus those exposed to HDM alone. On the basis of these data, we examined whether DEP exposure was similarly associated with increased asthma prevalence in children in the presence or absence of allergen exposure/sensitization in the Cincinnati Childhood Allergy and Air Pollution Study birth cohort. Early-life exposure to high DEP levels was associated with significantly increased asthma prevalence among allergic children but not among non-allergic children. These findings suggest that DEP exposure results in accumulation of allergen-specific T_H2/T_H17 cells in the lungs, potentiating secondary allergen recall responses and promoting the development of allergic asthma.

. . .

The Effect of Air Pollution on Lung Development from 10 to 18 Years of Age

W. Gauderman, *et al*, New England Journal of Medicine 351:11, p.1057 (2004)

Abstract Whether exposure to air pollution adversely affects the growth of lung function during the period of rapid lung development that occurs between the ages of 10 and 18 years is unknown. In this prospective study, we recruited 1759 children (average age, 10 years) from schools in 12 southern California communities and measured lung function annually for eight years. The rate of attrition was approximately 10 percent per year. The communities represented a wide range of ambient exposures to ozone, acid vapor, nitrogen dioxide, and particulate matter. Linear regression was used to examine the relationship of air pollution to the forced expiratory volume in one second (FEF1) and other spirometric measures.

Results: Over the eight-year period, deficits in the growth of FEV1were associated with exposure to nitrogen dioxide (P=0.005), acid vapor (P=0.004), particulate matter with an aerodynamic diameter of less than 2.5 μm (PM2.5) (P=0.04), and elemental carbon (P=0.007), even after adjustment for several potential confounders and effect modifiers. Associations were also observed for other spirometric measures. Exposure to pollutants was associated with clinically and statistically significant deficits in the FEV1 attained at the age of 18 years. For example, the estimated proportion of 18-year-old subjects with a low FEV1 (defined as a ratio of observed to expected FEV1 of less than 80 percent) was 4.9 times as great at the highest level of exposure to PM2.5 as at the lowest level of exposure (7.9 percent vs. 1.6 percent, P=0.002).

Conclusions: The results of this study indicate that current levels of air pollution have chronic, adverse effects on lung development in children from the age of 10 to 18 years, leading to clinically significant deficits in attained FEV1 as children reach adulthood.

Diesel Exhaust and Asthma: Hypotheses and Molecular Mechanisms of Action

RJ Pandya, *et al*, Environmental Health Perspectives 110 Supp 1: p.103-112 (2002)

Abstract: Several components of air pollution have been linked to asthma. In addition to the well-studied criteria air pollutants, such as nitrogen dioxide, sulfur dioxide, and ozone, diesel exhaust and diesel exhaust particles (DEPs) also appear to play a role in respiratory and allergic diseases. Diesel exhaust is composed of vapors, gases, and fine particles emitted by diesel-fueled compression-ignition engines. DEPs can act as nonspecific airway irritants at relatively high levels. At lower levels, DEPs promote release of specific cytokines, chemokines, immunoglobulins, and oxidants in the upper and lower airway. Release of these mediators of the allergic and inflammatory response initiates a cascade that can culminate in airway inflammation, mucus secretion, serum leakage into the airways, and bronchial smooth muscle contraction. DEPs also may promote the expression of the TH2 immunologic response phenotype that has been associated with asthma and allergic disease. DEPs appear to have greater immunologic effects in the presence of environmental allergens than they do alone. This immunologic evidence may help explain the epidemiologic studies indicating that children living along major trucking thoroughfares are at increased risk for asthmatic and allergic symptoms and are more likely to have objective evidence of respiratory dysfunction.

* * *

Short-term diesel exhaust inhalation in a controlled human crossover study is associated with changes in DNA methylation of circulating mononuclear cells in asthmatics

C. Carlston, *et al*, Particle and Fiber Toxicology 11:71 (2014)

Abstract: Changes in DNA methylation have been associated with traffic-related air pollution in observational studies, but the specific mechanisms and temporal dynamics therein have not been explored in a controlled study of asthmatics. In this study, we investigate short-term effects of diesel exhaust inhalation on DNA methylation levels at CpG sites across the genome in circulating blood in asthmatics. A double-blind crossover study of filtered air and diesel exhaust exposures was performed on sixteen non-smoking asthmatic subjects. Blood samples were collected pre-exposure, and then 6 and 30 hours post-exposure. Peripheral blood mononuclear cell DNA methylation was interrogated using the Illumina Infinium HumanMethylation450 Array. Exposure-related changes in DNA methylation were identified.

In addition, CpG sites overlapping with Alu or LINE1 repetitive elements and candidate microRNA loci were also analyzed. DNA methylation at 2827 CpG sites were affected by exposure to diesel exhaust but not filtered air; these sites enriched for genes involved in protein kinase and *NFkB* pathways. CpG sites with significant changes in response to diesel exhaust exposure primarily became less methylated, with a site residing within *GSTP1* being among the significant hits. Diesel exhaust-associated change was also found for CpG sites overlapping with Alu and LINE1 elements as well as for a site within *miR-21*.

Conclusion:
Short-term exposure to diesel exhaust resulted in DNA methylation changes at CpG sites residing in genes involved in inflammation and oxidative stress response, repetitive elements, and microRNA. This provides plausibility for the role of DNA methylation in pathways by which airborne particulate matter impacts gene expression and offers support for including DNA methylation analysis in future efforts to understand the interactions between environmental exposures and biological systems.

* * *

Diesel Exhaust Inhalation Causes Vascular Dysfunction and Impaired Endogenous Fibrinolysis

N. Mills *et al*, for the American Heart Association; Circulation 112:25, p.930-936 (2005)

Abstract:
Background: Although the mechanisms are unknown, it has been suggested that transient exposure to traffic-derived air pollution may be a trigger for acute myocardial infarction. The study aim was to investigate the effects of diesel exhaust inhalation on vascular and endothelial function in humans.

Methods and Results: In a double-blind, randomized, cross-over study, 30 healthy men were exposed to diluted diesel exhaust (300 µg/m3 particulate concentration) or air for 1 hour during intermittent exercise. Bilateral forearm blood flow and inflammatory factors were measured before and during unilateral intrabrachial bradykinin (100 to 1000 pmol/min), acetylcholine (5 to 20 µg/min), sodium nitroprusside (2 to 8 µg/min), and verapamil (10 to 100 µg/min) infusions 2 and 6 hours after exposure. There were no differences in resting forearm blood flow or inflammatory markers after exposure to diesel exhaust or air. Although there was a dose-dependent increase in blood flow with each vasodilator ($P<0.0001$ for all), this response was attenuated with bradykinin ($P<0.05$), acetylcholine ($P<0.05$), and sodium nitroprusside ($P<0.001$) infusions 2 hours after exposure to diesel exhaust, which persisted at 6 hours. Bradykinin caused a dose-dependent increase in plasma tissue plasminogen activator ($P<0.0001$) that was suppressed 6 hours after exposure to diesel ($P<0.001$; area under the curve decreased by 34%).

Conclusions: At levels encountered in an urban environment, inhalation of dilute diesel exhaust impairs 2 important and complementary aspects of vascular function in humans: the regulation of vascular tone and endogenous fibrinolysis. These important findings provide a potential mechanism that links air pollution to the pathogenesis of atherothrombosis and acute myocardial infarction.

* * *

Air Pollution–Associated Changes in Lung Function among Asthmatic Children in Detroit

T. Lewis, *et al*, Environmental Health Perspectives 113:8, p.1068–1075 (2005)

Abstract: In a longitudinal cohort study of primary-school–age children with asthma in Detroit, Michigan, we examined relationships between lung function and ambient levels of particulate matter ≤10µm and ≤2.5 µm in diameter (PM10and PM2.5) and ozone at varying lag intervals using generalized estimating equations. Models considered effect modification by maintenance corticosteroid (CS) use and by the presence of an upper respiratory infection (URI) as recorded in a daily diary among 86 children who participated in six 2-week seasonal assessments from winter 2001 through spring 2002. Participants were predominantly African American from families with low income, and >75% were categorized as having persistent asthma. In both single-pollutant and two-pollutant models, many regressions demonstrated associations between higher exposure to ambient pollutants and poorer lung function (increased diurnal variability and decreased lowest daily values for forced expiratory volume in 1 sec) among children using CSs but not among those not using CSs, and among children reporting URI symptoms but not among those who did not report URIs. Our findings suggest that levels of air pollutants in Detroit, which are above the current National Ambient Air Quality Standards, adversely affect lung function of susceptible asthmatic children.

* * *

Characterizing the Range of Children's Pollutant Exposure During School Bus Commutes

D. Fitz, *et al,* for the California Air Resources Board, Contract No. 00-322 (2003)

Abstract: To determine the range of children's exposures during their bus commutes, especially those conditions leading to high exposures, real-time and integrated measurements of pollutant concentrations were conducted inside five conventional diesel school buses, as well as a diesel bus outfitted with a particulate trap and a bus powered by natural gas. Measurements were made during 20 bus commutes on a Los Angeles Unified School District bus route from South Central Los Angeles to the west side of LA, with additional runs on a second urban route, a rural/suburban route, and to test the effect of window position.

Children's school bus commutes in Los Angeles appear to expose them to significantly higher concentrations of vehicle-related pollutants than ambient air concentrations and frequently higher concentrations than those measured on roadways. Concentrations of diesel vehicle-related pollutants such as black carbon and particle-bound PAHs were significantly higher on board conventional diesel buses when windows were closed. This was due to the intrusion of the bus's own exhaust, as demonstrated through the use of a tracer gas added to each bus's exhaust. When windows were open, increased ventilation rates markedly reduced this effect, although high peak concentrations were then observed when following other diesel vehicles. On-board concentrations of vehicle-related pollutants were also significantly higher on the urban routes compared to the rural/suburban route, indicating the importance of surrounding traffic density. Other related exposure scenarios such as bus loading and unloading, and time spent waiting at bus stops, were shown to make relatively insignificant contributions to children's exposure, due to the generally lower concentrations and the short times spent at those activities compared to bus commutes. Results from this study show that minimizing commute times, using the cleanest buses for the longest routes, and reducing bus caravanning and idling time will reduce children's exposure to bus-related pollutants.