STUDIES/ARTICLES - HIGHWAY POLLUTION

Summary of near-**highway health effects** studies
http://www.ehjournal.net/content/6/1/23

FULL TEXT

Environ Health. 2007; 6: 23.

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Near-highway pollutants in motor vehicle exhaust: A review of epidemiologic evidence of cardiac and pulmonary health risks

Doug Brugge,[1] John L Durant,[2] and Christine Rioux[3]

http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=1971259

There is growing evidence of a distinct set of freshly-emitted air pollutants downwind from major highways, motorways, and freeways that include elevated levels of ultrafine particulates (UFP), black carbon (BC), oxides of nitrogen (NOx), and carbon monoxide (CO). People living or otherwise spending substantial time within about 200 m of highways are exposed to these pollutants more so than persons living at a greater distance, even compared to living on busy urban streets. Evidence of the health hazards of these pollutants arises from studies that assess proximity to highways, actual exposure to the pollutants, or both. Taken as a whole, the health studies show elevated risk for development of asthma and reduced lung function in children who live near major highways. Studies of particulate matter (PM) that show associations with cardiac and pulmonary mortality also appear to indicate increasing risk as smaller geographic areas are studied, suggesting localized sources that likely include major highways. Although less work has tested the association between lung cancer and highways, the existing studies suggest an association as well. While the evidence is substantial for a link between near-highway exposures and adverse health outcomes, considerable work remains to understand the exact nature and magnitude of the risks.

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See also extensive References at link above

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Highway Pollution And Health Study In Boston, Somerville Funded By NIH
http://www.medicalnewstoday.com/articles/112138.php

Numerous good references on this page
http://www.somervillestep.org/background/health.html

State of the Air: 2009 Health Risks Overview
http://www.stateoftheair.org/2009/health-risks/overview.html
Download This Report

Living Near A Highway Affects Lung Development In Children, Study Shows
http://www.sciencedaily.com/releases/2007/01/070125185843.htm

ScienceDaily (Jan. 26, 2007) — Children who live near a major highway are not only more likely to develop asthma or other respiratory diseases, but their lung development may also be stunted.

Mobile Source Air Toxics
http://www.fhwa.dot.gov/environment/airtoxic/020306guidapc.htm
Mobile Source Air Toxics (MSATs) are a subset of the 188 air toxics defined by the Clean Air Act. The MSATs are compounds emitted from highway vehicles and non-road equipment. Some toxic compounds are present in fuel and are emitted to the air when the fuel evaporates or passes through the engine unburned. Other toxics are emitted from the incomplete combustion of fuels or as secondary combustion products. Metal air toxics also result from engine wear or from impurities in oil or gasoline.

Mobile Source Air Toxics
http://www.epa.gov/OMS/toxics.htm

The Effect of Fine and Coarse Particulate Air Pollution on Mortality: A National Analysis

http://www.ehponline.org/docs/2009/0800108/abstract.html

Environmental Health Perspectives Volume 117, Number 6, June 2009

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Abstract

Background: Although many studies have examined the effects of air pollution on mortality, data limitations have resulted in fewer studies of both particulate matter with an aerodynamic diameter of ? 2.5 µm (PM2.5 ; fine particles) and of coarse particles (particles with an aerodynamic diameter > 2.5 and < 10 µm ; PM coarse) . We conducted a national, multicity time-series study of the acute effect of PM2.5 and PM coarse on the increased risk of death for all causes, cardiovascular disease (CVD) , myocardial infarction (MI) , stroke, and respiratory mortality for the years 1999?2005.

Method: We applied a city- and season-specific Poisson regression in 112 U.S. cities to examine the association of mean (day of death and previous day) PM2.5 and PM coarse with daily deaths. We combined the city-specific estimates using a random effects approach, in total, by season and by region.

Results: We found a 0.98% increase [95% confidence interval (CI) , 0.75?1.22] in total mortality, a 0.85% increase (95% CI, 0.46?1.24) in CVD, a 1.18% increase (95% CI, 0.48?1.89) in MI, a 1.78% increase (95% CI, 0.96?2.62) in stroke, and a 1.68% increase (95% CI, 1.04?2.33) in respiratory deaths for a 10-µg/m3 increase in 2-day averaged PM2.5. The effects were higher in spring. For PM coarse, we found significant but smaller increases for all causes analyzed.

Conclusions: We conclude that our analysis showed an increased risk of mortality for all and specific causes associated with PM2.5, and the risks are higher than what was previously observed for PM10. In addition, coarse particles are also associated with more deaths.

Analysis Finds Elevated Risk From Soot Particles in the Air

http://www.nytimes.com/2009/06/03/science/earth/03soot.html?ref=us

By FELICITY BARRINGER

A new appraisal of existing studies documenting the links between tiny soot particles and premature death from cardiovascular ailments shows that mortality rates among people exposed to the particles are twice as high as previously thought.

Dan Greenbaum, the president of the nonprofit Health Effects Institute, which is releasing the analysis on Wednesday, said that the areas covered in the study included 116 American cities, with the highest levels of soot particles found in areas including the eastern suburbs of Los Angeles and the Central Valley of California; Birmingham, Ala.; Atlanta; the Ohio River Valley; and Pittsburgh.

The review found that the risk of having a condition that is a precursor to deadly heart attacks for people living in soot-laden areas goes up by 24 percent rather than 12 percent, as particle concentrations increase.

A variety of sources produce fine particles, and they include diesel engines, automobile tires, coal-fired power plants and oil refineries.

Comparing exposure within the New York and the Los Angeles metropolitan areas, the study found that the risks were evenly distributed in the vicinity of New York while some areas around Los Angeles, including neighborhoods near the Ports of Los Angeles and Long Beach, had elevated health risks.

The extended epidemiological analysis, which draws on data gathered from 350,000 people over 18 years, and an additional 150,000 people in more recent years, was conducted for the Health Effects Institute by scientists at the University of Ottawa.

The institute was created by the Environmental Protection Agency and the industries that it regulates with the goal of obtaining unbiased studies.

The link between fine particles, the diameter of which is smaller than a 30th of a human hair, and cardiopulmonary disease has been established for two decades, and the E.P.A. has regulated such emissions since 1997. In

2006, despite mounting evidence that the particles were deadlier than first thought, the agency declined to lower chronic exposure limits.

The United States Court of Appeals for the District of Columbia Circuit declared that decision inadequate, and the Obama administration is now considering what level is appropriate.

"AIR POLLUTION AND PARKINSON'S DISEASE IN SOUTHERN ONTARIO CITIES"

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Centre for Environment, University of Toronto
WINTER/SPRING 2008 ENVIRONMENT AND HEALTH SEMINAR SERIES
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Room 106, Health Sciences Centre, 155 College Str., at McCaul Str.

MURRAY FINKELSTEIN, Department of Family and Community Medicine, University of Toronto
(brief bio below)

"AIR POLLUTION AND PARKINSON'S DISEASE IN SOUTHERN ONTARIO CITIES"
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ABSTRACT:There is concern that industrial emissions of manganese (Mn) and the use of Mn-containing compounds as fuel additives might increase the population risk of Parkinson's Disease (PD)-like disorders. Associations between the diagnosis and treatment of PD and markers of exposure to vehicle exhaust and industrial emissions of Mn were investigated

within a cohort of 110,000 subjects in the cities of Toronto and Hamilton, Ontario. Methylcyclopentadienyl manganese tricarbonyl (MMT) has been added to Canadian gasoline since 1976 and steelmaking in Hamilton emits Mn to the air.
Using residential postal codes, subjects were mapped to: (1) residence locations close to traffic and to neighbourhood levels of NO2, as markers of Traffic Generated Air Pollution (TGAP); and, (2) neighbourhood levels of ambient Mn in Hamilton, as measured by the Mn fraction of Total Suspended Particulate. Subjects were linked to Ministry of Health administrative databases, 1992-1999, to identify physician's diagnoses of PD and prescriptions for L-Dopa containing medications. In Toronto, we found no association between PD and the markers of TGAP. In Hamilton, the odds ratio for a physician's diagnosis of PD was 1.034 (1.00 - 1.07) per 10 ng/m3 increase in Mn in TSP. The estimate of the "doubling exposure" for physician-diagnosed PD was about 150 ng/m3 Mn in TSP. Examination of prevalence curves suggested that exposure to ambient Mn advances the age of diagnosis of PD, consistent with the theory that exposure to Mn adds to the natural loss of neurons attributable to the aging process.

BRIEF BIO: Dr. Murray Finkelstein is a physician/epidemiologist with interest in the assessment of occupational and environmental hazards. He is an Associate Professor in the Occupational and Environmental Health Program at McMaster University, an Assistant Professor in the Departments of Family and Community Medicine and of Public Health Sciences at the University of Toronto, and a member of the Hart House Orchestra at the U of T.

Diesel fumes affect brain activity, study finds

http://www.cbc.ca/health/story/2008/03/11/diesel-fumes.html

Last Updated: Tuesday, March 11, 2008 | 2:17 PM

Diesel exhaust fumes not only stink, they may alter the way the brain functions, a study released Tuesday suggests.

In the journal Particle and Fibre Toxicology, researchers from the Netherlands, Sweden and the United Kingdom report that even a half hour's exposure to the fumes can put stress on the brain.

Previous research has suggested that very small particles breathed in from polluted air can end up in the brain, but "this is the first study to demonstrate functional changes in brain activity as a result of exposure to diesel exhaust in human subjects," the team writes.

Researchers monitored 10 male volunteers who spent an hour in a room filled either with

clean air or exhaust from a diesel engine. The exhaust-filled room was set to mimic the highest level that people might encounter in the environment or at work, for example on a busy road or in a garage.

Volunteers were connected to an electroencephalograph (EEG) to monitor the brain's electrical signals during exposure and for the hour afterwards.

Within 30 minutes, the participants in the exhaust room showed signs of stress on the EEG, indicating a change in the way the brain processes information.

The researchers said the effect continued in the hour after the participants left the room. "We can only speculate what these effects may mean for the chronic exposure to air pollution encountered in busy cities where the levels of such soot particles can be very high," lead researcher Paul Borm said in a release.

"It is conceivable that the long-term effects of exposure to traffic nanoparticles may interfere with normal brain function and information processing," he said, adding that further studies would be necessary to determine whether exposure has a lasting effect.

Such findings are significant, the researchers said, because this type of stress, as a consequence of particles depositing in tissue, has been linked to the development of Parkinson's and Alzheimer's disease.

Traffic exhaust can cause asthma, allergies and impaired respiratory function in children

Public release date: 9-Apr-2008
Karolinska Institutet

Children exposed to high levels of air pollution during their first year of life run a greater risk of developing asthma, pollen allergies, and impaired respiratory function. However, genetic factors are also at play. These are the results of a new study conducted under the BAMSE project.

The BAMSE project has monitored 4,000 children in Stockholm county from birth in order to assess whether exposure to traffic pollution during their first year of life affects the risk of developing asthma and allergies. Levels of traffic exhaust were measured at the site of the home. The results show that the children who were exposed to high concentrations of pollutants ran a 60 per cent higher risk of suffering of persistent asthma symptoms. Respiratory function was also adversely affected, and the children were much more likely to be allergic to airborne allergens, particularly pollen.

Studies were also made of how the risk of developing air pollution-related allergies is influenced by genetic factors. It was found that children carrying a variant of GSTP1 (glutathione S-transferase P1) gene, which is crucial to the body's ability to take care of air pollutants (the antioxidative system), run a greater risk of developing an allergy linked to traffic-related air pollution. According to new analyses, variants of another 'asthma gene', TNF (tumour necrosis factor), also affect sensitivity to air pollution. Children with a particular combination of GSTP1 and TNF variants run a considerably higher risk of developing allergies.

The children studied in the BAMSE project are now 12 years old, and an on-line follow-up survey of the children and their parents has now been launched. The answers to the survey will provide information about health, lifestyle and environmental conditions, including air pollution, during the children's lives.

Conclusions

1. Children who grow up in Stockholm are at greater risk of developing asthma, respiratory problems and pollen allergies if they live in areas where there are high concentrations of traffic pollution.
2. Not all children who live in areas with high levels of air pollution develop allergies. Whether they do or not is partly determined by genetic factors.
3. For the first time, data are now obtained for the BAMSE project using web-based techniques, which give more reliable answers.

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The BAMSE project is run by the Stockholm County Council's unit for Occupational and Environmental Medicine and the Institute of Environmental Medicine at Karolinska Institutet. Read more at www.folkhalsoguiden.se/bamse

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Road pollution blamed for higher allergy risk in kids

New evidence blames traffic-related pollution for increasing the risk of allergy and atopic diseases among children by more than fifty percent. What's more, the closer children live to roads, the higher their risk.

"[Children] living very close to a major road are likely to be exposed not only to a higher amount of traffic-derived particles and gases but also to a more freshly emitted aerosols which may be more toxic," wrote lead author of the research, Joachim Heinrich, Ph.D., of the German Research Center for Environment and Health at the Institute of Epidemiology, in Munich.

"Our findings provide strong evidence for the adverse effects of traffic-related air pollutants on atopic diseases as well as on allergic sensitization," wrote Dr. Heinrich. The results appeared in the second issue for June of the American Thoracic Society's American Journal of Respiratory and Critical Care Medicine.

The study examined nearly 2,900 children at age four and more than 3,000 at age six to determine their rates of doctor-diagnosed asthma and/or allergy with relation to long-term exposure to traffic-related pollution.

Both the four-year-old and six-year-old groups of children came from prospective cohort studies and were enrolled at birth in the metropolitan Munich area. Their exposure to traffic pollutants was calculated as a function of the distance of their homes from major roads at birth and at two, three and six years of age. Parents were given questionnaires about their child's respiratory diagnoses and symptoms, and their children were assessed for asthma, wheezing, sneezing and eczema. At six years of age, the children were tested for food allergies. Air was tested for particulate matter (e.g., soot) and nitrogen dioxide (NO2) at each of forty identified points near high-traffic areas once each season between March 1999 and July 2000.

After controlling for such individual characteristics as parental allergies, pet ownership, and number of siblings, researchers found significant positive associations between distance to the nearest road and asthmatic bronchitis, hay fever, eczema and allergic sensitizations. They also found a distant-dependent relationship between proximity to the road and risk of allergic sensitization, with those living closest to major roads having a nearly 50 percent greater risk of allergic sensitization.

Previous studies have found that pollutants and allergic sensitization are linked, but using distance from major roads as a proxy for pollutant exposure has been confused by the socioeconomic factors that are often closely linked to such locales. However, in Munich, as with other older European cities, the roads and buildings are structured so that economic advantages are not necessarily correlated with living further from the main thoroughfares. In this study, it was possible to determine that economic factors were not a confounding variable in the analysis, but there was a clear difference in the children's allergic development with relation to their proximity to a road.

"We consistently found strong associations between the distance to the nearest main road and the allergic disease outcomes," wrote Dr. Heinrich. "Children living closer than 50 meters to a busy street had the highest probability of getting allergic symptoms, compared to children living further away."

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Urban Air Pollution Profile Causes An Increased Airway Inflammatory Response

29 May 2008

Global increases in traffic, industrialisation, and expanding cities have all contributed to a rise in emissions and growing levels of air pollution, thus adding to an escalating concern surrounding their environmental and health-related impacts.

Over the last few decades, there has been mounting epidemiological and laboratory evidence regarding the negative short-term, as well as long-term, health effects of air pollutants on the respiratory and cardiovascular systems.

Ozone (O3) and diesel exhaust (DE) are two major contributors to traffic-related air pollution and have both been shown to trigger inflammation in the airways, causing symptoms such as wheezing, coughing and reduced lung function.

DE tends to reach its highest concentrations at peak rush hours, such as in the mornings. Conversely, O3 concentrations are inclined to culminate in the afternoons.

Therefore, Jenny Bosson (University Hospital, Umeå, Sweden) and her colleagues alleged

that exposure to this urban pollution profile may cause these compounds to exhibit synergistic or additive properties in the airways.

In order to investigate the consequences of this sequential exposure pattern, healthy subjects underwent two separate exposure series within controlled walk-in chambers. These comprised a one-hour morning exposure to DE or filtered air followed five hours later by a two-hour exposure to O3.

Bronchial rinse samples were obtained via bronchoscopy 24 hours after the start of each morning exposure, with inflammatory cells and immune cell factors assessed.

Healthy subjects exposed in sequence to environmentally relevant levels of DE and O3 demonstrate significantly increased pro- inflammatory cells, revealing a potentially adverse amplification in airway inflammation.

Currently, standard limits for each pollutant are set independently of each other. These novel findings provide a basis towards comprehending the cumulative airway effects when exposed to an urban air pollution profile and may indicate a need for future co- regulations of exposure limits.

Title of original article-
Diesel exhaust exposure enhances the ozone-induced airway inflammation in healthy humans

The European Respiratory Journal is the peer-reviewed scientific publication of the European Respiratory Society (more than 8,000 specialists in lung diseases and respiratory medicine in Europe, the United States and Australia).

European Respiratory Journal

Article URL: http://www.medicalnewstoday.com/articles/108869.php

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Medical officer wants idling limited to 10 seconds
Updated: Thu Jul. 03 2008 6:36:12 PM

ctvtoronto.ca
http://toronto.ctv.ca/servlet/an/local/CTVNews/20080703/idling_bylaw_proposal_080703/20080703/?hub=TorontoNewHome

Toronto's Board of Health has passed a proposal from the city's medical officer of health that aims to limit the time vehicles can idle to just 10 seconds.

A feasibility study will be conducted after Dr. David McKeown's initiative received support by

board members on Thursday.

Under Toronto's current anti-idling bylaw, drivers in vehicles that are running for more than three minutes can be ticketed. The fine for the infraction is $125.

McKeown says more needs to be done to clean the air because figures show pollution kills 1,700 residents in Toronto every year.

Harmful emissions from idling vehicles contribute to the deaths, he says.

Health officials say cutting down on unnecessary idling will save people money on gas, which may change some drivers' attitudes because fuel prices continue to rise.

McKeown says city workers who drive Toronto's fleet of vehicles already abide by the 10-second rule. He says officers will have a much easier time enforcing his proposed bylaw.

"It's a lot easier for an enforcement officer to tell when you've been idling the vehicle for 10 seconds than to wait around to see if you've idled for three minutes," McKeown said.

The Board of Health is also asking the provincial and federal governments to look into making it mandatory to put devices in vehicles that would automatically shut off the engines if idled too long.

With a report from CTV Toronto's Naomi Parness

Epidemiologists find molecular clues to air pollution's impact on youngsters
Date: Sun, 20 Jul 2008 23:58:02 -0400

Is China's Pollution Poisoning Its Children?

http://www.sciam.com/article.cfm?id=chinas-children-of-smoke&print=true

Epidemiologists find molecular clues to air pollution's impact on youngsters
By Dan Fagin

Editor's Note: This story will be published in the August issue of Scientific American.

A few heaping piles of scrap metal and a rusty coal shed are all that is left of the power plant that until recently squatted like an immense, smoke-belching dragon in the middle of Tongliang, a gray city of 100,000 in south-central China. As we walk toward the shed, a Belgian Shepherd begins barking furiously, jerking its iron chain and baring sharp teeth. A brown-eyed face peeks out from the open doorway—it belongs to a girl in a stained shirt, holding a tabby cat that jumps away to hide under a slab of concrete as we approach. The

girl is no more than six or seven years old and appears to be living in the shed with her father, who watches us warily from within.

The delegation of local officials who are taking us on a tour of the site are embarrassed; they want to hustle us along to a nearby office to show us an elaborate scale model of an extravagant (by Tongliang standards) 900-unit housing development planned for the property. But Frederica Perera is intrigued. She strides toward the girl and gives a friendly "ni hao" and a smile. The girl smiles back before retreating back into the shadows with her father.

Children, after all, are why Perera is here. She is looking for connections between air pollution and disease, especially in children who were exposed to pollutants in the womb. The director of Columbia University's Center for Children's Environmental Health, Perera helped to pioneer the field of molecular epidemiology, which applies the tools of molecular analysis to identify genetic and environmental factors that contribute to disease. She and other molecular epidemiologists who focus on environmental links to illness increasingly do much of their work in the developing world, where pollution is so ubiquitous that its complex connections to health can be calibrated even in small study populations. But their conclusions should also apply in places such as the U.S., Europe and Japan, where environmental exposures are subtler and their effects more difficult to measure in small-scale studies.

Wherever they work, what distinguishes the approach of molecular epidemiologists is their search for biological indicators that closely correlate with toxic exposures and illness. Often these markers take the form of chemicals bound to DNA or of changes in gene structure or activity that match up with particular types of contaminants and disease. Now that DNA microarrays and other screening technologies are making it much easier to measure many of those biomarkers, routine use of such tools could, at least theoretically, save lives by identifying populations at risk from specific pollutants.

The science is still controversial, however, because relatively few candidate molecular biomarkers of susceptibility, exposure or early disease have been fully validated—that is, proved to herald future illness—and because it is very difficult to factor out confounding variables such as diet and genetic predisposition that may be at least as important as exposure to pollutants in causing various ailments. What has proved even more difficult is getting a handle on how those disparate risks may be interacting to affect health.

As a result, more than 25 years after Perera's first paper on the topic, molecular epidemiology has progressed more slowly than its architects had initially hoped, and the consensus among researchers is that no matter how enticing it sounds in theory, real-world complexities have limited its usefulness. Initial enthusiasm for the idea that changes in a few specific biomarkers—the tumor-suppressing protein p53 is a prominent example—could be reliable indicators of early illness has faded as researchers have identified much more complicated etiologies, involving cascades of biochemical changes, for many diseases. "You could say that the reception was a little overenthusiastic early on. There have been some

premature claims," Perera acknowledges. "The promise of using biomarkers for early detection and custom-managed treatment has turned out to be not so easy."

But now, in Tongliang, Perera believes she has found the best test case yet for environmental epidemiology at the molecular level—and she and her Columbia colleague, Deliang Tang, are getting results to back up her optimism. How they made their discoveries is almost as interesting as what they found.

A "Biological Dosimeter"

Ever since she began studying biomarkers in 1979, the ones that have interested Perera the most are PAH-DNA adducts, which she and Tang are now measuring in the white blood cells of children who were exposed to exhausts from the Tongliang power plant. PAHs, or polycyclic aromatic hydrocarbons, are a large family of compounds formed by the incomplete combustion of organic material—especially coal, but also other fossil fuels, cigarettes and even barbecued meat. They are among the most widespread and harmful air pollutants in the world. What interests Perera most about PAHs is their sticky molecular structure. Many PAHs readily form tight, covalent bonds with DNA. Those fused pollutant-DNA complexes, or adducts, can disrupt replication of the genome during cell division, altering the functions of genes that promote or suppress disease.

The coal-burning power station that loomed over Tongliang was a Vesuvius of PAHs, and its closure in 2004 changed environmental conditions in the city virtually overnight. That makes Tongliang something very rare in the world of epidemiology: a feasible laboratory for measuring the before-and-after health impacts of air pollutants. The city is still far from pristine, but passing cars no longer kick up clouds of black soot from the street and families can hang their wash outside to dry for more than a few minutes without their white shirts turning gray. The air-pollution monitors that the Columbia team installed around Tongliang confirm the improvements: airborne concentrations of one of the most important PAHs, benzo(a)pyrene, or BaP, fell by about 30 percent between 2002 and 2005. Other PAHs declined even more.

The changes that interest Perera the most, however, are taking place in the bodies of the city's youngest residents. Since 2002 she and Tang, along with Tin-yu Li of Chongqing Children's Hospital, have been studying 450 children who live within two kilometers of the plant site by testing their DNA and measuring their physical and mental development starting at birth. The researchers' preliminary analysis shows that children born in 2002, when the power plant was still operating, have smaller heads and score worse on developmental tests than those born in 2005, a year after the plant closed. There are also differences at the molecular level: concentrations of BaP-DNA adducts were about 40 percent higher in the white blood cells of newborn babies in Tongliang in 2002 than in those of children born three years later.

Perhaps most meaningful of all, in the children born in 2002, measured concentrations of BaP-DNA adducts closely correlated with head circumference and developmental test scores.

In other words, the more damage a child's DNA suffered in the womb, the more likely he or she was to be born with a smaller head and to score worse on tests of motor skills and overall development as a toddler. The correlations were weaker among babies born in 2005, suggesting that air pollution becomes less of a risk as overall levels drop. Children born in 2005 will probably be slightly less likely to get cancer, according to Perera, whose previous work suggests that adduct counts correlate with cancer risk.

The Tongliang data, along with the results of earlier studies she conducted in Poland and New York City, suggest that measurements of adducts in white blood cells are reliable "biological dosimeters" for estimating the impact of PAHs on neurodevelopment, Perera says. That being the case, testing for adducts could someday become part of a pediatrician' s arsenal for identifying children who are at high risk for developmental problems and thus need early intervention, she observes.

The 2002/2005 comparison is "a very powerful finding," remarks molecular epidemiologist John D. Groopman of Johns Hopkins University. "One of the critical steps in the validation of biomarkers is to demonstrate that if you modulate the biomarker, you can show an effect on a health outcome."

"I'm in awe of what Dr. Perera has accomplished," adds John F. Rosen of Children's Hospital at Montefiore in Bronx, N.Y., a longtime lead-poisoning researcher who has also worked in China. "Translating her clinical results unquestionably will advance child health in China and the rest of the world."

Finding Tongliang

A fine mist was falling the morning I arrived in Tongliang with Perera and Tang. The hills surrounding the city on three sides seemed as blurred as they must have looked back in the days when the coal plant was running. Most of the electricity in this part of China comes from hydropower, but because snowmelt does not swell the Yangtze River until the spring, many of the smaller cities have relied on primitive coal-burning plants that lack even basic pollution controls to fill the gap during the winter months. Tongliang's power plant consumed more than 4,000 tons of coal a month between November and May, and that coal was especially problematic because it contained very high concentrations of sulfur and thus did not burn completely. PAH-laden ash and exhaust gases would pour out of the plant's 279-foot smokestack and settle over the low-lying city like a thick blanket.

Back in 2000, Perera had been searching for just such a place to build on her two decades of research into the role of PAH-DNA adducts as indicators of disease risk. Her initial studies—the first ever in human subjects—had measured the adducts in the lung tissue of adult cancer patients [see "Uncovering New Clues to Cancer Risk," by Frederica P. Perera; Scientific American, May 1996], and she went on to measure them in mothers and children living in polluted neighborhoods of New York City and the industrial city of Kraków, Poland. What she found is that people exposed to air pollution had higher adduct levels in their blood and that those high levels in turn correlated with the presence of genetic mutations

that were known to be risk factors for cancer and developmental problems in young children. Children in cities where the air was cleaner, Perera determined, had fewer adducts and were less likely to suffer from growth deficits.

Still, her studies were small, and she could not rule out the possibility that unmeasured lifestyle differences, instead of pollution, might explain the differences in health and in adduct levels that she found between mothers and children who lived in polluted cities and those who did not. Now Perera wanted to take the next step by finding one city in which emissions of PAHs were abruptly reduced, allowing a before-and-after comparison in a single, discrete population.

China, with its extreme environmental problems and an authoritarian government capable of shutting down a major polluter in one fell swoop, was the obvious place to look. And Tang was the best person to direct the study Perera envisioned. A physician and Shanghai native, Tang did his doctoral training in public health in Perera's lab and was now her frequent research collaborator. For his study he would have to train a small army of Chinese doctors and nurses to collect placentas and cord blood from mothers enrolled in the study and to administer cognitive tests to the children as they grew. He would also need to parley with an array of government officials, from Beijing bureaucrats to provincial apparatchiks, to secure the cooperation of hospitals, arrange for lab space, import pollution-control equipment and export blood samples—all very politically sensitive tasks.

Perera and Tang investigated 12 candidate sites before settling on Tongliang, where its sole power plant was scheduled to close as part of a government program to replace inefficient coal-burning plants. Tongliang was a good fit not only because the plant was set to shut down but also because the city had relatively few other important sources of air pollution aside from vehicle traffic. Natural gas had already replaced wood- and coal-burning stoves in the city, which had no large factories. The four local hospitals that agreed to participate were just large enough to collectively generate enough cases to satisfy the statistical requirements of the study Perera and Tang planned: 150 nonsmoking women whose pregnancies coincided with the months the plant operated. Additional mothers and newborns would be tested in later years, after the power plant closed.

But when Perera and Tang arrived in Tongliang in the spring of 2002 to begin recruiting pregnant women for the study, they found themselves in the middle of a controversy. The question of whether to close the power plant had been a simmering issue for years in Tongliang. Some local mothers had even stood outside during government meetings in silent protest against continued operation—an extraordinary step in China. Now city officials, worried about the economic impact, were considering retrofitting the plant or moving it to the edge of the city instead of shuttering it. The Columbia researchers had to wait for months for a resolution. Ultimately, publicity over their planned study helped to tip the balance in favor of closure. The old smokestack spewed its final cloud of gray smoke in May 2004.

Persistent Complications

Three anxious young fathers, all of them smoking cigarettes, slump in the crowded central hallway of Tongliang County Maternal Hospital, not far from two “No Smoking” signs. Smoking is endemic among Chinese men—half of the male population and two thirds of adult men younger than 25 light up regularly—and the nurses and doctors seem to have given up trying to enforce a ban.

In a room at the end of the corridor, medical personnel are lavishing attention on a young boy named Junshan Li, who was born in the spring of 2002, when the power plant was still going strong. Li is one of the original 150 subjects of the Tongliang study, but there are no signs today that he is anything but a healthy, active five-year-old— active enough to have broken his collarbone a week earlier in a playground accident. Li is at the hospital today not because of the collarbone injury but for his yearly developmental assessment for Perera and Tang’s study. At the moment, he is perched on the edge of a chair and excitedly shouting out numbers in Chinese—“ba!” ... “san!” ... “qi!”—in response to simple arithmetic questions posed by a tester, a young pediatrician named Xu Tan. Her goal is to assess Li’s growth both mentally and physically; after the test, Tan will weigh him and measure his height and head circumference.

The scene in the hospital illustrates a key challenge of molecular epidemiology. The growth and developmental deficiencies Perera and Tang are scrutinizing for links to prenatal exposure to PAH pollution are subtle and can have multiple causes—including secondhand tobacco smoke such as that emanating from the fathers smoking at the other end of the hallway. The researchers have tried to deal with the problem of alternative causes by enrolling only nonsmoking mothers with low-risk pregnancies and by asking mothers about their education, family smoking habits, and exposure to PAHs via grilled meats and other foods, as well as some other possibly confounding explanations. The investigators have also taken measurements of neurotoxic metals and antioxidants in blood, because those could also affect child development. So they are reasonably confident that the correlations they have uncovered between adduct counts in Tongliang children and several important measures of growth and learning stem mostly from exposure to air pollution.

Though statistically significant, the differences between Tongliang children born in 2002, when the power plant was still open, and those born in 2005, after it had closed, are small: a few millimeters in head circumference and height, an ounce of body weight, a point or two on a developmental test. According to Perera, the results suggest that the 2002 children will be slightly more likely to be slower learners and to need extra help at school and will develop fine-motor skills later on average than their counterparts born in 2005.

These kinds of subtle health effects have always been a source of contention in biomarker research. In the 1970s and 1980s Herbert L. Needleman, now at the University of Pittsburgh, pioneered the study of lead levels across populations by grinding up baby teeth and measuring trace levels of the metal, eventually finding correlations with diminished learning capacity and delinquent behavior. But the indistinct nature of the neurological problems Needleman was seeing, and the very low levels of lead he was measuring, opened

his work to fierce criticism from the lead industry. Ultimately, his findings were replicated and are now widely accepted as a key justification for removing lead from gasoline and paint. Moves to crack down on secondhand smoke, similarly, have cited studies that measured blood and urine levels of cotinine, the most important breakdown product of nicotine. Cotinine levels in pregnant mothers and newborns have become extensively used markers in research into links between environmental tobacco smoke and a broad range of developmental problems in children.

There is an additional complication in drawing conclusions about health effects by measuring molecular biomarkers. Just because concentrations of lead, cotinine or PAH-DNA adducts are relatively easy to measure in the bloodstream does not mean that the same dose is reaching the brain or other organs where meaningful damage can occur. Earlier adduct studies, some of them by Perera, have suggested that white blood cells are a reasonable proxy for target organs such as the brain and lungs, but contaminants are rarely distributed uniformly throughout the body, and metabolic differences can cause huge variations among individuals even if they are part of a cohesive population that breathes the same air or drinks the same water.

Adducts do have one important advantage over blood measurements of lead and cotinine: they are indicators not just that a contaminant is present in the body but that it is having a discernible effect, in this case by altering DNA molecules. Here, too, however, there are some big uncertainties because no consensus exists on how the formation of adducts could lead to developmental problems in children. In cancer research, where Perera did her initial work with adducts, the connection is somewhat clearer because an adduct's ability to disrupt accurate genomic copying during cell division could trigger mutations and other genetic changes that give rise to malignant cells. But for developmental deficits in children, the theories are more nebulous.

One of the leading ideas about how PAHs may affect the brain involves the "neural pruning," or controlled nerve cell death, that occurs naturally as the developing brain adjusts to its environment and becomes more efficient by discarding synapses it does not need. The presence of PAHs may alter brain function by extending this process, called apoptosis, to essential synapses as well—both in the womb and in the child's early life. Another prominent theory is that PAHs disrupt a fetus's ability to obtain nutrients and oxygen by occupying molecular receptor sites in the placenta. The pollutants may also trigger the release of metabolism-altering enzymes in fetuses and young children and may also alter levels of growth-regulating hormones. The likeliest answer, some experts suggest, is that most or perhaps even all these mechanisms are taking a toll on the brains of children exposed to high levels of air pollution.

"One of the things we've come to learn over the past 10 years is how many pathways there are in many common diseases," says Groopman, whose studies in China and elsewhere have focused on the interaction of aflatoxins with human hepatitis B virus in inducing liver cancer. Aflatoxins, which are produced by Aspergillus fungi, are a ubiquitous food contaminant in China and Africa. "With aflatoxin and liver cancer, you're dealing with just

one compound and with a specific disease that is very common in countries like China. There are no other confounding sources," he points out. PAHs and childhood development, he adds, "are a much more complicated story."

Next Steps

The next steps, Perera and Groopman agree, will be to scale up and drill down. Larger studies with greater statistical power, involving perhaps thousands of children, may be able to find stronger correlations between PAH exposures and specific developmental problems. Meanwhile investigators will also be delving into the intricacies of neural chemistry in the search for new biomarkers that will allow them to better measure the precise changes in the brain that give rise to growth and learning problems.

That search is already taking scientists into the realm of epigenetics, which is the study of heritable, environmentally induced changes that alter the functions of genes without changing their underlying sequence of DNA codes, as PAH adducts do. According to Perera, some evidence already exists that PAHs can lead to epigenetic changes in gene activity that cannot be identified by looking for breaks or disruptions in the genetic code itself. Because adducts are not a proxy for those epigenetic changes, Perera and other molecular epidemiologists are starting to turn to other biomarkers, such as DNA methylation, which is the attachment of methyl groups (CH3) to genetic material. Methylation typically silences genes, and some evidence suggests that methylation increases with PAH exposure and prevents genes from giving rise to proteins involved in suppressing some diseases, including cancer.

If epigenetic changes turn out to be crucial in altering a child's capacity to grow and learn, then counting methyl groups may end up being a better dosimeter for pollution's impact on the brain than counting PAH-DNA adducts. The Tongliang study may help settle that question, because Perera and Tang plan to analyze all their Tongliang blood samples for DNA methylation and perhaps for other epigenetic biomarkers as well.

Someday doctors may be able to test for a battery of biomarkers—both genetic and epigenetic—to assess a child's overall risk for a wide range of health and developmental problems. For now, though, children such as the girl in the abandoned coal shed in Tongliang will have to rely on their governments to protect them from PAHs and other harmful air pollutants, and Perera never misses a chance to prod public officials to do so. "Tongliang is important because it shows that governments can take specific actions to reduce exposures," she asserts. "Instead of just guessing, we can measure the improvements." The ability to measure cause and effect is especially important in China and other fast-growing countries that are making hard choices about whether to continue to rely heavily on coal or move to cleaner but more expensive energy sources.

The complexities and uncertainties of molecular epidemiology, Perera says, should not obscure the overall message of the data she has accumulated during 29 years spent studying the health effects of air pollution in Finland, Poland, China and her own

neighborhood near Columbia in upper Manhattan. That message is as relevant in developed nations as it is in heavily polluted China, she explains, because PAHs are a ubiquitous pollutant capable of affecting children even at relatively low concentrations. In New York City, where airborne PAH levels are more than 10 times lower than in Tongliang, “we have been able to measure the effects in reduced fetal growth and neurodevelopmental impacts,” Perera notes. “This is not some vague, theoretical threat that may or may not turn out to be valid with more study. We have all the evidence we need to reduce these exposures right now.”

Even as Perera and Tang continue to analyze their Tongliang data, they are on the prowl for opportunities to launch a much larger study based on the same before-and-after premise as the work in Tongliang. “It would require the magic of finding just the right kind of place, in just the right setting,” she says. “We’ve got our eyes peeled for that.”

Note: This article was originally published with the title, "China's Children of Smoke".

Exposure To Traffic-related Air Pollution Linked To Onset Of Allergic Diseases In Children

Allergy To Road Traffic:
Exposure To Traffic-related Air Pollution Linked To Onset Of Allergic Diseases In Children

http://www.sciencedaily.com/releases/2008/07/080712144742.htm

ScienceDaily (July 17, 2008) — Allergic diseases appear more often in children who grow up near busy roads according to a new study involving several thousand children.

Under the direction of the Helmholtz Zentrum München, a German research group studied in a longitudinal study, over six years, whether associations are identifiable between the onset of atopic diseases and exposure to air pollutants originating from traffic.

The scientists based their analysis, on the one hand, on the corresponding distance of the parental home to streets busy with traffic, and on the other hand, modeled values, for the respective residencial addresses of the children, of air pollution with fine dust, diesel soot and nitrogen dioxide.

The research team led by Dr. Joachim Heinrich of the Institute of Epidemiology of the Helmholtz Zentrum München compared, with this, the data of 3,061 six-year old children from Munich and its surroundings. From birth, their development has been tracked within

the scope of the so-called GINI and LISA studies. The studies are led by Prof. Dr. H.-Erich Wichmann of the Helmholtz Zentrum München, and, among other things, are aimed at the study of behavioral and environmental risk factors for allergic diseases. In the current analysis, the results of medical research and regular parental interviews were considered. Moreover, the appearance of the specific IgE antibodies against common allergens in blood serum was tested in children at the age of 6.

The scientists were able to estimate individual values of exposure of children to fine dust and nitrogen dioxide, with the help of calculation models. It was shown that an escalation of asthmatic bronchitis and allergic sensitization to pollen and other common allergens occurred with increasing exposure to fine dust. Increased exposure to nitric oxide was linked to increases in eczema.

Connections were noted, in particular, between the appearance of asthmatic bronchitis, hay fever, eczema and allergic sensitization, on the one hand, and residential environment, on the other: compared with their contemporaries living in more distant places, children who lived less than 50 m from a very busy main road were between 1 % and 50 % more likely to contract these diseases. Statistical analysis of the data showed a lower risk with increasing distances to the main roads.

Joachim Heinrich and his colleagues consider the results of their research to be clear evidence of the disadvantageous effects of air pollution from traffic on the causes of allergies and atopic diseases. In the past, epidemiological studies on this subject failed to supply a clear picture, although the effects of laboratory experiments and inhalation studies are well-known.

Journal reference:

V. Morgenstern et al. Atopic Diseases, Allergic Sensitization, and Exposure to Traffic-related Air Pollution in Children. American Journal of Respiratory and Critical Care Medicine, 2008; 177 (12): 1331 DOI: 10.1164/rccm.200701-036OC
Adapted from materials provided by Helmholtz Zentrum Muenchen - German Research Centre for Environmental Health.
Allergy To Road Traffic: Exposure To Traffic-related Air Pollution Linked To Onset Of Allergic Diseases In Children. ScienceDaily. Retrieved July 18, 2008, from http://www.sciencedaily.com /releases/2008/07/080712144742.htm

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OSU STUDY SHOWS EXPOSURE TO BAD AIR RAISES BLOOD PRESSURE

http://researchnews.osu.edu/archive/rajagop.htm

Public Release: 28-Jul-2008
Arteriosclerosis, Thrombosis, and Vascular Biology

COLUMBUS, Ohio – The air people breathe while walking in the park, working in the garden or shopping downtown may be unhealthy enough to seriously spike their blood pressure, a new study suggests.

Cardiovascular researchers at The Ohio State University Medical Center are the first to report a direct link between air pollution and its impact on high blood pressure, or hypertension. If the results from these animal studies hold up, this could be important for human health.

"We now have even more compelling evidence of the strong relationship between air pollution and cardiovascular disease," said Sanjay Rajagopalan, section director of vascular medicine at Ohio State's Medical Center and co-author of the study. This builds upon previous research from Rajagopalan's team published in the journals *JAMA*, *Circulation* and *Inhalation Toxology*.
Researchers exposed rats to levels of airborne pollutants that humans breathe everyday, noting the levels were still considerably below levels found in developing countries such as China and India, and in some parts of the U.S.

Sanjay Rajagopalan

Researchers found that short-term exposure to air pollution, over a 10-week period, elevates blood pressure in those already predisposed to the condition.

The results appear online and are scheduled for publication in an upcoming issue of *Arteriosclerosis, Thrombosis, and Vascular Biology*, a journal published by the American Heart Association.

"Recent observational studies in humans suggest that within hours to days following exposure, blood pressure increases," Rajagopalan says.

In a highly-controlled experiment, hypertensive rats were placed in chambers and exposed to either particulate matter or filtered air for six hours a day, five days a week, over a period of 10 weeks. At week nine, researchers infused angiotensin II, another pollutant, into mini-pumps within the chambers and monitored responses in blood pressure over one week.

The air pollution level inside the chamber containing particulate matter was comparable to levels a commuter may be exposed to in urban areas with heavy traffic such as downtown Manhattan. “Pre-exposure to air pollution markedly increased blood pressure responses following infusion of angiotensin II,” added Rajagopalan.

According to the U.S. Environmental Protection Agency (EPA), the four most common pollutants emitted into the air are particulate matter, ozone, nitrogen dioxide and sulfur dioxide. Air pollution is commonly the result of industrial emissions, coal burning, power plants and automobile exhaust.

“This study provides guidance for the EPA to change pre-existing stringent standards in the effort to reduce air pollution,” says Rajagopalan. “Our study also confirmed a need for a broader based approach, from the entire world, to influence policy development.”

“This study provides guidance for the EPA to change pre-existing stringent standards in the effort to reduce air pollution,” says Rajagopalan. “Our study also confirmed a need for a broader based approach, from the entire world, to influence policy development.”

Qinghua Sun, first author of the study, will analyze vascular function in humans before and after the upcoming summer Olympics in Beijing, China.

With stringent laws to ensure good quality during the games, it is anticipated that the air quality will improve significantly in and around Beijing. “We expect to find a tangible impact on vascular function and blood pressure because ultimately the only thing that will have changed is levels of air pollution,” says Sun.

Researchers at the University of Michigan, the U.S. Environmental Protection Agency, the Institute of Statistical Science and the New York University School of Medicine participated in the study.

Along with Rajagopalan and Sun, other Ohio State researchers involved in the study were Peibin Yue, Zhekang Ying and Arturo J. Cardounel. Funding from the National Institutes of Health supported this research.

According to the World Health Organization (WHO), more than three million premature deaths each year can be attributed to air pollution, with more than half of the population residing in developing low- and middle-income countries where air pollution levels are at their highest. For example, severe air pollution in Beijing, China, where the average concentration is well above five times that of levels typically found in the U.S., is the result of rapid industrial development, urbanization and increased traffic into the capital. WHO relies on scientific evidence and considers its implications when determining air quality

guidelines.

Many U.S. Public Schools in 'Air Pollution Danger Zone'

http://www.healthnews.uc.edu/news/?/7358/

CINCINNATI—One in three U.S. public schools are in the "air pollution danger zone," according to new research from the University of Cincinnati (UC).

UC researchers have found that more than 30 percent of American public schools are within 400 meters, or a quarter mile, of major highways that consistently serve as main truck and traffic routes.

Research has shown that proximity to major highways—and thus environmental pollutants, such as aerosolizing diesel exhaust particles—can leave school-age children more susceptible to respiratory diseases later in life.

"This is a major public health concern that should be given serious consideration in future urban development, transportation planning and environmental policies," says **Sergey Grinshpun**, PhD, principal investigator of the study and professor of environmental health at UC.

To protect the health of young children with developing lungs, he says new schools should be built further from major highways.

"Health risk can be mitigated through proper urban planning, but that doesn't erase the immediate risk to school-age children attending schools that are too close to highways right now," he adds. "Existing schools should be retrofitted with air filtration systems that will reduce students' exposure to traffic pollutants."

The UC-led team reports its findings in the September 2008 issue of the *Journal of Environmental Planning and Management*, an international scientific journal. This is believed to be the first national study of school proximity and health risks associated with major roadways.

For this study, Grinshpun's team conducted a survey of major metropolitan areas representative of all geographical regions of the United States: Atlanta, Boston, Cincinnati, Denver, Philadelphia, Los Angeles, Memphis, Minneapolis and San Antonio.

More than 8,800 schools representing 6 million students were included in the survey. Primary data was collected through the U.S. Department of Education's National Center for Education Statistics.

Schools within this data set were then geocoded to accurately calculate distance to the nearest interstate, U.S. highway or state highway.

Past research on highway-related air pollution exposure has focused on residences located close to

major roads. Grinshpun points out, however, that school-age children spend more than 30 percent of their day on school grounds—in classrooms, after-school care or extracurricular activities.

"For many years, our focus has been on homes when it comes to air pollution. School attendance may result in a large dose of inhaled traffic pollutants that—until now—have been completely overlooked," he adds.

These past studies suggest this proximity to highway traffic puts school-age children at an increased risk for asthma and respiratory problems later in life from air pollutants and aeroallergens.

This includes research from the UC Cincinnati Childhood Allergy and Air Pollution Study (CCAAPS) which has reported that exposure to traffic pollutants in close proximity to main roads has been associated with increased risk for asthma and other chronic respiratory problems during childhood.

Grinshpun's team found that public school students were more likely to attend schools near major highways compared to the general population. Researchers say the rapid expansion of metropolitan areas in recent years—deemed "urban sprawl"—seems to be associated with the consistent building of schools near highways.

"Major roads play an important role in the economy, but we need to strike a balance between economic and health considerations as we break ground on new areas," says Alexandra Appatova, the study's first author. "Policymakers need to develop new effective strategies that would encourage urban planners to reconsider our current infrastructure, particularly when it comes to building new schools and maintaining existing ones."

The state of California, for example, has passed a law prohibiting the building of new schools within 500 feet (168 meters) of a busy road. New Jersey is moving a bill through the legislature to require highway entrance and exit ramps to be at least 1,000 feet from schools.

This study was funded in part by grants from UC's Center for Sustainable Urban Engineering and the National Institute of Environmental Health Sciences. UC's Patrick Ryan, PhD, and Grace LeMasters, PhD, also participated in this study. Appatova was an intern in UC's department of environmental health when the study was being conducted.

Air pollution poses heightened risk to heart patients: study

Last Updated: Wednesday, September 10, 2008 |
http://www.cbc.ca/health/story/2008/09/10/heart-air-pollution.html
CBC News

Tiny particles in polluted air hamper the heart's ability to conduct electrical signals, raising the risk for people with heart disease, who should avoid traffic pollution after leaving

hospital, researchers say.

Pollution from cars and industrial factories is known to trigger heart attacks.

The American Heart Association and the American College of Cardiology already recommend that some heart patients, particularly those who have had heart attacks, avoid driving for several weeks, especially in heavy traffic, because of the stress.

"Our study provides additional rationale to avoid or reduce heavy traffic exposure after discharge, even for those without a heart attack, since traffic exposure involves pollution exposure as well as stress," lead researcher Dr. Diane Gold said in a release Tuesday.

The team from Harvard University in Boston collected data on 48 patients who had been hospitalized for heart attack, unstable angina or worsening symptoms of coronary artery disease.

The subjects, who were between 43 and 75 years old, wore portable electrocardiograph machines for 24 hours. Researchers also visited the patients two to four weeks after discharge and three more times over a year.

Effect greatest in first month

Researchers found that when levels of tiny particles in air pollution and black carbon from traffic exhaust increased, there were changes in the electrical conductivity of the heart called ST-segment depression, which may indicate inadequate blood to the heart or inflamed heart muscle.

Higher black-carbon levels over the previous day were linked with a 1.5-fold increased risk of ST-segment depression, according to the study.

The effects were greatest within the first month after hospitalization, and for patients who had been hospitalized for a heart attack or had diabetes, the researchers reported in the journal Circulation.

The average daily levels for all pollutants in the study were below accepted or proposed national air-quality standards in the U.S.

It's not known how the carbon and air particles lead to ST-segment depression.

"Further research is needed to evaluate whether the pollution-related ST-segment depression that we see is related to increased heart muscle inflammation, reduced oxygen flow, oxidative stress, or increased risk of arrhythmias," Gold said.

"We think that our findings, which are definitely subclinical, may represent a process that increases clinical risk for people with symptomatic coronary artery disease."

$PM_{2.5}$ Constituents and Oxidative DNA Damage in Humans

Environ. Sci. Technol., Article ASAP

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Publication Date (Web): April 1, 2009

http://pubs.acs.org/doi/abs/10.1021/es803337c

Abstract

Previous studies suggested that certain constituents of ambient $PM_{2.5}$ can induce or increase oxidative stress in biological systems. The present study is designed to examine whether exposure to traffic generated particles increases the burden of oxidative stress in humans and to identify specific $PM_{2.5}$ constituents responsible for pollution-induced oxidative stress. We recruited two nonsmoking security guards who worked at a university campus gate by a heavily trafficked road. Pre- and post-workshift spot urines were collected on each of the 29 days of measurement. Concentrations of $PM_{2.5}$ mass and 126 chemical species were measured at the worksite and a campus background site simultaneously. Urine samples were analyzed for 8-hydroxy-2′-deoxyguanosine (8-OHdG). Factor analysis and linear mixed-effects regression models were used in statistical analyses. Three clusters of $PM_{2.5}$ species were identified, including PAHs, metals, and polar organic compounds. Urinary concentrations of 8-OHdG increased by >3 times following an eight-hour workshift in participants. Pre-workshift urinary concentrations of 8-OHdG were associated with $PM_{2.5}$ concentrations at the background site. Post-workshift 8-OHdG concentrations were significantly and positively associated with $PM_{2.5}$ mass, PAHs, and metals, but not polar organic species, measured at the worksite. Our findings provide direct evidence in humans that PM compositions are important in increasing oxidative stress burdens. Our results support that PAHs and metals are biologically active constituents of $PM_{2.5}$ with regards to the induction of oxidative DNA damages in the human body.

- Abstract http://pubs.acs.org/doi/abs/10.1021/es803337c
- Full Text HTML http://pubs.acs.org/doi/full/10.1021/es803337c
- Hi-Res PDF[201 KB] http://pubs.acs.org/doi/pdf/10.1021/es803337c
- PDF w/ Links[137 KB] http://pubs.acs.org/doi/pdfplus/10.1021/es803337c

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Study Links Maternal Exhaust Exposure to Childhood Asthma

By Eddy Ball
April 2009

http://www.niehs.nih.gov/news/newsletter/2009/april/study-links.cfm

"This research is aimed at detecting early signs of asthma risk, so that we can better prevent this chronic disease that affects as many as 25 percent of children in Northern Manhattan and elsewhere," Perera explained. (Photo courtesy of Columbia University's Mailman School of Public Health)

Second author Tang took the lead in performing experiments for the basic research component of the study and made major contributions to design, data analysis and write-up of the study. (Photo courtesy of Shuk-mei Ho)

Chief author Shuk-mei Ho maintained, "Our data support the concept that environmental exposures can interact with genes during key developmental periods to trigger disease onset later in life and that tissues are being reprogrammed to become abnormal later." (Photo courtesy of the UC Academic Health Center)

A recent proof-of-principle study, funded in part by NIEHS, reports preliminary evidence of an association between transplacental exposure to traffic-related polycyclic aromatic hydrocarbons (PAHs) and childhood asthma among a cohort in New York City — where more than 25 percent of children are affected by the disease. The seven-member team of researchers at Columbia University and the University of Cincinnati maintain that their study is the first to "examine the effects of prenatal exposure to ambient air pollutants on DNA methylation patterns in genes potentially associated with the asthma phenotype in the offspring."

Lead authors on the study (http://www.plosone.org/article/info:doi/10.1371/journal.pone.0004488) , published online in *PLoS ONE*, were Frederica Perera, Dr.PH. (http://www.mailmanschool.org/msphfacdir/profile.asp?uni=fpp1) , professor of environmental health sciences and director of the Columbia Center for Children's Environmental Health (CCCEH) and NIEHS grantee Wan-yee Tang (http://tools.niehs.nih.gov/portfolio/sc/detail.cfm?appl_id=7514004), Ph.D., of the University of Cincinnati (UC). The principal investigator and corresponding author was Shuk-mei Ho, Ph.D. (http://www.eh.uc.edu/dir_individual_details.asp?qcontactid=702) , chair of the Department of Environmental Health at UC.

The paper outlines a novel study design for identifying biomarkers and surrogate disease endpoints that could serve as what the authors call a "new blueprint" for use in population-based studies. The authors described their approach as "environmental epigenetics" — a research focus that incorporates analysis of epidemiologic data with unbiased investigation into epigenetic alterations associated with disease to identify the most promising candidate genes associated with the population data. The approach is based on the concept that environmental exposures can interact with genes during key developmental periods to trigger disease onset later in life.

Subjects in the study were nonsmoking Dominican and African-American women from the Washington Heights, Central Harlem and South Bronx areas of New York City. The women

were members of a CCCEH cohort who were willing to complete prenatal air monitoring and collection of a maternal and/or umbilical cord blood sample at birth. Childhood asthma in the offspring was verified by parental report of a doctor's diagnosis.

Using this approach with unbiased profiling by methylation sensitive restriction fingerprinting, the researchers were able to identify 31 candidate genes that showed differential methylation patterns between those with maternal PAH above and those with levels below the median in the cohort of 20 children. From that group of genes, they were able to narrow the field to six candidates that are known genes with CpG islands in the 5' promoter flanking region using computer-based, or *in silico*, analysis.

The team found a positive and significant association between methylation of a 5'-CpG island in a gene known as *acyl-CoA synthetase long-chain family member 3 (ACSL3)* and the level of maternal PAH exposure and parental reports of asthma symptoms in offspring prior to age five. *ACSL3* is one of the candidate genes critical to T-helper cell differentiation that may induce polarization toward or away from an allergic phenotype. T cells are important in the production of cytokines and other asthma mediators. The researchers reported that additional testing showed methylation status was predicted with 75 percent sensitivity and 82 percent specificity — suggesting strongly that the methylation of *ACSL3* is a putative epigenetic marker associated with PAH exposure and asthma.

In their conclusion, the study's authors described their work as "an important first step" in much-needed research to help scientists understand a theoretically preventable disease by pinpointing environmental triggers and establishing the mechanisms that initiate this complex condition. Further research is needed, they wrote, "to identify an epigenetic profile related to PAH-associated childhood asthma and determine whether reprogramming events associated with transplacental exposure to PAHs increase risk of childhood asthma."

Citation: Perera F, Tang WY, Herbstman J, Tang D, Levin L, Miller R, Ho SM. (http://www.ncbi.nlm.nih.gov/pubmed/19221603?ordinalpos=3&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_DefaultReportPanel.Pubmed_RVDocSum) 2009. Relation of DNA methylation of 5'-CpG island of ACSL3 to transplacental exposure to airborne polycyclic aromatic hydrocarbons and childhood asthma. PLoS ONE 4(2):e4488. doi:10.1371/journal.pone.0004488.

Addressing a Newly Recognized Gap in Asthma Research

This paper by Perera et al. addresses a major research priority area described in a recently published report (http://pats.atsjournals.org/cgi/content/full/6/1/1) by the National Heart, Lung and Blood Institute Working Group on its "Pediatric Pulmonary Diseases Strategic Planning Workshop," held July 9-10, 2008. The group outlined multiple opportunities for leading-edge research into epigenetic influences on lung programming and translation of early life epigenetic programming to specific disease states.

Two of the study's authors, Rachel Miller, M.D., and Ho had identified the same research need in an earlier review (http://www.ncbi.nlm.nih.gov/pubmed/18187692?ordinalpos=4&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_DefaultReportPanel.Pubmed_RVDocSum) , "Environmental Epigenetics and Asthma: Current Concepts and Call for Studies," that appeared in the March 2008 issue of the *American Journal of Respiratory and Critical Care Medicine*. They reviewed research into the genetic and environmental components of

asthma as they called for novel approaches to understand the role of epigenetic alterations by applying newly developed technologies to epidemiologic studies.

HEI is a nonprofit corporation chartered in 1980 as an independent research organization to provide high-quality, impartial, and relevant science on the health effects of air pollution. Typically, HEI receives half of its core funds from the US Environmental Protection Agency and half from the worldwide motor vehicle industry (see HEI Sponsors). Other public and private organizations periodically support special projects or certain research programs.

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http://www.healtheffects.org/
