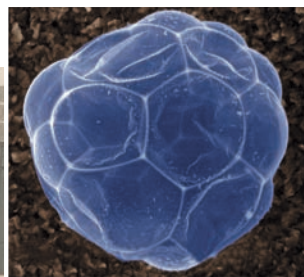


## Road RAGE?

### The Role of Diesel Particulate Matter in Lung Inflammation

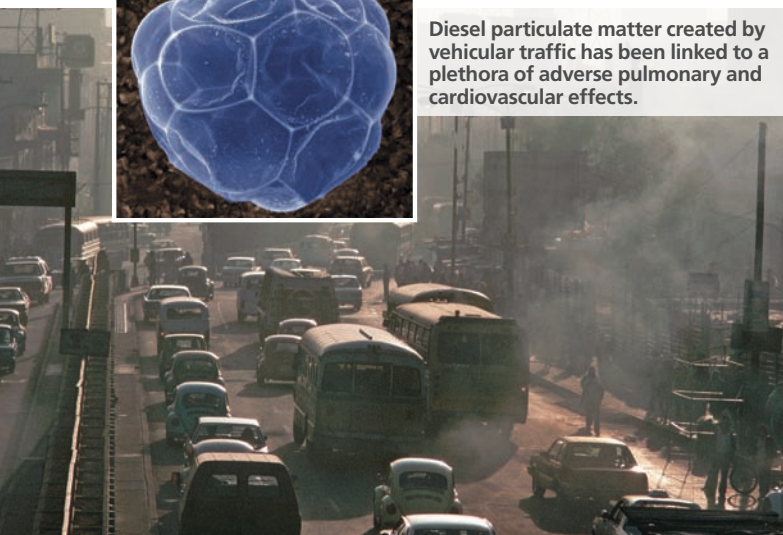
Diesel particulate matter (DPM) is a nearly ubiquitous environmental pollutant. It is known to be inflammatory and is linked to a plethora of health effects including asthma, chronic obstructive pulmonary disease, and pulmonary fibrosis. New research sheds light on which components of DPM are harmful to the lung and what mechanisms they trigger [*EHP* 119(3):332–336; Reynolds et al.].

The authors focused on receptors for advanced glycation end-products (RAGE), cell-surface proteins expressed in many cell types.



Diesel particulate matter created by vehicular traffic has been linked to a plethora of adverse pulmonary and cardiovascular effects.

Previous research performed in the same laboratory documented that



## Climate Change and Children's Health

### Protecting and Preparing Our Youngest

Climate change is expected to bring increased frequency and intensity of rainstorms, snowstorms, heat waves, and other extreme weather events. Numerous studies indicate climate change is already contributing to a greater overall burden of disease. A new review uses a children's health framework to summarize the latest data on the projected increasing burden of climate change–related disease for children [*EHP* 119(3):291–298; Sheffield and Landrigan]. The authors also discuss prevention strategies they believe should be incorporated into public health programs.

For 2000 the World Health Organization (WHO) estimated climate change contributed to more than 150,000 deaths and 5.5 million lost disability-adjusted life years worldwide. More than 88% of this burden occurs in children under age 5 years, even though the overall pediatric burden of disease is only 5% in high-income countries and 31% in low- and medium-income countries.

Children are inherently sensitive to the climate because they are physiologically and metabolically less effective than adults at adapting to heat and other climate-related exposures. Rapid development and higher exposures per unit of body weight make them more vulnerable to environmental exposures, and their diet and behavior may expose them to different agents than adults might typically encounter. More expected future years of life provides more time

RAGE can be activated in response to cellular stress resulting from exposure to particles in cigarette smoke. The authors hypothesized that exposure to DPM generated by fuel combustion could induce RAGE in the epithelial cells lining the lungs.

The team studied effects of DPM exposure in human primary pulmonary epithelial cells and R3/1 cells, an immortalized alveolar type 1 cell line derived from rats. They found that the quantities of *RAGE* messenger RNA and protein increased by approximately 100% in both cell types after exposure to DPM for 2 hours, compared with controls. By demonstrating that RAGE is indeed upregulated following exposure to DPM, the authors identified a surface signaling mechanism involved in inflammatory responses triggered by DPM exposure.

From there, the scientists identified some of the downstream signaling effects associated with RAGE upregulation. Their gene reporter experiments showed DPM exposure caused significant translocation of nuclear factor  $\kappa$ B (NF- $\kappa$ B), a potent proinflammatory mediator, into the nucleus of R3/1 cells, where it can promote the expression of more than 200 genes. Through experiments involving the inhibition of RAGE with small interfering RNA (siRNA), the team confirmed that DPM-induced NF- $\kappa$ B activation is mediated in part by RAGE expression.

The scientists also documented that exposure to DPM increased the synthesis and secretion of two NF- $\kappa$ B targets (IL-8, a chemokine, and MCP-1, a cytokine) by the R3/1 cells. These molecules were secreted to a lesser extent, but were not completely inhibited, in cells transfected with siRNA for RAGE prior to DPM exposure, which suggests other factors and pathways also are involved in inflammatory responses to DPM.

The new research is also significant for contradicting conventional wisdom that only “fresh” DPM is biologically active. The work suggests that even “aged” DPM that has been suspended in the atmosphere for more than a decade is capable of biological activity, which has important public health implications given the abundance of this pollutant in the atmosphere.

**Kellyn S. Betts** has written about environmental contaminants, hazards, and technology for solving environmental problems for publications including *EHP* and *Environmental Science & Technology* for more than a dozen years.

for exposure to new or worsening hazards, and a dependence on caregivers means children can't always control their surroundings or remove themselves from harm.

In the current review, the authors analyzed health outcomes expected to result from increased temperatures, increasing frequency and severity of extreme weather, and sea-level rise. These include higher rates of vectorborne diseases such as malaria and dengue and of diarrheal disease, more exposure to extreme weather and to toxic chemicals (for instance, as weather changes affect patterns of pesticide use), and greater risks of poverty and of displacement due to sea-level rise, crop failure, and food insecurity. Other impacts include malnutrition and problems related to increased exposures to allergens and air pollution. Risk varies across socioeconomic levels and geographic locations.

The authors write that prevention strategies to help alleviate children's burden of disease should incorporate climate change adaptation into current programs as well as monitor children's exposures and environmental health indicators in a manner that is internationally consistent—as proposed by the WHO. They emphasize that new climate-sensitive disease-prevention programs should strive not only to protect children and parents in the short term but also prepare children to be resilient adults in the years to come. They also point to health impact assessments as an emerging tool to help shape smart policies that can solve multiple existing problems and head off future burdens.

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