### THE PATH AHEAD

## Particulate Matter Is a Surprisingly Common Contributor to Disease

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#### Abstract

Particulate matter is a huge contributor to indoor and outdoor air pollution and a significant factor in many major diseases. Those living in cities, and especially those working in traffic or living near roads, have substantially increased risk of several diseases, especially autoimmune, cardiovascular, respiratory, and neoplastic. Intervention is primarily based on reducing exposure and using appropriately sophisticated air cleaning systems.

#### Particulate Matter

According to the US Environmental and Protection Agency (EPA),

Particulate matter (PM), also known as particle pollution, is a complex mixture of extremely small particles and liquid droplets that get into the air. Once inhaled, these particles can affect the heart and lungs and cause serious health effects.<sup>1</sup>

It contains aerosols and solid particles like dust, soot, smoke, and dirt. Of particular clinical importance, PM absorbs and adsorbs many types of toxic chemicals such as diverse polycyclic aromatic hydrocarbons and volatile organic compounds, which significantly contribute to their toxic health effects.<sup>2</sup>

PM is categorized according to particle size. Particles that are 2.5 to 10 micrometers in diameter are considered "coarse" and designated as  $PM_{10}$ . These larger particles are typically found near dusty roadways and industrial activity. *Fine particles* are defined as 0.1 to 2.5 micrometers in diameter and are designated as  $PM_{2.5}$ . Ultrafine particles (UFP), also called nanoparticles, are less than 0.1 micrometers in size. They are more soluble than larger particles and are designated as  $PM_{0.1}$ .

#### Sources of Particulate Matter

**Cities.** In general, the larger the population center, the greater the amount of air pollutants due to multiple sources of combustion (vehicles, barbeques, smoking, etc) and industrial activity. To help address the health problems due to city pollution, in 1970, the US Congress passed the Clean Air Act, which set limits for emissions from stationary and mobile sources of pollution.<sup>3</sup> The EPA now regulates the 6 worst air pollutants: particle matter, ozone, carbon monoxide, sulfur oxides, nitrogen oxides, and lead. Of these, particle matter and ozone cause the most physiological damage.

**Diesel and Biodiesel.** Those smoking diesel vehicles are as toxic as they look. Diesel exhaust particles are probably the most toxic component of urban outdoor air pollutants. They are a mixture of carbon particles, organic chemicals, heavy metals, and free radicals. The oxidative damage they cause is not only to enzymes and cell membranes, but also to DNA, as demonstrated by elevated urinary 8-OHdG level.<sup>4,5</sup> This damage is especially serious in those with the highest exposure to diesel exhaust, such as traffic officers.<sup>6,7</sup>

The effort to decrease diesel exhaust toxicity has led to the use of low-sulfur diesel fuels and biodiesel. Unfortunately, the results have been far less beneficial than expected. Low-sulfur diesel and biofuels put out less sulfur oxides and approximately 26% less total PM. However, 100% biodiesel (typically from waste cooking oil) reduced total PM by only 9%.<sup>8</sup> Unfortunately, although the total mass of PM from the biodiesel fuels is lower than for regular diesel, they produce much more of the ultrafine particles that penetrate the lungs more deeply, resulting in greater toxicity.<sup>9</sup> Also, although biodiesel exhaust has lower sulfates, they also produce higher levels of nitrogen oxides than regular diesel exhaust.<sup>10</sup> Researchers have

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studied mixing biodiesel with regular diesel, typically a 50/50 ratio. These biodiesel blends have the benefit of producing far fewer PAHs (polyaromatic hydrocarbons) and VOCs (volatile organic compounds) than standard diesel fuel. Unfortunately, they also produce higher levels of PM, CO, and sulfur compounds. Researchers who studied animals exposed to each type of exhaust surprisingly found that biodiesel resulted in greater adverse cardiovascular, hematological, and proinflammatory changes than regular diesel.<sup>11</sup> Overall, currently available biodiesel, especially blends, do not appear to have much impact on reducing total outdoor air pollution from diesel engines.

#### **Toxic Effects of PMs**

Key to understanding the widespread physiological damage done by PMs is that their toxicity is most definitely not limited to the contact areas of the lungs. Particles less than 10 micrometers in diameter are readily absorbed in the lungs and then distributed throughout the body. For example, animal research shows that PM containing iron oxide, India ink, and titanium dioxide that were initially found in alveolar macrophages were found a day later also in the liver, kidney, heart, tracheobronchial and mediastinal lymph nodes, anterior and posterior nasal cavity, brain, and blood.12 These toxic particles also enter the body through other routes, such as transport by the olfactory nerve into the brain.<sup>13</sup> Once these toxic particles are in the tissues, they are very difficult to eliminate. Animal research shows PM in the brain, heart, spleen, liver, and lungs a full 6 months after just a single exposure.<sup>14</sup> Anyone with daily exposure—such as when living in a city or near a major road or a job working near vehicles or other sources of combustion-have these particles with their adsorbed toxicants causing constant damage throughout their body.

These particles cause significant oxidative damage in whatever tissue they land in.<sup>15,16,17</sup> They have been associated with increased mortality, primarily from autoimmune, cardiovascular, respiratory, and neoplastic diseases.<sup>18,19,20,21</sup>

#### Diseases Most Affected by PM

**Mortality.** The higher the body load of PMs, the greater the incidence of many diseases, with resultant increased mortality. People living in larger, more polluted cities are 15% to 17% more likely to die a premature death than people living in areas with cleaner air.<sup>19,20,22</sup>

**Cardiovascular.** PM<sub>10</sub> has been shown to increase the levels of platelets, fibrinogen, and C-reactive protein.<sup>23,24</sup> In addition, PMs disrupt the autonomic function of the heart as evidenced by increased heart rate and cardiac arrhythmias and decreased heart rate variability.<sup>25</sup>

**Simply Living Close to a Major Roadway Increases Risk of Dying From an Acute Heart Attack.** In a study of 3886 people with acute myocardial infarction, those living 200 to 1000 meters from a major roadway were 13% more likely to have a fatal heart attack than those living over 1000 meters away. Living 100 to 200 meters away increased this risk to 19%, whereas those who lived within 100 meters had suffered a 27% increased risk of a fatal myocardial infarction (MI).<sup>26</sup>

**Cancer.** The California state EPA's office of Environmental Health Hazard Assessment asserts:

In fact, long-term exposure to diesel exhaust particles poses the highest cancer risk of any toxic air contaminant evaluated by OEHHA. ARB estimates that about 70 percent of cancer risk that the average Californian faces from breathing toxic air pollutants stems from diesel exhaust particles.<sup>27</sup>

People occupationally exposed to diesel exhaust have a 19% to 68% higher risk of lung cancer than nonexposed populations. In contrast, gasoline exhaust has only a weakly positive, nonsignificant association.<sup>28</sup> These risk ranges have been confirmed in a number of studies.<sup>29,30,31,32</sup>

The federal EPA has determined that benz[a] anthracene, benzo[a]pyrene, benzo[b]fluoranthene, benzo[k]fluoranthene, chrysene, dibenz[a,h]anthracene, and indeno[1,2,3-c,d]pyrene are probable human carcinogens.<sup>33</sup> Benzo[a]pyrene is the main lung carcinogen in cigarette smoke<sup>34</sup> and vehicular exhaust.<sup>35</sup> Both PM and PAHs are known to damage mitochondria and suppress their proper functioning.<sup>36,37</sup>

Respiratory. Exposure to diesel exhaust has been linked to the development of asthma in adults, which persists even after exposure ceases.<sup>38</sup> Several studies have shown a strong correlation between childhood asthma and respiratory problems and exposure to vehicle exhaust. Children living within 100 meters of a freeway had significantly more cough, wheeze, rhinitis, and diagnosed asthma compared with those living further away.<sup>39</sup> The intensity of truck traffic and the concentration of black smoke in the schools were both significantly associated with chronic respiratory symptoms. A study in Italy found that the amount of truck traffic on the street that children resided was significantly associated with increased risk of bronchitis (odds ratio [OR], 1.69), bronchiolitis (OR, 1.74), and pneumonia (OR, 1.84) as well as persistent phlegm (OR, 1.68) and wheezing (OR, 1.86) that was severe enough to limit speech.40

Many studies have found that living in the center of large cities significantly decreases baseline lung function compared to those living in the suburbs.<sup>41</sup> The greatest associations were found with NO<sub>2</sub> and PM<sub>10</sub>.

**Immunological.** Animal models have shown that exposure to diesel emission particles increases immunoglobulin E (IgE) reactivity to ovalbumin.<sup>42</sup> The problem appears both direct and indirect probably through an adjuvant mechanism. The authors of this study stated,

The possibility cannot be excluded that diesel emission particles, which are kept buoyant in the environmental atmosphere of urban districts, may exert an adjuvant activity for IgE antibody production after being inhaled into the human body and have some relation to the mechanism of the outbreak of allergic rhinitis caused by pollens in Japan. Another study found that living along main roads lined with older cedar trees (heavier pollen release) and heavy traffic had higher rates of cedar pollen allergy (13.2%) than those living in cedar forest areas with low traffic (5.1%).<sup>43</sup>

As levels of urban PM<sub>2.5</sub> exposure go up, so has the level of circulating anti-dsDNA antibodies, a classic marker for systemic lupus erythematosus (SLE).<sup>44</sup> The higher the levels of PM<sub>2.5</sub>, the higher the risk for SLE, Sjogren's syndrome, scleroderma, polymyositis, and dermatomyositis.<sup>45</sup> PM<sub>10</sub>, NO<sub>2</sub>, and CO have all been shown to be risk factors for juvenile onset SLE, with each 13.4  $\mu$ g/m<sup>3</sup> increase in PM<sub>10</sub> increasing disease risk by 34%.<sup>46</sup>

**Neurological.** Exposure to particulate matter less than 2.5 micrometers in diameter  $(PM_{2.5})$  is one of the most significant factors in cognitive dysfunction and decline. Computerized cognitive testing in children revealed a strong negative association between cognitive development and exposure to  $PM_{2.5}$ .<sup>47</sup> A study of cognitive function of older men (average age of 71 years) found clear dysfunction in proportion to vehicular exhaust  $PM_{2.5}$ .<sup>48</sup> Those men with the highest level of exposure had a mental decline that equaled 1.9 years of aging. A similar study in women between the ages of 70 and 81 years found a cognitive decline equivalent to 2 years of aging.<sup>49</sup>

#### Intervention

As with virtually all other toxins, avoidance of exposure is the critical first step. This starts with simple actions such as not smoking in the home, not having an open fireplace, not driving a diesel vehicle, and removing shoes before entering the home, which reduces the amount of PM and PAH tracked into the home. The other strategies are more challenging. Obviously, living rurally greatly decreases exposure, but for everyone else, appropriate air filters provide many benefits.

Best are whole-house air cleaners. Second best are appropriate filters in areas where people spend the most time, such as bedroom and kitchen. Electrostatic pleated air filters, rated at least a MERV 7, on home HVAC units can dramatically reduce the levels of PMs—depending upon their design.<sup>50</sup> Less costly filters with MERV ratings below 6 only reduce PM by less than 10%. MERV 7 filters significantly decrease levels of the circulating dust, which carries the majority of indoor air pollutants. The best methodology is a dedicated high-quality air purifier.<sup>51</sup>

A number of studies have shown that home air purifiers in communities with high outdoor air pollution produce measurable physiological benefits, such as reduction of inflammatory markers.<sup>52</sup> In this controlled study (which used sham units with no filters for comparison), the air purifiers reduced indoor PM about 60% and high-sensitivity C-reactive protein (hs-CRP) levels dropped by over 30%.

Directly protecting personal air space, such as by using face masks, has been shown to significantly affect endothelial function in persons in the highly polluted city of Beijing.<sup>53</sup>

There are, of course, many strategies for decreasing the damage from PMs (eg, anything that increases glutathione), but most critical is simply stopping exposure.

#### In This Issue

# Mitochondrial Function, Obesity, and Personalized Lifestyle Medicine

Associate Editor Jeff Bland, PhD, leads off the issue continuing his thoughtful discussion of how we can be thinking about personalized medicine. His review of the crucial role of mitochondria in health and ways to optimize function is an important read.

I was very encouraged by John Weeks' tally of the many advances made by this field in gaining federal recognition and inclusion. As the health care crisis grows, appears there is increasing willingness to look for solutions outside the box that got us into this mess.

Managing editor, Craig Gustafson, brings us 2 intriguing interviews. It would be hard to overstate the importance of the work of Heather Zwickey, PhD, in engaging the naturopathic profession in research and helping the whole field of integrative medicine become more rigorous in our thinking on psychoneuroimmunology. His second interview is of Leslie Stone, MD; Michael Stone, MD; and nutritionist Emily Rydbom, telling us about their application of sophisticated nutritional intervention to improve pregnancy outcomes. This is a substantive discussion of so many key factors that must be considered to provide new lives a better opportunity for health.

We so often talk about integrative medicine as combining the best of both worlds. But how often do we actually research the combination of natural products with conventional drugs? I therefore am pleased to provide you such research by Yi Bai, MD; Su-liang Ouyang, MD; Ya-jun Bai, MD; and Dai-hong Wu, MBA, who objectively evaluated the use of fluoxetine with electroacupuncture in the treatment of a difficult pain disorder.

We continue the excellent series on probiotics written by Keren E. Dolan, MS, CNS; Jessica M. Pizano, MS, CNS; Crystal M. Gossard, MS, CNS; Christy B. Williamson, MS, CNS; Cathleen M. Burns, MS, RD; Margaret G. Gasta, MS, RDN, CCN; Heather J. Finley, MS, RD, LD, CEDRD; Emily C. Parker, MS, RD; and Elizabeth A. Lipski, PhD, CNS, CCN, BCHN, IFMCP. Fascinating review of the impact of probiotics on skin health.

Lara and I just finished building a very nice—and large—raised vegetable garden. One of my sisters sent me a book on biodynamic gardening to help us do it right. While reading the beautiful book I was stunned by how similar they approach plant health to how we treat patients—get nutrients in, keep toxins out. This way of caring for plants comes from anthroposophical medicine, one of our intellectual forerunners. I think you will find the article by Ricardo R. Bartelme, MD, on this medical philosophy of great interest. An excellent case report demonstrates the strength of integrative approaches for patients. Kathleen O'Neil-Smith, MD, and. Melissa S. Barber, MSc, show how restoring proper gut function helps a young child recover from atopy and irritable bowel syndrome (IBS).

Associate Editor Bill Benda, MD, finishes the issue as usual with provocation. (I actually wrote this before I read his BackTalk because this is virtually always the case ...) Yup, another poke in the eye to get our attention.

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