Air quality and its impact on transplants

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As Civil and Environmental Engineering Professor Jamie Schauer travels around the world studying air pollution, he tenaciously reminds people that pollution is a human health issue. That is especially crucial when it comes to particulate matter, an airborne mix of microscopic solid particles and liquids that can arise from any number of sources. Particulate matter varies widely from place to place, and so do its potential health effects.

"I believe that different components of particles are what drive different pathways of disease," Schauer says.

In an effort to trace those pathways, Schauer says, environmental engineers need to collaborate with the medical profession to establish scientific connections between specific health problems and specific kinds and sources of pollution. He recently partnered with UW-Madison transplant surgeon Joshua Mezrich to examine how pollution impacts patients after a lung transplant.

Previous research has shown that lung transplant recipients who live near major roads are at higher risk of developing bronchiolitis obliterans syndrome, in which the body's immune system attacks the new lung. But this research didn't establish a clear medical reason why that should be. And, Mezrich says, except for some people who specialize in lung transplants, it hasn't really provoked the organ-transplantation community to pay more heed to environmental impacts.

"Lung transplants do a lot worse," Mezrich says. "In five years, half of

the grafts will be lost. There's something very different about lungs, and maybe part of that is this interface with the environment, and maybe it's something else."

It's hard to single out any one culprit for this disproportionate rate of rejection among lung transplant recipients, because transplant patients and their immune systems are already battling so many stresses.

But the two researchers are investigating whether particulate matter has a unique way of setting off the immune system. The research combines Mezrich's expertise in organ transplant tolerance with Schauer's intricate methods for chemically analyzing samples of air pollution. Schauer and his research group developed samples of cigarette smoke, wood smoke and diesel exhaust, then tested those samples on cultures derived from mice lungs.

And in a paper published in December 2013 in the journal *PLOS One*, Schauer and Mezrich showed that the pollution samples increase the formation of Th17 cells, a type of white blood cell that commonly attacks tissue in autoimmune diseases.

Mezrich hopes that by establishing specific mechanisms by which pollution impacts organ rejection—and by publishing his work more frequently in transplant journals, as opposed to immunology or toxicology journals—such research will convince his fellow transplant surgeons to get serious about how pollution affects their patients. In the *PLOS One* paper, Mezrich and Schauer noted that further exploration of these pathways could help doctors develop treatments that head off rejection, such as prescribing medication to block the aryl hydrocarbon receptor, a protein that binds to particulate matter and touches off the production of Th17 cells.

Beyond these processes that directly link particulate matter to an

autoimmune response, Mezrich says it's possible that pollution could have more subtle and indirect effects on transplant tolerance. If a person spends years inhaling foreign particles, Mezrich says, it's possible that activity puts the immune system on alert, making it all the more likely to attack when a new organ enters the picture.

"It would make sense to me that, say, if you're caught in a house fire or exposed to a really high level of particulate matter pollution, you'd want your immune system to get activated," Mezrich says. "But I could see over time, if you're constantly exposed to that, it could cause a scenario where you have a lot of inflammation and it could become pathologic."

When it comes to tracking down other disease pathways, Schauer's ability to gather samples of the world's incredibly varied pollution and make it translate to experiments on the molecular level will be crucial. Particulate matter can pose a threat even outside of industrialized or urban areas; Schauer points out that one-third of the world's population still gets its heat from burning solid fuels, including wood, coal, crop waste, and dung. The better we understand how those sources of particulate matter are impacting human health, the more we can prioritize targeting specific forms of air pollution. Schauer believes that environmental engineers and medical researchers can approach that task by working together to craft a forensic approach.

"A lot of people I work with in the medical field have never considered environmental conditions before, have never worked with an engineer before," Schauer says.

In this case, the language of engineering and environmental chemistry gives Mezrich an opportunity to change the conversation in the medical community. "I'd like to be able to present it to transplant people and say, 'look, pollution is causing all these bad things,' but to Jamie that represents so many things that can change over time," Mezrich says.

"Even if you find something at the cellular level, what are people really being exposed to?"

More information: van Voorhis M, Knopp S, Julliard W, Fechner JH, Zhang X, et al. (2013) "Exposure to Atmospheric Particulate Matter Enhances Th17 Polarization through the Aryl Hydrocarbon Receptor." *PLoS ONE* 8(12): e82545. DOI: 10.1371/journal.pone.0082545

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