How Inhaled Dust Harms the Lungs

Seven years ago, an Environmental Protection Agency statistician stunned researchers studying the effects of air pollution on health when he reported analyses indicating that as many as 60,000 U.S. residents die each year from breathing federally allowed concentrations of airborne dust (SN: 4/6/91, p. 212). This and subsequent studies figured prominently in EPA's decision last year to ratchet down the permitted concentration of breathable particles in urban air—and in human airways (SN: 7/5/97, p. 6).

At the time, many industrialists argued that they shouldn't have to pay for better pollution control because science had yet to suggest a plausible biological mechanism by which breathing low concentrations of urban dust might sicken or kill people.

Now, scientists at the University of Texas Houston Health Science Center describe how they uncovered what they think may be one of the basic elements of that toxicity.

On the alert for foreign debris, a community of white blood cells known as alveolar macrophages patrols small airways of the lung. When these cells encounter suspicious material, they identify it and send out a chemical clarion call to rally the immune system cells best suited to disabling and disposing of such matter.

The trick is to recruit only as many troops as are needed. If they call in too many, the lung can sustain inflammatory damage from friendly fire. Alongside the small troop of macrophages that stimulates defense measures, a larger squadron of macrophages halts immune activity when it threatens the host.

Andrij Holian and his coworkers in Houston have found that people with healthy lungs normally have 10 times as many suppressor macrophages as stimulatory ones. In people with asthma and other chronic lung diseases—who face an increased risk of respiratory disease from inhaling urban dust—that ratio may be only 3 to 1. The reason for the difference is not known.

In a report to published in the March ENVIRONMENTAL HEALTH PERSPECTIVES, Holian's team describes test-tube studies of human alveolar macrophages. The macrophages showed no response to ash collected from the Mount St. Helen's eruption. However, when exposed to airborne dust from St. Louis and Washington, D.C., most of the suppressor macrophages underwent apoptosis, or cellular suicide, while the stimulatory ones survived unaffected. Ash from burned residual oil, a viscous boiler fuel, proved even more potent at triggering suppressor cell suicides.

If this test-tube system models what's actually happening in the human lung, Holian told SCIENCE NEWS, the different responses of the two classes of lung macrophages could result in an overly aggressive immune response to normal triggering events. Indeed, he says, it would be the first step in a cascade that can end in inflammatory lung injury. "We may one day be able to target this upstream event and prevent that injury."

"This is, I think, an important contribution to the overall story," says Daniel L. Costa of EPA's pulmonary toxicology branch in Research Triangle Park, N.C.

Studies by EPA suggest that certain metals—especially iron, vanadium, nickel, and copper— in smoke from combustion of fossil fuels trigger particularly aggressive inflammatory responses by lung cells. Costa says these metals play a "preeminent" role in the toxicity of airborne particulates. When EPA researchers removed the metals, they also removed the toxicity, he says. Moreover, he notes, these metals tend to reside on the smallest water-soluble particles in urban air—the fraction targeted for more aggressive controls under the new rules.

Studies of dust from Washington, D.C., and St. Louis suggest how particles in air damage the lungs.

John Vandenberg, assistant director of EPA's National Health and Environmental Effects Research Laboratory in Research Triangle Park, says Holian's results are "a nice complement to our studies." *—J. Raloff*

Uric acid linked to multiple sclerosis

Mice paralyzed by a disease resembling multiple sclerosis can walk again after receiving daily injections of uric acid, a compound that occurs naturally in the body.

Treatment lessened symptoms and lengthened survival, report researchers from Thomas Jefferson University in Philadelphia. Sixty percent of untreated animals died within 4 weeks of the disease's onset, but almost 90 percent of the mice treated with the highest doses of uric acid were alive 8 weeks later.

"Before the treatment kicked in, the mice had total hind limb paralysis," says immunologist D. Craig Hooper, a coauthor of the study published in the Jan. 20 PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES. "When we stopped the treatment, they had a little limp."

The mice were given experimental allergic encephalomyelitis (EAE), a mouse disease that causes chronic bouts of paralysis much like multiple sclerosis in humans (SN: 12/6/97, p. 356). Hooper and his colleagues had reported earlier that they could prevent most EAE symptoms by giving mice uric acid before inducing the disease.

Now, the researchers report that uric acid treatment can reverse, not just prevent, the progression of EAE.

The team also found lower amounts of uric acid in 46 people with multiple sclerosis than in 46 people with other neurological diseases. In a review of 20 million Medicare and Medicaid patient records, the team discovered almost no overlap between multiple sclerosis and gout, a disease caused by excess uric acid. The combined evidence suggests a relationship between low uric acid concentrations and multiple sclerosis in people, Hooper says.

In both multiple sclerosis and EAE, the immune system seems to attack the myelin sheath that insulates the nerves of the brain and spinal cord. Uric acid inactivates peroxynitrite, a compound generated by the immune system to combat invading viruses and bacteria. Thus a deficiency in uric acid might lead to attacks on normal tissue.

However, the idea that low uric acid concentrations cause multiple sclerosis is controversial, says neuroimmunologist Henry F. McFarland of the National Institute of Neurological Disorders and Stroke in Bethesda, Md. He adds that accurately inferring disease causes from patient records is hard, particularly for a difficult-to-diagnose disease like multiple sclerosis.

Stephen Reingold, a neurophysiologist at the National Multiple Sclerosis Society in New York, cautions that "the vast majority of things that work in EAE prove not very promising in multiple sclerosis." Nevertheless, he adds, "this is an intriguing, provocative finding. It needs to be followed up." *—M. Jensen*