# Chemistry of Airborne Particulate -- Lung Interactions Revealed

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Exactly how airborne particulates harm our lungs still puzzles epidemiologists, physicians, environmental scientists, and policy makers. Now California Institute of Technology researchers have found that they act by impairing the lungs' natural defenses against ozone.

"I've long been perplexed by the inconclusive debates, based on epidemiological and clinical evidence, over whether the causative agent is particle size or some unspecified chemical component. I always felt that some missing chemistry might be associated with particle effects," says A. J. Colussi, a senior research associate in environmental science and engineering at Caltech and author of the study.

The researchers harnessed breakthroughs in chemistry to focus on what happens when air meets the thin layer of antioxidant-rich fluid that covers our lungs, protecting them from ozone, an air pollutant that pervades major cities. "We found new chemistry at the interfaces separating gases from liquids using a technique that continuously monitors the composition of these interfaces," Colussi says.

Adapting an innovation in mass spectrometry by Nobel laureate John Fenn of Virginia Commonwealth University, the Caltech team studied how aqueous ascorbic acid, the essential antioxidant also known as vitamin C and present in lungs' fluid layer, reacts with ozone gas.

Under normal physiological conditions, ascorbic acid instantly scavenges ozone, generating innocuous byproducts. However, the researchers discovered that when the fluid is acidic--a pathological condition found in asthmatics--ascorbic acid instead reacts with ozone to form potentially harmful compounds called ozonides.

"I immediately wondered whether ozonides would injure living tissues," Colussi comments. Indeed, he found literature reports that an ozonide is the active component of a plant extract used in Chinese medicine 2,500 years ago to treat malaria. Synthetic ozonide surrogates are currently used to target the malaria parasite: when the parasite disrupts red blood cells, the reduced iron that is released converts ozonides into cytotoxic free radicals on the spot. The nearby cells that the free radicals damage include the parasite.

The Caltech researchers inferred that inhalation of fine airborne particulates is an essential cofactor for ozonide production. The finer a particle is, the more acidic it is, so when particles are inhaled, they lower the lung pH. Most particulates also carry iron. In the lungs, then, the particularly harmful combination of ascorbic acid, ozone, low pH, and iron should trigger an acute inflammatory response.

To study the conditions that create ozonides, the team conducted experiments in which ascorbic acid solutions are sprayed, converting the liquid into fine droplets. When this mist is crossed by a stream of ozone gas, reactions at the interface of liquid and gas create products that are ultimately ejected from the droplets and then identified by a mass spectrometer.

Fenn had shown why the ions detected by this technique come exclusively from the droplets' interfacial layers, Colussi says. For the Caltech team, the approach provided a means to discover that ozonide yields are markedly enhanced in an acidic setting, when pH falls below five (pH 7 is neutral), and that ozonides are produced at the gas-liquid interface but not in bulk solution.

"Epidemiologists had consistently found significant increases in emergency-room admissions and cardiorespiratory deaths during episodes of high levels of both atmospheric ozone and particulates in several American and European cities, and they didn't know why. Now we have a plausible hypothesis about how ozone and particulates potentiate their harmful effects synergistically," Colussi says. Indeed, the National Academies recently confirmed a link between ozone and premature death.

"This is a chemical breakthrough with wide implications ranging from lung physiology to environmental policy," remarks Colussi. He intends to continue the study in vivo.

"Our tissues, except the stomach, were designed to function at about pH 7," Colussi notes. For example, asthmatics alleviate breathing difficulties by inhaling nebulized bicarbonate solutions at pH 8 to counteract low lung pH just like Tums does for heartburn.

The study appears this week in the early online edition of the *Proceedings of the National Academy of Sciences.* Other authors are Shinichi Enami, a postdoctoral scholar in environmental science and engineering, and Michael Hoffmann, Caltech's Irvine Professor of Environmental Science and Dean of Graduate Studies.

Source: Caltech