

Ozone exposure throws monkey wrench into infant lungs

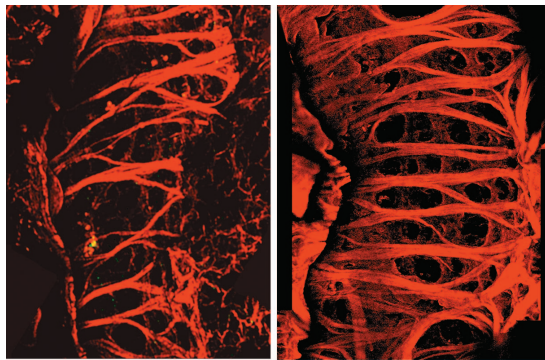
The lungs of asthmatic infants undergo irreversible structural changes when they breathe in polluted air—those results, released in March in Denver, had clean air advocates clamoring for better standards. The fact that the infants are rhesus macaques makes the results no less alarming. The monkeys are the closest models for human lungs, and researchers say they have every reason to believe the same pollution-driven alterations occur in children.

“Many people are now exposed to ozone at ground level above the US standard, and admissions to hospitals for asthma attacks are increasing,” says David Bates, co-editor of the Health and Clean Air newsletter and former dean of medicine at the University of British Columbia. “The two things are almost certainly linked.”

Ozone exposure disrupts nerve and airway branch formation in lungs and forces a dramatic reorganization of airway muscles, according to data from Charles Plopper, developmental biologist at the University of California in Davis. His results stunned many prominent asthma researchers at the annual meeting of the American Academy of Allergy, Asthma and Immunology.

“It’s been very exciting from a scientific point of view, but from a public health standpoint it’s a pretty disquieting situation,” Plopper says. The loss of three to five generations of airway branches is particularly striking because scientists had believed until now that the branch number is fixed *in utero*.

Many factors resulting from ozone exposure conspire to make animals hypersensitive to allergens and to have a more severe asthma attack, Plopper says. What’s more, the developmental changes may negatively affect lung function throughout the animal’s life, regardless of future air quality. The most worrisome



Monkey business: Smooth-muscle bundles in distant bronchioles of infant rhesus monkeys exposed to house dust-mite allergen (right) change in orientation and increase in size and density.

while lung tissue develops postnatally for two years; in children, the same development takes eight to ten years.

The team exposed one-month-old macaques to ozone that mimicked Mexico City levels and a Los Angeles pattern: 0.5 parts-per-million ozone, eight hours a day for five days, followed by nine days of clean, filtered air. A primary component in smog, ozone is known to trigger and aggravate allergic responses that can bring on asthma attacks. The researchers repeated this cycle for five months and then allowed the monkeys to recover with six months of clean air.

The monkeys showed typical immune system and cellular responses seen with asthma. Autopsies revealed a disrupted and rearranged respiratory system. Smooth muscle, which controls airway constriction and relaxation, increased in mass and was realigned to be mostly perpendicular to the airway. Airways were thinner and shorter than in control monkeys.

There is some evidence that Plopper’s observations in monkeys may extend to children. X-rays of otherwise healthy children living in Mexico City show inflamed and over-inflated lungs, says Lilian Calderon-Garcidueñas, an environmental toxicologist at University of North Carolina, Chapel Hill. “The changes in these guys are amazing,” she says of the monkeys. “We probably have something like that happening also in children exposed to ozone.”

Kendall Powell, Denver

Slashed state budgets strangle ailing US research

While US scientists bemoan proposed cuts in federal research funding, more bad news is on the way. State legislators are now considering budgets that would gut many science programs by the end of the year. The cuts, which will affect some of the nation’s most research-intensive regions, compound belt-tightening at top biomedical research philanthropies.

Individual states are faltering under the combined loss of state tax revenues and valuable federal money. In order to pay for basic services, states like New Jersey—which faces a \$5 billion deficit—are cutting what they see as nonessential programs. “We’re at a point that’s lower than we’ve ever been be-

fore,” says John Tesoriero, executive director of the New Jersey Commission on Science and Technology.

In February, Tesoriero says, New Jersey governor James McGreevey proposed eliminating funding for all state grant programs, including arts, science and technology grants. Tesoriero’s commission, which supports academic and early-stage corporate research in the state, has already had its budget reduced from \$25 million to \$14.5 million in the past year. Under the new plan, that budget would be eliminated, and researchers who now receive five-year grants would find their funding abruptly cut off.

New Jersey is not the only state facing such

drastic cuts. California is considering eliminating state-funded technology programs and Michigan is slashing its Life Sciences Corridor project by more than half; several other states are contemplating similar cuts.

Philanthropies are not likely to pick up the slack, either. After watching its endowment shrink from a high of \$13 billion in 2000 to its current \$10 billion, for example, the Howard Hughes Medical Institute has begun reviewing all of its programs and trimming many of them. In March, the Institute announced that it would phase out its prestigious pre-doctoral training grants, saving an estimated \$17 million annually.

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