

Mutagens in air: They may be a gas

While the release of chemical pollutants into the air poses a health threat, the greater danger may lie in the by-products of the subsequent interaction of those chemicals in the presence of sunlight. Or at least that's what is suggested by a mutagenicity study appearing in the *MARCH ENVIRONMENTAL SCIENCE AND TECHNOLOGY*. It shows that toluene, a fairly simple and nonmutagenic hydrocarbon found in virtually all urban air, can be converted photochemically into gas-phase mutagens.

Paul B. Shepson of Northrop Services Inc. in Research Triangle Park, N.C., says that to date almost all mutagenicity studies of urban air pollutants have focused on compounds known as polynuclear aromatic hydrocarbons (PAHs), which are adsorbed onto airborne particulates. "But there's no evidence that this [research focus] is justified," he says. "Though we know PAHs are mutagenic, no one has really addressed the question of the extent to which gas-phase hydrocarbons contribute to the overall mutagenic activity of urban air."

The Ames test performed by Shepson and colleagues at Northrop, together with

researchers at two local Environmental Protection Agency laboratories, examined the ability of toluene and its breakdown products to induce mutations in bacteria. The test is widely used as a preliminary gauge of a material's potential hazard as a cancer-causing agent.

Because the chemistry of an urban atmosphere changes greatly over the course of a day, the researchers focused on the mix of hydrocarbons that would exist at both 3 hours and 6.7 hours after a typical atmospheric mix of toluene, oxides of nitrogen (NO_x), water and clean air was pumped into closed reaction chambers and allowed to react in the presence of light. These particular temporal snapshots of toluene photochemistry were selected, Shepson says, because the mix of photochemical products present "was as different in the two cases as possible." That's because at 6.7 hours, reactive nitric oxide was no longer present.

To do the Ames test, these chemical mixes had to be held in a constant steady-state rate of reaction for 18 hours, something not possible in the ambient atmosphere. In each test, bacteria were exposed to: (1) "clean air" only; (2) the initial mix of toluene, nitrogen dioxide, nitric oxide and water—but no light; (3) the irradiated mix of hydrocarbons that would be present at 3 or 6.7 hours; and (4) that latter mix minus any solid particles.

The first two exposure regimes were not mutagenic. Like the third test atmosphere, however, the gas-only reaction products showed strong mutagenic activity. Further analysis suggested that formaldehyde and peroxyacetyl nitrate (PAN) contribute to this gas-phase mutagenic activity. That in itself is important, Shepson says, "because there are a large number of hydrocarbons in the atmosphere that produce both PAN and formaldehyde in photooxidation processes."

More surprising, he says, is his group's subsequent finding of a similar photochemically induced mutagenicity among the breakdown products of an even smaller organic chemical, propylene (C₃H₆). And when the researchers studied wood-smoke mixtures, "we got a large mutagenicity response there with gas-phase products," he says.

However, with potentially thousands of photooxidation products present in the irradiated wood-smoke mixture, "it's absolutely hopeless to try and determine what caused the response," he says. That's one reason his team plans to focus more attention on propylene. Explains Shepson, "We feel we should start with the simplest case and try to understand that before we move on to more complex ones."

In any case, concern remains that important and largely unrecognized gaseous mutagens may be prevalent in urban air.

— J. Raloff

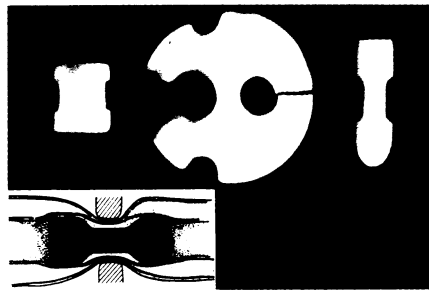
Pulling the plug on sterilization

When a woman has her fallopian tubes "tied," the sterilization effected can be forever. Contraceptive counselors do not recommend tubal sterilization to women seeking a reversible form of contraception, because reversal, which requires removal of the damaged section of the tube and exacting microsurgery to reconnect it, frequently doesn't work.

C. Irving Meeker of the Maine Medical Center in Portland and Wilfred Roth of the University of Vermont in Burlington set out to develop a device to make sterilization more reversible, and have come up with the gizmo at right. The idea is to protect the fallopian tube (see inset) from being crushed, so that no microsurgery is required for reversal.

They have implanted the device in 18 baboons for 6 to 18 months. Within a year of removal, 10 of the 18 got pregnant. This 56 percent conception rate compares to a 65 percent rate in unsterilized baboons, representing "a high degree of reversibility for the method," they report in the *MARCH OBSTETRICS & GYNECOLOGY*.

For insertion, a small slit is made in the abdomen and the plug (far right) is threaded into the fallopian tube through its open end near the ovary. The clip (center) is placed around the plug and tube, and the lock (near right) fits into the clip to hold it shut. The egg, released from



the ovary into the fallopian tube, is stopped by the plug and reabsorbed by the body.

To reverse the procedure, the lock and clip are removed and the plug is either eased out of the tube or taken out through a small slit. The researchers plan to start testing in humans when they receive Food and Drug Administration approval.

Meeker says he hopes the device will prove useful for women in their 20s who are not planning to have more children but may change their mind. He anticipates it could also be valuable in underdeveloped countries like China, where strong political pressure for sterilization is resisted by couples with one child who worry that something may happen to their only offspring. "For them," says Meeker, "the possibility of reversal becomes extremely important."

— J. Silberner

Do kinks and twists denote DNA damage?

Radiation and chemicals often damage a cell's DNA. Fortunately, there is a natural repair mechanism to undo most of that damage. But what is it that these enzymes must repair? And how do dispatched repair squads find the damage? Using computers to model the most likely stable structure of two types of photochemically induced damage, chemists in Berkeley, Calif., think they may have spotted the answers—bends and a partial unwinding of the DNA's characteristic double helix in the damaged cells. A report of their work appears in the March 15 *SCIENCE*.

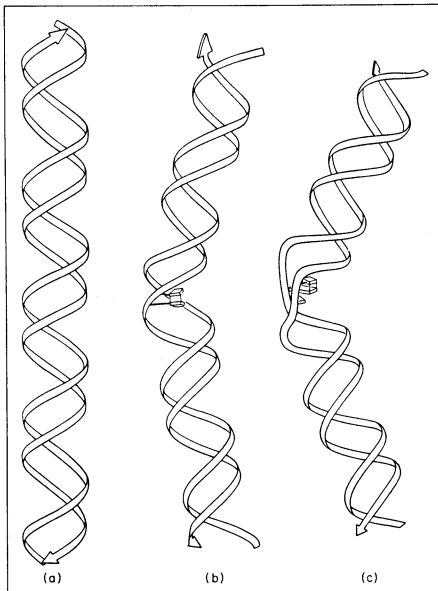
Creation of certain dimers, bound pairs of identical subunits, is the most widely studied radiation-induced DNA change. Upon irradiation with ultraviolet (UV) light, two adjacent structures—thymines—along a strand of DNA may fuse into a thymine dimer. These dimers present roadblocks to normal DNA synthesis and are likely to spawn mutations if they are not repaired before the cell's DNA undergoes replication.

Another well-studied DNA lesion occurs when cells exposed to the drug psoralen (often used for treating the skin disease psoriasis) are subsequently irradiated with long-wavelength UV light. Here the psoralen molecule chemically binds to a

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nucleic-acid base on each of two strands of DNA. If this psoralen cross-link is not repaired, the affected cell will die.

Scientists believe that the DNA repair mechanism must recognize the structural changes these damaging chemical bonds cause. "Our goal was to see what kinds of changes in the overall DNA structure are induced by this photo-damage," says Stephen R. Holbrook, a staff scientist at Lawrence Berkeley Laboratory, "and our results are that the DNA becomes bent [at the site of damage] by a moderate angle in the thymine dimer formation, and by a very large angle in the psoralen cross-link." David Pearlman at the University of California at Berkeley computed the helical kinks, or bend angle, induced in the DNA as 27° for the dimer and 46.5° for the psoralen cross-link (shown in the illustration as b and c, respectively).



Healthy, linear DNA (a) shown with dimer (b) and psoralen cross-linked (c) models.

The researchers also noted a characteristic alteration in the helical coiling of the double-strand DNA at the point of damage. Normal DNA has 10 base pairs per full turn, meaning that DNA turns 36 degrees for every base pair. In the damaged DNA, the chemists' models showed a change in that winding angle. For dimers, instead of winding 36°, affected base pairs coiled only 16.3°. In the psoralen cross-link, the 87.7° twist in the opposite direction actually causes the affected portion of the helix to completely unwind (structure c).

"I should emphasize," Holbrook says, "that this is a proposal." Although the contortions were suggested by computer models based on the best available X-ray crystallographic data on dimer and cross-link DNA damage, he notes that they have not yet been visually observed. Milan Tomic, a student now working with the team, is attempting to isolate enough psoralen-linked base pairs to make that possible.

— J. Raloff

Out of the pork barrel, into the fire

"A million dollars here, a million there, and soon it begins to add up to real money." This political chestnut—a favorite quote at budget time—can readily be applied to recent concerns about the success some universities have had in obtaining federal funds for the construction of new facilities. During the last two years, about two dozen universities have together collected more than \$100 million for new buildings by going directly to Congress and lobbying for special appropriations.

"These actions establish a dangerous precedent," says a new report from the National Science Board's (NSB) Committee on Excellence in Science and Engineering. "If this becomes common practice, it could seriously undermine the U.S. system of merit competition for research funding that has been so successful during the recent period of U.S. scientific dominance."

The furor started two years ago when Columbia University in New York and Catholic University of America in Washington, D.C., hired Schlossberg-Cassidy and Associates, a Washington lobbying firm, to help them get funding for new laboratories. The effort was successful, bringing \$8 million to Columbia and \$13.9 million to Catholic University (SN: 7/23/83, p. 52).

Because of this success, says NSB Chairman Roland W. Schmitt, "there's enormous pressure on other university presidents, who also have an intense need, to go and do likewise. I think there's a danger of the dam bursting."

The NSB report lists 15 universities that have already benefited from bringing their problems directly to Congress. For example, Florida State University in Tallahassee, which happens to sit in the district of Rep. Don Fuqua (D-Fla.), chairman of the House science and technology committee, obtained \$7 million to establish a supercomputer center. Northwestern University in Evanston, Ill., received \$16 million to build a "basic industry" research institute. In addition to these 15 schools, another seven institutions received funds for libraries or demonstration projects.

The problem, says Charles E. Hess of the University of California at Davis, who chaired the NSB committee, is that many of these proposals were brought up late in the budget process on the House floor and were approved without any discussion. "To me, you're not only bypassing science review, but essentially you're bypassing all review," he says.

Theodore Litovitz, director of Catholic University's Vitreous State Laboratory, doesn't understand why there is such a fuss. "The money is for a building, not for research," he argues. "There are so many other buildings that have gone up based on government funds. Buildings have never been peer-reviewed."

"The reason why it's such a large issue," says Robert M. Rosenzweig, president of the Association of American Universities (AAU) in Washington, D.C., "is that it can't be limited to facilities. The same pressures that lead to the targeting of a building will eventually spill over into decisions about what research is going to be supported in that building." In late 1983, the AAU along with the National Academy of Sciences issued statements condemning "special-interest amendments to funding legislation" (SN: 11/19/83, p. 329).

In addition, money intended for other purposes may go into building facilities. Such reallocations have already taken some funds, especially at the Department of Energy, away from research projects, says Rosenzweig.

In the late 1960s and early '70s, the National Science Foundation (NSF) did provide funds for building or renovating research facilities, Hess points out. Now, NSF has new programs for supercomputer (SN: 3/2/85, p. 135) and engineering research centers (SN: 2/16/85, p. 102). But this isn't enough.

"The present spurt of direct appeals for congressional action on academic projects," says the NSB report, "is symptomatic of an underlying need in many U.S. academic institutions for facilities support. This need is not adequately addressed by present funding mechanisms in either the public or the private sector."

"Until there's some regular funding for renovation and construction of facilities," says Rosenzweig, "the temptation to use the direct congressional route is going to be too great for some to resist."

The report recommends the holding of a special conference as soon as possible to consider these issues. "This conference is to be a catalyst," says Schmitt. It will bring together university administrators, researchers, people from the financial community, state and federal officials and others to share ideas and to map out a strategy for meeting university needs. "The solution cannot be a federal solution alone," says Schmitt. Planning for the conference, which may take place as early as next summer, is just beginning.

Meanwhile, Congress is scrutinizing the federal budget for the fiscal year 1986. There are already a significant number of university requests for special appropriations, says one congressional committee staff member.

"It's hard to know how many," says Rosenzweig. "It's in the nature of these things that they don't happen until late in the budget process."

— I. Peterson