Nitrosamines: Scientists on the Trail of Prime Suspect in Urban Cancer

In the last few months an increasing number of scientists and public interest activists have become disturbed by one of the most potent—and baffling—of all chemical carcinogens: nitrosamines. Nitrosamines, a well-established class of animal carcinogens, are already regulated in food by the federal government. But since last summer they have been discovered in urban air, soil, water, and sewage treatment wastes, in places ranging from New York City to the Kanawha Valley of West Virginia.

Scientists are saying that the possible threat to human health from this apparently widespread pollutant is of "grave concern"—but no one is sure what to do about it. Unlike other pollutants, such as vinyl chloride, which comes from a limited number of sources, nitrosamines are generated from other chemicals found almost everywhere in the environment. Control of these so-called "precursor" chemicals, to prevent spontaneous formation of nitrosamines in the environment, could pose a regulatory nightmare—forcing the government to set new standards for the chemical and automobile industries, for public utilities, for the tobacco industry, and others. An investigation of the way the Air Force transports and stores fuel for its strategic missiles may also be needed.

The discovery could have even broader significance in unraveling one of the mysteries of cancer epidemiology. For several years, epidemiologists have been baffled by the observed statistical correlation between high levels of nitrogen dioxide (NO_2) and the high incidence of cancer in many urban areas. Yet neither NO_2 nor nitric oxide (NO), for which NO_2 is an indicator, have been demonstrated to cause cancer. However, combined with water under certain conditions, both NO and NO_2 can form nitrous acid, which then combines with amines to form nitrosamines.

Thus, it could be that the nitrosamines, and not the NO_2 itself, are the culprits responsible for some urban cancers. Says Richard J. Hickey, one scientist who has established such correlations:

> Nitrosamines are a possible route by which a fruitful explanation could be developed to explain the significant correlation we and others have found between atmospheric levels of NO_2 and urban cancers.

One reason that nitrosamines may be a special environmental problem is that they are formed from amines that are found almost everywhere. Amines, which are substitution products of ammonia, are produced in the decomposition of proteins. They are present in pesticides, drugs, and foods and are used in industrial processes. Amines react with nitrous acid to form nitrosamines. The reaction can take place under many circumstances, including those in the human digestive system and in the atmosphere.

The other precursor, nitrous acid, is formed from nitrites, which are in meats and in fertilizers, and from nitrates. It is also formed from NO_2 and NO, both of which are principal products of oil, coal, and gas combustion, including motor vehicle exhausts.

For years, government research and regulation has focused on nitrosamines in food. Nitrites and nitrates are used to give color to preserve fish and meat; both have been limited by the U.S. Department of Agriculture for many years, partly because of their potential as carcinogens. For example, when nitrite-cured bacon is cooked, the nitrite changes to nitrous acid and reacts with amines in the meat to form the potently carcinogenic nitrosamine, dimethyl nitrosamine, or DMN.

In 1973, the USDA convened a panel of outside experts to review the nitrosamine problem. Last November, following the group's recommendations, USDA proposed more stringent standards for nitrite in meats and proposed banning nitrates entirely.

Nitrosamines in the environment did not come to public attention until last summer, when Ralph Nader's Public Interest Research Group asked Thermo Electron Corporation, a Waltham, Mass., instrument manufacturer, to take atmospheric nitrosamine measurements in several places, including a missile fuel plant in Baltimore, Md. Thermo Electron had developed a new instrument that reduces the time for nitrosamine detection from 10 hours to approximately 1 hour, and which is capable of detecting all of the 50 or so common nitrosamine compounds in far smaller amounts than was previously possible. The instrument had been developed as an aid to cancer research; recently, however, scientists at the Environmental Protection Agency (EPA) have confirmed that it can also measure nitrosamines in air, water, and soil.

Thermo Electron found quantities of DMN [0.3 microgram per cubic meter ($\mu g/m^3$)] in its initial readings of the air on the property of the FMC Corporation, which uses nitrosamines in the manufacture of fuel for Air Force Minuteman missiles. Subsequently, even higher levels, in the range of 1 to 10 $\mu g/m^3$, were found in readings taken by Thermo Electron, the EPA, and FMC itself—alarming local residents, FMC workers, state and city health officials, and even the Maryland congressional delegation. The Air Force has decided simply to shut the plant down as of 1 April and to make the Minuteman fuel by another method in which nitrosamines are not used. Nonetheless, the FMC fuel is still stored and transported by the Air Force around the country, and, of course, is located in the missiles in their silos in the upper Midwest.

The FMC situation was a special case since it seems to be the only place in the country where nitrosamines are emitted directly. More alarming, from a national public health standpoint, was the discovery of DMN and other nitrosamines in areas where there are no known sources of nitrosamines. These include Baltimore, upwind of the FMC plant (0.02 to 0.1 $\mu g/m^3$); the Kanawha Valley towns of Charleston and Belle (trace levels to 0.07 $\mu g/m^3$; and even on the Cross Bronx Expressway in New York City (0.8 $\mu g/m^3$). Water samples at some of these locations also confirm the presence of nitrosamines, as do samples of the discharge taken from sewage treatment plants.

The findings have aroused skepticism, to be sure. One question, largely laid to rest by recent tests, has been whether Thermo Electron's instrument was producing the nitrosamines it measured. Another question came from laboratory tests showing that sunlight breaks down atmospheric nitrosamines in a few hours. Some argue, however, that this would not occur in the real, urban atmosphere.

"Great potential for harm to the public health exists," concluded Ralph Nader and Samuel Epstein, the Case Western Reserve University environmental toxicologist, in a letter to EPA Administrator Russell E. Train last summer. Thermo Electron's principal investigator, David Fine, concluded a recent presentation of his latest measurements—including the one in New York City—with the remark: "The recent finding of nitrosamines in the air, water, and soil of urban environments ... may present an unacceptable health hazard and is therefore of grave importance."

Scientists are still trying to work out just how grave the problem is. One nongovern-

ment calculation shows that a person ingests 0.5 μg of DMN if he eats four slices of cooked bacon (with the nitrite level permitted by the old standard). He inhales 0.8 μg after smoking a pack of cigarettes (it is well established that nitrosamines form in cigarette smoke). Fine has calculated that, by comparison, a person breathing air containing 1 $\mu g/m^3$ of DMN for 24 hours will inhale 10 to 14 μg of DMN.

On a clear day in Belle, West Virginia, where DMN levels of 0.1 $\mu g/m^3$ were measured, a person would inhale 1 to 1.4 μg of DMN—still more than the amount he would have taken in after eating the bacon or smoking the pack of cigarettes. James Smith, an EPA scientist who has reviewed calculations of relative exposures to nitrosamines, says that exposures of humans to atmospheric nitrosamines are probably "in the same ball park" as exposures from food and cigarettes.

An important missing piece of information, however, is how nitrosamines behave in the human respiratory system. Jean French, an EPA epidemiologist, says that while nitrosamines have been shown to form from precursors in the digestive system, "a counterpart of such a demonstration in the respiratory system hasn't been tried.... This is a bad void in the research." If indeed they form there, nitrosamine exposure in the population may be more than that even now supposed.

Cancer researchers have tested nitrosamines on dogs, monkeys, parakeets, rats, mice, hamsters, guinea pigs, and even on rainbow trout. Each group has contracted a significant number of cancers. Moreover, each has developed a variety of kinds of cancer—suggesting that nitrosamines do not limit their harmful effects to one organ.

Animal studies have also shown that, in low doses, nitrosamines seem to activate other, weak carcinogens, such as benzo(*a*)pyrene, to act more potently. Reviewing this and the other evidence of its harmfulness, an EPA report in 1974 concluded, "as a family of carcinogens, the nitrosamines have no equals."

But relating all this evidence in animals to the likely human experience is another matter. At present there is no data linking nitrosamines to cancer in humans. Establishing that it does or does not cause human cancers would be a formidable research task. Nonetheless, some researchers say they should be considered a public health menace on the basis of animal data alone. Says one:

> There is no evidence linking nitrosamines to cancer in man, but that may be because the cancers they produce are so common that they don't stand out as unusual. Vinyl chloride was easy to track down because it produces such an odd cancer. With the nitrosamines, however, it is reasonable to assume that man is not a god

ERDA Gives Boost to Breeder Program

The Energy Research and Development Administration (ERDA) has decided to continue a "strong research effort" to develop a liquid metal fast breeder reactor that might become a key factor in supplying nuclear energy in the next century. The renewed commitment to the controversial breeder program appears to belie hints that surfaced last summer that the agency's zeal for the breeder might be waning.

The new commitment was signified in two events that occurred late last month. On 20 December, ERDA announced an internal reorganization aimed at putting "particular emphasis on the Liquid Metal Fast Breeder Reactor (LMFBR) program." A new Division of Reactor Development and Demonstration was formed that will be devoted exclusively to LMFBR activities, while other activities that had formerly been handled in the same administrative unit were spun off into a second new division. Richard W. Roberts, ERDA's assistant administrator for nuclear energy, said the reorganization will give the LMFBR the "dedicated attention it requires."

Then, on 31 December, Robert C. Seamans, Jr., ERDA administrator, announced his findings after reviewing the LMFBR program's final environmental impact statement, which analyzed the various environmental, economic, technological, and social issues involved in widespread deployment of breeders. Seamans concluded, in essence, that the impact statement supported the need for a vigorous research and development program to determine whether the breeder is a viable energy option, but that at least one more impact statement should be prepared and considered before ERDA decides—probably by 1986—whether the breeder is acceptable for widespread commercial deployment. Should ERDA decide in the affirmative, it would then be up to industry to decide whether to invest in the breeder option or use some alternative source of energy, and it would be up to the Nuclear Regulatory Commission to decide whether to license such breeders.

These latest steps by ERDA reverse the impression which emerged last summer that the agency was backing slowly away from its commitment to the breeder, a reactor that produces more nuclear fuel than it consumes. One event which gave that impression was the publication of ERDA's national plan for energy R & D. That plan seemed to treat solar energy and fusion on a par with the breeder as potential long-range energy options, a scenario that caused dismay in the nuclear industry. "They acted as if all three horses came out of the gate at the same time and were running in the same race," complained a spokesman for the Atomic Industrial Forum, the industry trade group. "That was not a realistic appraisal. We have the breeder technology fairly well in hand, but we've never built a solar generating station or a fusion reactor." A second event that reinforced the impression was ERDA's announcement that it was reducing its fiscal year 1976 budget for the breeder by $60 million. But much of that money could not have been spent anyway because of delays in the program. Some observers believe ERDA made the announcement to defuse opposition in Congress, where the breeder budget for long-range items subsequently survived a major attack by votes of 227 to 136 in the House and 66 to 30 in the Senate.

The latest plan as approved by Seamans calls for construction of a demonstration plant (the Clinch River Breeder Reactor Plant); a prototype large breeder reactor; and a commercial reactor that would go critical in 1993. Seamans said a decision on commercialization could be made in 1986, and that carrying out the R & D program would not constitute "an irreversible commitment to widespread commercial use." But J. Gustave Speth, of the Natural Resources Defense Council, an opponent of the breeder, calls such an assertion "nonsense." He argues that, after billions of dollars have been spent on the breeder and a large private and public bureaucracy has been built up in support of the breeder, the decision on commercialization will be "foreclosed." The total cost of the breeder program through 1986 is projected at about $10 billion.

Opponents of the breeder argue that it will be beset by technologic and economic uncertainties and that it is environmentally dangerous, since it is based on highly toxic plutonium, the stuff of which bombs are made. But proponents contend that the problems can be overcome and that the breeder will be essential to meet future energy demands.—PHILIP M. BOFFEY

and that if every animal group tested has succumbed to it then man will succumb as well.

Nitrosamines are also prime suspects in the quest for what one scientist calls "the defining factor in urban cancers." William Lijinsky, a well-known nitrosamine researcher at Oak Ridge National Laboratory, along with Epstein, pointed a finger at this possibility in a 1970 article in *Nature*. "In our view, any group of chemical carcinogens significantly implicated in human cancer must be both widespread and multipotent. Such chemicals are the nitrosamines. . . ."

Hickey, in a 1970 study cross-checking disease rates in 38 U.S. urban areas with a host of environmental chemicals, found that NO_2 cross-correlated with seven out of eight categories of cancer and with heart disease. (Sulfur dioxide, sulfates, and heavy metals also correlated with several cancers.) In his paper, published by the Regional Science Research Institute in Philadelphia, Hickey speculated that this might be due to nitrous acid's role as a mutagen, which could make the population more susceptible to disease. However, now that nitrosamines have been found in the urban atmospheres, Hickey agrees that they could form part of the explanation.

However, French, the EPA epidemiologist, doubts that nitrosamines by themselves—or any single compound—will prove the missing link in explaining the urban cancer rate. She suggests that urban air may contain other substances, such as benzo(*a*)pyrene, that may act along with nitrosamines in a harmful manner. "If you eliminated nitrosamines entirely, you'd still have cancer. They are only one of the possible causes."

It is too early to predict what kind of action the government might take on the issue of environmentally occurring nitrosamines. Clearly, since USDA has concluded that certain amounts in food are unacceptable, it would be hard for the EPA not to take action. Epstein, who has often prodded federal agencies over environmental and occupational health issues, complains: "It's absurd for the government to have entirely different policies for the same compound, based on the fact that it happens to occur at several different places in the ecosystem."

Nader and Epstein, in their summer letter to Train, argued that the key factor in nitrosamine occurrence in the atmosphere could turn out to be nitrogen oxides and argued strongly that therefore EPA should not go through with a proposed relaxing of emission standards of these oxides for automobiles. Clarence Ditlow, of the Nader group, goes further and charges that the EPA has tried to downplay the nitrosamine issue because EPA is already politically committed to relaxing these standards.

However, other people who have examined the potential regulatory problems posed by environmental nitrosamines argue that standards limiting the amines—which come by and large from industrial sources—may be the easier method of control.

Clearly, much more research and study will have to be done before anyone knows for certain what levels of nitrosamines are in the environment, how they behave there, and where they come from. But however complicated this knowledge turns out to be, it may help to cut the Gordian knot faced by research scientists who are trying to figure out the probable causes of urban cancers.—DEBORAH SHAPLEY

Edward Goldsmith: Blueprint for a De-industrialized Society

The *Ecologist*, despite its title, is not a scientific journal. Its editor, who frequently has harsh things to say about science and scientists, refers to it affectionately as a "propaganda paper." Published from the rural depths of Cornwall, England, the *Ecologist* is in essence a political magazine devoted to environmental issues. Its positions are usually uncompromising. It advocates the dismantling of industrial economies and the return to a rural society embodying small-scale technology and rustic virtues. It styles itself the "Journal of the Post Industrial Age."

Such a program is akin to redressing the 18th-century ideal of the Noble Savage in modern clothes. It is clearly of limited persuasiveness to anyone who thinks that the present style of civilization can and should be preserved. Nevertheless, the *Ecologist*'s plans for the world are worth considering whether one agrees with them or not. The idea of a past Golden Age, simpler, purer, and somehow recapturable, is deeply rooted in Western and other cultures. The *Ecologist* wields more influence than might be expected for the advocate of so extreme a stance. Its circulation of 10,000 copies is small but respectable (*Nature*, for example, *Science*'s English counterpart, has a circulation of about 20,000). The *Ecologist* sells about 1000 copies in the United States, and has three heads of state (those of Tanzania, Zambia, and Papua New Guinea) among its personal subscribers. Its dramatic credo, the *Blueprint for Survival*, has sold some 500,000 copies in 3 years and has been adopted as an election platform by political parties in England, New Zealand, and Tasmania. In national elections held 2 months ago the Values Party of New Zealand polled 5 percent of the vote, which observers regard as an impressive showing for a new party.

The editor of the *Ecologist*, and coauthor of the *Blueprint for Survival*, is Edward Goldsmith. Teddy, as he is known to his friends, wants to de-industrialize the world; his brother Jimmy is a self-made millionaire who is one of England's most successful entrepreneurs.

Goldsmith is a man of refreshing individuality. He stood as a candidate for parliament in the last election, touring his would-be constituency on camelback for the purpose of emphasizing that other forms of transport would no longer be available in 20 years time. The principal plank in his campaign was soil erosion. The issue, he persuasively contends, is "far more important than the price of beer, equal pay for women, or the other fatuities they debate in parliament." If that makes him sound like a male chauvinist, well, he appeared at a recent conference in Houston wearing a tie emblazoned with boar heads and the monogram MCP.

An engaging and impulsive talker, Goldsmith has the uninhibited delight in knowledge of the self-taught, which to some extent he is. After taking his bachelor's degree at Oxford in 1950, he became, he says, a permanent student. His military service on the allied staff in Berlin did not prevent him from spending 4 hours a day in the library, and he continued his studies when he moved to Paris to manage a small electronics factory.

Ten years ago Goldsmith came into a small private income which has made it possible for him to follow his own interests. Through several vacations spent in Africa he became concerned about the