High-dose inhalation cancer tests suggested

A new study conducted by and for the federal government concludes that inhaling a single large dose of a known carcinogen can cause cancer in one species of laboratory animal.

The report goes so far as to suggest that short-term, high-dose laboratory studies of other known carcinogens "may be appropriate for government and private researchers."

Conducted for the Consumer Product Safety Commission, the $700,000 research project examined the effects on rodents of inhaling doses as high as 50,000 ppm of vinyl chloride, a known liver carcinogen. Previously, most inhalation-based carcinogenicity studies with animals have involved comparatively small doses of chemicals given routinely over relatively long periods of time. The current study was performed by Dr. Bernard McNamara and coworkers at the Chemical Systems Laboratory at the U.S. Army Aberdeen Proving Grounds in Maryland.

Started in 1975, the vinyl chloride study exposed groups of mice and rats to single one-hour doses of vinyl chloride gas in air of 50,000, 5000, 500, 50, and 0 (controls) ppm. In addition, other groups of the rodents were given 10 one-hour exposures to 500 ppm vinyl chloride five days per week for two weeks. Yet another group of the animals received 100 one-hour exposures to the chemical at 50 ppm, five days per week for 20 weeks. All were then kept in cages for the remainder of their lives, usually about two years.

A reproduction study conducted simultaneously, however, failed to detect any mutagenic or carcinogenic effects in succeeding generations of rodents whose forebears had been exposed to vinyl chloride vapors.

But the carcinogenicity study, particularly the single-exposure experiments, seems to be the focus of study. Several important points arose from the study. For example, only mice and not rats demonstrated any carcinogenic effects from one exposure to vinyl chloride. And the single-dose experiments produced only adenomas, or benign tumors, generally at the highest single-dose levels, virtually all of which subsequently failed to progress to carcinomas, or malignant tumors.

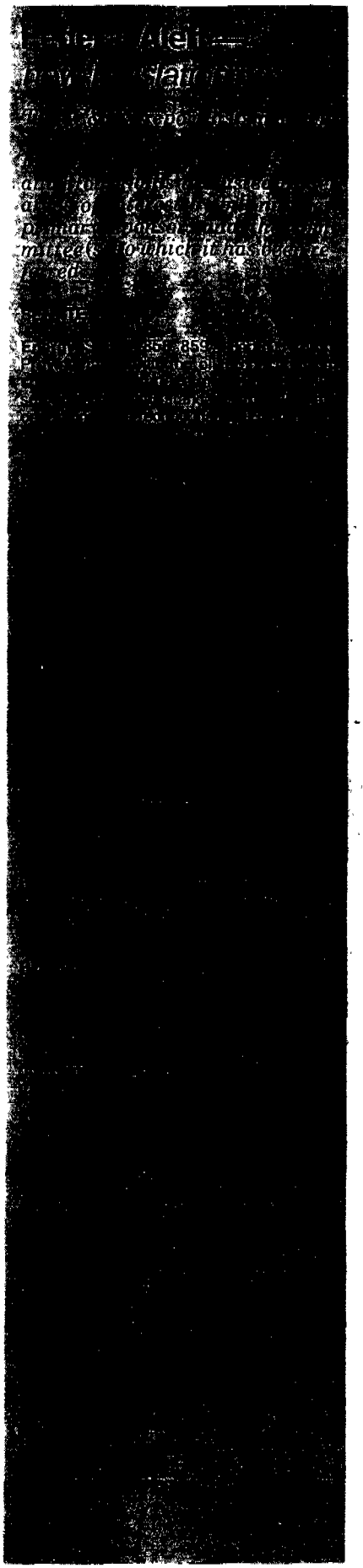
Moreover, and perhaps more important, the report notes that pneumonitis, a condition of acute, localized lung inflammation, "was evident in all animal (mice) groups exposed to vinyl chloride in doses of 500 ppm or more." Most toxicologists believe that a dose of a chemical that makes an animal acutely ill should not be used in a carcinogenicity study because it can produce results unrelated to a compound's cancer-inducing potential.

Specifically, the study found that nearly 33% of the mice exposed to 50,000 ppm of vinyl chloride for one hour developed adenomas of the lung; about 17% of the mice exposed to 5000 ppm also developed adenomas; at 500 ppm 13%, and at 50 ppm 10.1%. By contrast, 10.0% of the animals used as controls (no exposure) developed adenomas.

Progression to carcinoma, the report notes, "was minimal" among the mice. Only three of the 137 mice (2.2%) exposed to 50,000 ppm of the plastic monomer later developed carcinoma of the lung. At lesser doses a barely perceptible increase in carcinomas was found. For example, at the next lowest dose of 5000 ppm of vinyl chloride for one hour, one mouse out of 143 (0.7%) eventually developed a pulmonary carcinoma.

All of which leads to skepticism among industrial toxicologists. Dow Chemical toxicologist Perry Gehring, for instance, says that because of the high level of pneumonitis among the test mice, "the relevance of the results is highly questionable." He notes, too, that only mice and not rats were affected by the vinyl chloride exposure. "Adenomas in the lungs of mice," Gehring says, "have a very high spontaneous background," particularly when the mice are in physiologically stressful situations such as nearly being anesthetized by vinyl chloride gas.

Yet the Consumer Product Safety Commission in releasing the study concludes that its "findings further support the thesis that a single exposure to a high dose of vinyl chloride, or perhaps other similarly acting carcinogens, could pose a risk of cancer to humans." Dow's Gehring observes that long before vinyl chloride was recognized as a liver carcinogen in the early 1970's, "we knew that 3000 ppm or higher levels were not uncommon—we should have tumors all over the place [now.]" □



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