ity of building the quadrants in smaller units that could pass through the St. Lawrence Seaway and be assembled in Lake Erie or Lake Michigan has not been ruled out.) Also, four different parts of the country could be given contracts for building the four arc-shaped platforms. (Already, a bid has been received from a Japanese shipbuilding firm experienced in building supertankers.) Since these four quadrants—and the linac structure and the experimental hall structures—could be built simultaneously in different shipyards, as much as 2 years could be saved relative to the time needed to construct a fixed synchrotron.

Only in the last few weeks has the last and thorniest problem been solved: the problem of radiation beamed toward a particular part of the city adjacent to the harbor in question. If an emergent beam were aimed toward a certain portion of the city, persons living there would receive, during a typical month, five or ten times the permissible dose (from muons, which are fundamentally aquatic and can travel freely in water). The solution is to mount a 5-hp outboard motor tangentially at the outer edge of the platform and keep the motor running continuously, so as to rotate the entire accelerator at the rate of one revolution per week and thus distribute the radiation uniformly along the entire harbor-front. The direction of rotation will be the same as that of the protons in the accelerator, so as to add to their speed; even a slight increase is significant if the particles are already traveling at a speed almost equal to that of light.

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Carcinogenic Risk

Although G. M. Williams and J. H. Weisburger (Letters, 1 July, p. 6) refer to "safe" levels of carcinogens, their letter sheds no light on means by which these may be established. They assert that carcinogens can be divided into genotoxic and epigenetic agents but do not discuss the reality that the mechanism by which any carcinogen acts is unknown. That many carcinogens are genotoxic is known, although in those instances in which we can roughly quantify carcinogenicity and genotoxicity there is no quantitative relationship between the two, even within chemical families of known carcinogens. Nevertheless, it is not known that any carcinogen induces tumors through genotoxicity, and there is no known difference between tumors induced by, for example, "nongenotoxic" carcinogens, such as nitrosodiethanolamine or methapyrilene, and those induced by other carcinogens. Dose-response relationships in carcinogenesis are observed with these, as with other carcinogens.

Furthermore, whether or not there is one or more mechanisms by which carcinogens act is irrelevant to the assessment of risk in large populations, perhaps millions, of people to a substance shown to be carcinogenic in animals. Normally, we test a compound at high doses in small groups of animals and extrapolate the risk to the lower doses to which humans may be exposed. At these low doses errors in calculation can be enormous, particularly when the difference in length of exposure can be 60 years for man versus 2 years for a rat or mouse.

To calculate the "carcinogenic risk" at low doses that would be reliable to protect human health would require using huge numbers of animals (tens of thousands per group), which would be prohibitively expensive, even if practical. The safest course is to continue to treat any substance identified as a carcinogen as if it posed a reasonable risk to the human population and to regulate it accordingly.

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Williams and Weisburger are correct in their assertion that there are different kinds of carcinogens but not in concluding that there are "two distinct classes." The evidence for genotoxic or nongenotoxic mechanisms of carcinogenicity is not as available as they imply. The term "genotoxicity" covers a universe of events from single base changes, additions, or deletions in DNA to chromosome and chromatid deletions and rearrangements and to the gain or loss of chromosomes. More recently, the term has also been extended to include other effects on DNA or chromosomes, such as sister chromatid exchanges, induction of DNA strand breaks, or unscheduled incorporation of thymidine into the cell nucleus. The term "epigenetic" has been used as a catchall to categorize chemical carcinogens that do not appear to be genotoxic, but the term is not defined in the negative sense (lacking genotoxicity) and provides no information on mechanisms of action.

Since Ames and his colleagues (*1*) began demonstrating that the majority of carcinogens were mutagenic in *Salmonella typhimurium*, results from this test have been used as the basis for the identification of chemicals as "genotoxic carcinogens." Recently, however, additional studies have shown that many chemicals originally judged nonmutagenic based on their lack of mutagenicity in *Salmonella* can cause mutation, chromosome aberrations, aneuploidy, or sister chromatid exchanges in eukaryotic microorganisms, insects, or cultured mammalian cells (*2*). Additionally, some carcinogens that were not mutagenic in *Salmonella* when tested by the original protocol were mutagenic when modified protocols or different metabolic activation procedures were used (*3*). At this time, however, too few chemicals that are not mutagenic in *Salmonella* have been tested adequately in other genetic toxicity assays and for carcinogenesis to know the predictability of results from the other genetic toxicity tests for carcinogenicity. Furthermore, other modifications of DNA or chromatin that could result in heritable phenotypic changes in mammalian cells (*4*) are not commonly explored.

If a carcinogen has not been tested for a variety of genetic endpoints, including some from in vivo genetic toxicity tests, it is inappropriate to classify it as "nonmutagenic." A recent IARC Working Group (*5*) has also concluded that ". . . at present, no classification of carcinogens could be exhaustive or definitive." Mutagenicity and rodent cancer data are too sparse to support general statements on carcinogenic thresholds for chemicals that have not been shown to be mutagenic.

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Erratum: In the article "Sulfur diagenesis in Everglades peat and origin of pyrite in coal" by Z. S. Altschuler *et al.* (15 July, p. 221) the equation at the bottom of the middle column on page 221 had a misprint; it should have read

$$Fe^{2+} + S_x^{2-} + HS^- \rightarrow FeS_2 + S_{x-1}^{2-} + H^+$$

Erratum: In the article "Yellow rain experts battle over corn mold" by Eliot Marshall (News and Comment, 5 August, p. 527), Pat Hamilton was incorrectly identified as a poultry scientist at the University of North Carolina. Hamilton is at North Carolina State University.