Letters

Estimating the Greenhouse Effect

In October, the U.S. Environmental Protection Agency (EPA) issued a report entitled "Can we delay a greenhouse warming?" The report was widely interpreted as answering that question essentially in the negative. In the words of Philip Shabecoff of the *New York Times* (*1*): "[The] warming trend, the result of a buildup of carbon dioxide in the atmosphere, is both imminent and inevitable." And "no strategy . . . even a total ban on the use of fossil fuels, could do more than delay the warming effect a few years."

A careful reader of the EPA report will recognize the need for some important qualifications to such statements. First, most students of the CO_2 issue would agree, I think, that some warming is probably unavoidable, perhaps an increase of 1° or 2°C in global annual average temperature, depending in part on the still-uncertain sensitivity of climate change to increasing atmospheric CO_2. But much higher temperature increases, like 5° to 10°C, which could conceivably result from full exploitation of the world's recoverable resources of fossil fuels, are by no means unavoidable. Although an immediate, total ban on fossil fuels (not exactly the case considered by EPA, but close to it) is entirely unrealistic, some future modification in the use of fossil fuels, in order to limit CO_2, might well be a practical possibility.

Second, the limited effect of large reductions in assumed future use of fossil fuels on the time when the calculated global temperature rise would reach 2°C, as presented by EPA, resulted in part from a large contribution to the calculated warming by infrared-absorbing gases other than CO_2, for example, methane, nitrous oxide, and chlorofluoromethanes. Their ever-increasing contributions to the warming were held fixed as functions of time, while the CO_2 contribution from fossil fuels was markedly reduced. In low-CO_2 scenarios, the other "greenhouse" gases contributed up to 80 percent of the calculated temperature rise.

It is generally recognized that the other greenhouse gases may be important; but neither their future sources and atmospheric concentrations nor their effect on climate can be estimated at all accurately at present. The EPA calculations may or may not prove to be correct. The implicit assumption that future sources and concentrations of the other greenhouse gases could not be controlled is probably incorrect.

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Reference

1. P. Shabecoff, *New York Times*, 18 October 1983, p. A1.

Cancer Prevention: Setting Priorities

The article "Cost-effective priorities for cancer prevention" by Milton C. Weinstein (1 July, p. 17) may offer a significant and potentially useful approach to the complex issue of setting research priorities for the prevention of human cancer. Weinstein's approach, however, appears to overlook a fundamental cost that may have a major impact on his cost-effectiveness analysis. Specifically, the cost of the total background of research that is necessary before any chemical is seen as an important candidate for rodent bioassay testing is likely to be less by several orders of magnitude than the cost of research needed to identify and justify any anticarcinogen as a legitimate candidate for human trials. For example, strongly positive responses for a new industrial chemical in one or more short-term screening tests may be sufficient justification to warrant rodent bioassay testing and subsequent governmental action. These data can be obtained for a total cost that certainly should not exceed the cost of the rodent bioassay itself.

By contrast, inhibitors of experimental chemical carcinogenesis can become legitimate candidates for human study only after exhaustive animal studies to determine species, organ, and carcinogen specificity; potency; toxicity; and most important, mechanism of action. Thus, to the estimated $4 million cost of the human trials of β-carotene should be added the cost of all the relevant worldwide human and animal experimentation that preceded and contributed to its recognition as a legitimate candidate for human anticancer trials. Although estimates of this cost are difficult to arrive at, one may suspect that they greatly exceed the $4 million cost of the actual human trials for anticarcinogenicity that Weinstein uses as his basic cost estimate. For example, a computer search of the Medline database reveals approximately 5700 articles relating to vitamin A dating back through 1966, with more than 10 percent of these relating directly to cancer research. If one estimates approximately $30,000 of research funds expended per publication, this represents an actual recent cost of 18×10^6 to 170×10^6, covering expenditures over only the past 17 years, to gather the data essential to identify retinoids as safe and potentially effective candidates for human trials. As Weinstein recognizes, β-carotene may represent a current best case for his arguments. The model will, of course, lack general validity if it applies to only a few such special cases. More recently recognized candidates as potential inhibitors, such as indole-3-carbinol and other plant phenolics, must undergo similar extensive, and costly, prior basic research if they are to prove fit for human trials. When such large factors are included as part of the real costs that must precede human trials, the cost-effective attractiveness of this approach over rodent bioassays cannot be as great as that estimated by Weinstein and, in fact, may disappear.

Weinstein has raised a very important issue. It is imperative, however, that administrative decisions on allocation of scarce research funds should not be based on cost-effectiveness models until these models are thoroughly scrutinized.

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Weinstein's approach to priority-setting for cancer research uses examples that are clearly not comparable. The results from extensive preliminary testing in both animals and humans must provide persuasive evidence of the value and safety of any proposed dietary intervention trial. Thus, the $4 million cited