

quickly threw aboard some plastic pipe and electrical cable, our sailors (and one good plumber) could have these units all hooked up for water, electric, and sewage services on the trip over.

Add up what it will cost Japan to build temporary housing for 100,000 families in Kobe. That would cost five times as much and take five times as long—while the earthquake survivors freeze through the winter. And none of this temporary housing could later be moved to Tokyo if an earthquake hits there.

Here in the United States, our disaster officials should realize they have overlooked the obvious. They should organize and sign up the owners and suppliers of camper units and recreational vehicles to respond to national disasters. This is how the U.S. Forest Service obtains the equipment it needs to respond quickly to major forest fires. Local fire departments should be given the federal money to organize these emergency shelters.

We must be ready to avoid the tragedy of Kobe if real disaster strikes one of our major cities.

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Risk Assessments of Low-Level Exposures

We read with interest Philip H. Abelson's editorial of 9 September (p. 1507) about risk assessment of low-level exposures. None of the subsequent responses (Letters, 18 Nov., p. 1141), however, offer suggestions for addressing the issue he raised. The approaches currently available to address this issue are (i) experimental studies of administered doses of toxicants or radiation exposure to animals; (ii) studies of unintentional or occupational exposure to humans; (iii) human environmental studies of effects at naturally occurring doses in certain locales; and (iv) meta-analysis of low-dose human exposure studies.

Even though these approaches can address low-dose effects, each has limitations. For example, in option i, applying results obtained from animal studies to humans is questionable because of interspecies variation in metabolism, which will likely yield different responses to doses among species. As Abelson points out, the linear model for extrapolating high-dose effects to very low doses is doubtful. This is especially the case if the high-dose exposure was received suddenly, or if the range between the lowest received dose and the dose used in predic-

tion of effects is large (greater than one order of magnitude). Linear extrapolation also disregards repair mechanisms in organisms (1, 2). These caveats apply regardless of whether the study is of animals or humans.

With regard to option ii, studies of acute (high) doses depend on the occurrence of rare and unintentional events such as explosions. Occupational studies are limited by sample size and increasingly stringent regulation of human exposures. For example, the Hanford worker study (3) yielded dose-response parameter estimates with wide confidence intervals.

Natural-dose, locale-based studies (option iii) depend on the availability of reliable measurements of effects, doses, and confounding factors. Epidemiologic (geographic cohort) studies of naturally occurring (background) radiation have been conducted (4); however, these studies typically occur on an ad hoc basis as funds are available and as appropriate locales are identified.

A meta-analysis of multiple low-dose human exposure studies (iv) can produce results with more statistical power than any of its constituent studies; however, if there are too few studies or the study results are heterogeneous, meta-analysis may not lead to a definitive conclusion. Also, methodological questions have been raised about

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the proper interpretation of meta-analysis of observational studies (5). Pooling of individual data from different sources may avoid some of the limitations of meta-analysis (6); however, any analysis remains subject to the problem that estimation of small effects requires large samples.

In addition to these four approaches, alternative epidemiologic investigations of mortality and morbidity could be performed. These studies can be characterized generally as ecological or individual. Often, the former can be conducted from existing mortality and environmental data (7). Although these studies are comparatively inexpensive, they suffer from the "ecological fallacy" and are considered useful only for hypothesis-generating purposes by many investigators (8).

For valid assessment of the effects of low-dose exposures in humans, large samples will be required. Such samples could be obtained by routine collection of mortality data from vital statistics or morbidity data from disease registries. Although state mortality statistics are already being gathered by the U.S. National Center for Health Statistics, information about confounding factors and exposure is not readily available. It could, however, be collected. Existing cancer registries, although useful, do not cover the entire United States, and the quality of state-based

registries varies greatly (9). We could obtain much larger and more useful samples from these registries if they were standardized and expanded to all states. For both mortality and morbidity, the resulting data would allow retrospective case-control or dose-response analyses. For some exposures, such as background radiation and air pollution, an individual's dose can be inferred from his or her locale (residence history); such studies could be initiated without direct measurement of toxicant body burdens. In other cases, the exposure dose would need to be obtained by direct sampling.

We agree with Abelson that major efforts should be made to study the effects of low-level toxicant exposures. Although experimental studies are important in order to understand basic mechanisms of exposure effects, the health effects of low-dose exposures on humans can be better understood by conducting large-scale, coordinated, epidemiologic investigations. The long-term commitment of resources required should be weighed against the societal cost of limited knowledge about the effects of low-dose exposures.

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Oswald Ennemoser (Letters, 18 Nov., p. 1145) provides what he says is evidence for lack of a threshold regarding exposure to ionizing radiation, using data collected from "nearly 96,000 workers in the nuclear industry," which he says are the most comprehensive available. At first glance, an increased leukemia mortality of 2.2 per sievert seems alarming, but the 90% confidence interval ranges from 0.1 to 5.7. Is 0.1 significantly different from 0.0? Not at the 95% confi-

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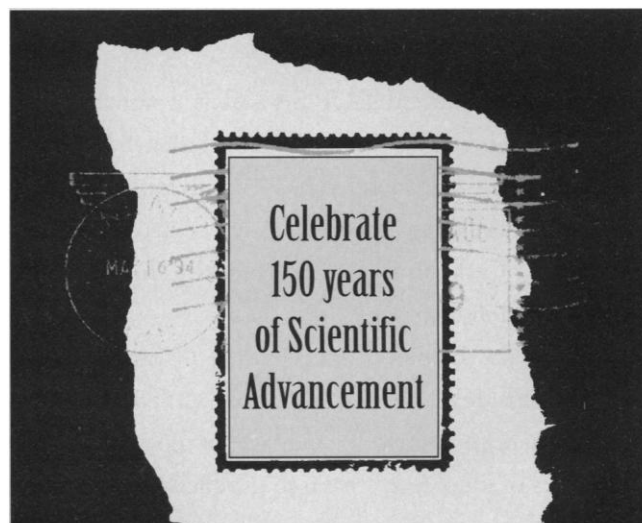
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dence level most scientists (and even the Environmental Protection Agency) use. Types of cancer other than leukemia showed no effects (90% range -0.39 to $+0.30$). If the data were subdivided into multiple groups of cancer types, one group, leukemia, could show a seemingly positive result. False-positive results would be expected in one out of each ten groups if the loose 90% significance level is used.

If such a thorough investigation of persons exposed to industrial levels of radiation is unable to come up with more convincing evidence of low-level effects of radiation, then the risk, in my opinion, is so small it is indistinguishable from zero. Thank you, Dr. Ennemoser, for confirming Philip H. Abelson's editorial conclusions (9 Sept., p. 1507).

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Other Lipopeptides

Carol Potera's Research News article "From bacteria: A new weapon against fungal infection" (29 July, p. 605) suggests that Montana State University's Gary Strobel and his colleagues determined the structures of new

antimycotic lipopeptides called the pseudomycins and discovered that they contained the unusual amino acids chlorothreonine, hydroxyaspartic acid, and diaminobutyric acid. These amino acids were previously found in similar lipopeptides (the syringomycins, the syringostatins, and syringotoxin) by researchers affiliated with our laboratories at the University of Rome (Alessandro Ballio), the University of Tokyo and Nara Institute of Sciences and Technology (Akira Isogai), and Utah State University (Jon Takemoto) (1). Like the pseudomycins, these latter lipopeptides are produced by the plant bacterial species *Pseudomonas syringae*. In all of these lipopeptides, chlorothreonine and hydroxyaspartic acid occur with serine and dehydroaminobutyric acid in a highly conserved sequence. The pseudomycins simply are the latest additions to this family of interesting bioactive bacterial metabolites. The complete structures of the pseudomycins were recently elucidated by Ballio and his colleagues (2).

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Corrections and Clarifications

Several authors' changes should have been included in the response by D. B. Wheeler *et al.* to the technical comment "Identification of calcium channels that control neurosecretion" (4 Nov., p. 830). A sentence reading, "Comparisons with experiments using higher concentrations of carrier protein (1.0 mg/mL) revealed no significant differences in the rate of efficacy of ω -Aga-IVA action" should have been inserted before the last sentence in the legend of figure 1. The measure "30 nM" (not 20 nM) should have appeared 19 lines from the bottom of the last column on page 830. The second-to-last sentence in that paragraph should read, "Increasing the duration of exposure to 30 nM ω -Aga-IVA from 20 min (1) to 45 min revealed significant inhibition of synaptic transmission ($n = 9$). Reference "(15)" (not 16) should have appeared seven lines from the top of the first column on page 831.

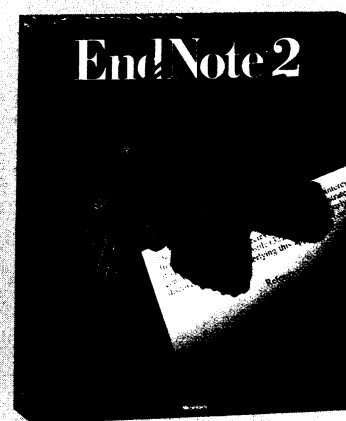
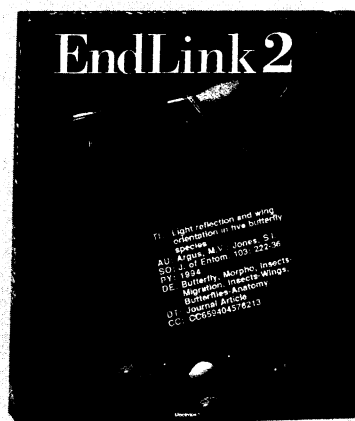
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