often conflicting issues that were discussed at the conference.

The overall purpose of the conference was not only to facilitate an eclectic discussion on the complex issue of informed consent, particularly in the context of Alzheimer's disease, but to use the information gained from the conference as the basis to develop a set of comprehensive guidelines that might be useful to the clinician investigators and patient subjects alike who are, or at some point in the future will be, participating in such a research protocol. To this end, we have now assembled a task force specifically for the purpose of identifying and developing such guidelines. This task force is scheduled to meet very soon and the goal of the task force deliberations will be to make every attempt to develop a set of guidelines that would be conducive to eliciting and facilitating sound research in the most ethical context. These guidelines will be published along with the proceedings of the conference.

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In the thought-provoking article by Kolata on Alzheimer's disease, Kenneth Davis is quoted as saying, "If we wait to do our research until patients come who have made penultimate wills, we may find ourselves waiting for Godot." I believe there must be thousands of people, some of whom ultimately will suffer from this terrible affliction, who would be willing to prepare a penultimate will volunteering to be studied by invasive techniques designed only to help mankind. It would add dignity to the leaving of this life to make one last contribution. Even the possibility of shortening life in that dreadful condition of incompetence would not deter many people.

Why not put this to a test? Interested groups could prepare a model will and give those presently with a sound mind and a willing heart an opportunity to sign up.

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NCI's Drug Program

I would like to comment on the article "Cancer institute's drug program reproved" (News and Comment, 20 Nov., p. 887). In May 1978, as part of a multicentered study sponsored by the Brain Tumor Study Group (BTSG) of the National Cancer Institute (NCI) on the chemotherapy of malignant gliomas with nitrosoureas, we notified the BTSG of the occurrence of nephrotoxicity in four of our patients. The circumstances of the nephrotoxicity were unusual. It developed insidiously in the patients several months after administration of the nitrosoureas, BCNU and methyl-CCNU, had been stopped; during the period of administration the routine tests of renal function were normal; the patients lived long enough to develop the nephrotoxicity. This heretofore unrecognized delayed renal toxicity was reported by Schacht and co-workers in our group (*1*) and independently by Harmon *et al.* (*2*).

Although toxicological studies in animals had revealed that the nitrosoureas were associated with acute nephrotoxicity, this differed substantially from the delayed nephrotoxicity reported by us and referred to at the congressional hearings. The acute nephrotoxicity occurred during administration of the drug and was accompanied by pyuria and hematuria. In our letters to the BTSG and to our institutional review board (to whom we were obligated to report), we stated that we did not know the incidence of the delayed nephrotoxicity and could find no literature on it.

Shortly after sending our letters, we received a reply from the NCI, who had reported our observations to Bristol-Myers (the manufacturers of the drug). The BTSG then initiated a detailed survey of the other participating centers, but even after a few more cases of delayed nephrotoxicity were found its incidence was still not known. The incidence was important because these drugs allowed 15 percent of patients with a formerly 100 percent lethal disease (malignant glioma) to live more than 2 years. If only a few of these long-term survivors developed the delayed nephrotoxicity, the drug could still be available for the other patients. With more sophisticated (and costly) tests than those usually required we could detect the nephrotoxicity sooner and stop administration of the drug. Unfortunately, as there are still no drugs available that are as effective as the nitrosoureas, we also could not offer more chemotherapy.

In all of my dealings with the BTSG and NCI (with whom I am no longer associated) I have found them to be careful, concerned, helpful, and diligent.

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1. R. G. Schacht, H. D. Feiner, G. R. Gallo, A. Lieberman, D. S. Baldwin, *Cancer* **48**, 1328 (1981).
2. W. E. Harmon, H. J. Cohen, E. E. Schneeburger, W. E. Grupe, *N. Engl. J. Med.* **300**, 1200 (1979).

Radioactive Waste Disposal

Several articles have appeared recently in *Science* which propose approaches for the storage of radioactive wastes. The approach of Winograd (26 June, p. 1457) appears to depend on the long-continued confinement of ground water to depths well below some craters remaining from nuclear weapons testing while the approach of Bredehoeft and Maini (17 July, p. 293) appears to depend on the long-term stability of ground-water flow patterns in selected areas. I cannot help wondering whether these approaches deserve further consideration at this time given the prediction of climatologists [see, for example, (*1*)] that the first distinguishable symptom of an ever-increasing carbon dioxide concentration in the atmosphere may be expected to be significant shifts in global precipitation patterns, which must ultimately affect the global distribution and flow of ground water.

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1. W. W. Kellogg and R. Schware, *Climate Change and Society: Consequences of Increasing Atmospheric Carbon Dioxide* (Westview, Boulder, Colo., 1981).

We note first that, on page 47 of their book, Kellogg and Schware state, "From what has been said above about the many uncertainties in our knowledge of the response of the climate system to an increase in atmospheric carbon dioxide, it appears to be a futile exercise at this time to try to make a detailed prediction of what the future warmer Earth will be like." Moreover, the one future scenario they present (figure 11.3, p. 49) indicates drier than modern soil moisture for most of the United States, including the Southwest. Nevertheless, Alpher's generalization deserves a response.

Certainly a major shift in climate of long duration could change certain ground-water regimes. However, the deep sedimentary rock flow systems, discussed by Bredehoeft and Maini, respond extremely slowly to external changes. For example, fresh ground wa-

ter has been found in the shallow sediments off the Atlantic Coast from New Jersey to Cape Cod. The common interpretation (*1*) suggests that this is the result of lower sea level during periods of Pleistocene glaciation. Even after at least 8000 years, the ground-water system has not equilibrated with the present sea level.

At the Nevada Test Site, the great depth to the water table beneath Yucca Flat (up to 660 meters), and many other valleys of the south-central Great Basin, is controlled by the regional subsurface extent of a highly transmissive carbonate-rock aquifer that also has a topographically low discharge point. That these deep water tables are not a result of the modern, arid to semiarid climate of the region is best seen by comparing Yucca Flat with Emigrant Valley, an intermontane basin bordering Yucca Flat on the northeast. The water table beneath Emigrant Valley is as shallow as 30 meters, yet both valleys have the same climate. The shallow water table beneath Emigrant Valley reflects extremely low transmissivity of the metasedimentary rocks surrounding this valley, not higher precipitation. Details on the hydrogeology (*2*) of both valleys and estimates of water level rises in the carbonate-rock aquifer in response to future, wetter climates (*3*) are available. Briefly, future, wetter climates—reflecting some combination of increased precipitation and reduced temperature—are unlikely to raise the water table significantly in Yucca Flat. Of far greater importance to the unsaturated zone notion advanced, a future increase in precipitation is likely to cause more frequent and deeper infiltration of water through the unsaturated zone than occurs at present. Nevertheless, as pointed out explicitly and at some length in Winograd's article, several barriers to radionuclide mobilization and migration remain in the event of a change to a wetter climate; namely, the high sorptive capacity of the valley fill and underlying zeolitized tuffs, the engineered capillary barrier, and a presumed low solubility of the waste form. Any radionuclides somehow reaching the carbonate-rock aquifer despite these barriers would additionally be diluted, as discussed by Winograd.

Alpher's general concern that "an ever-increasing carbon dioxide concentration in the atmosphere . . . must ultimately affect the global distribution and flow of groundwater" is unwarranted when one examines the specific waste disposal strategy of putting wastes in thick unsaturated zones within the arid- to semiarid southern Great Basin. The deep ground-water system discussed by Bredehoeft and Maini do not respond rapidly to changes in climate; their stability under the right setting can be assured for thousands, if not tens of thousands, of years.

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2. I. J. Winograd and W. Thordarson, *Geol. Soc. Am. Mem. 110* (1968), pp. 35–48; *U.S. Geol. Surv. Prof. Pap. 712-C* (1975).
3. I. J. Winograd and G. C. Doty, *U.S. Geol. Surv. Open-File Rep. 80-569* (1980).

Myeloma, Not Melanoma

Arnold Demain's article (27 Nov., p. 987) on industrial microbiology is excellent. However, there is one minor mistake in the article. Somehow, in the third column of page 993, myeloma (a tumor of the bone marrow characterized by the excessive production of either the "heavy" or the "light" chain of the antibody molecule) is confused with melanoma (a form of skin cancer). In the technique for the production of monoclonal antibody introduced by Kohler and Milstein (*1*), a hybrid of myeloma and immunized spleen cell is used.

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1. G. Kohler and C. Milstein, *Nature (London)* **256**, 495 (1975).

Erratum. In the letter from Senator Warren B. Rudman (29 Jan., p. 456), a quote from testimony by Ronald Lamont-Havers was incorrectly printed. The correct quote is as follows: "What I would be concerned about, in saying that, would be the fact that funds are then set aside, protected funds, which would prevent one of our own investigators not being supported. That's all I'm concerned about. I'm not really concerned about whether or not there's funding. I'm concerned about protecting my own investigators as far as their funding, and any reduction in funds within that system is going to have a perturbation within our system."

Erratum. In figure 1 of the report by D. Regan and K. I. Beverley (8 Jan., p. 194), the photograph on the left should have appeared on the right, and vice versa.