

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 re-proved" (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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References

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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References

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-