The May/June issue of Cancer Chemotherapy Reports shows that its readers are being stimulated by some of the articles in the Journal to the degree of sending in some provocative letters. As is often the case, the “letter-to-the-editor” format frequently permits a contributor more freedom in his views in that one need not respond to those pressures which result from multiple critical reviews of a formal manuscript. Such freedom often provokes the innovative thinking that can occasionally be achieved with a single well-mixed martini; in all fairness however, others might view these letters as being more likely to be the result of five or six martinis.

Chacon à son gout! Adamson submits a letter from the National Cancer Institute presenting a hypothesis concerning the structural basis for antitumor activity and cardiotoxicity of the drugs daunomycin and adriamycin. These antibiotics have certainly represented a major new thrust in chemotherapy and Dr. Adamson suggests that the sugar moiety may be critical in cell penetration, whereas the chromophore portion of the molecule is the key to antitumor activity. Certainly, this hypothesis can be tested by proper rational chemical syntheses based on this viewpoint.

Similarly, another letter by Cysyk, also from the National Cancer Institute, suggests the development of a methylphosphonate derivative of cytosine arabinoside to circumvent tumor resistance, a rapidly developing phenomenon in man. Certainly cytosine arabinoside has antitumor activities in a variety of human and animal tumors and one would hope that the author’s suggestion will be tested.

Two other letters from such diverse areas as the U.S. Missile Command at the Redstone Arsenal in Alabama, and the Royal Victoria Infirmary at Newcastle upon Tyne, England, from Allan and Norman, and from Dickson respectively present their reactions to a previous commentary dealing with Adjuvant Temperature Effects in Cancer Therapy (CCR, Vol. 57, p. 373, 1973). Dr. Dickson notes that temperature effects in cancer are now so well established that it would be
somewhat wasteful to put much effort into experimental models. His main concern is that temperature effects in animals will not be predictive for the clinic and he urges a more prompt clinical application of heat as an adjuvant to cancer therapy. Allan and Norman present the interesting view, with some supporting data, that the water structures in malignant and normal cells differ and these differences may be expected to be exaggerated by temperature changes and therein cause the observable relative thermosensitivity of tumor cells as compared to normal cells. This theory is interesting and would lend itself to a careful study. One thing is clear, however. When scientists at the U.S. Missile Command in Redstone Arsenal can write expertly on the physical state of water in normal and malignant tissues and its modification by temperature this would seem to indicate at least that flowers of academic freedom yet bloom in the United States.

Four more articles in this issue of CCR, i.e., those reviewed by outside experts, while perhaps not exhibiting the blitheness of view of these letters, do contain areas of particular interest to clinicians. For example, Sakamoto writing from Denver, Colorado, advances the idea that the peripheral neuropathy associated with vincristine is related to the preceding physical activity of the patient. Those people more active prior to and while receiving vincristine exhibit less neuropathy. Dr. Sakamoto believes that his idea can be tested by physicians with greater access to patients under such therapy.

Fondy et al. writing from Syracuse University make the interesting observation that in many rodent systems undergoing experimental chemotherapy there may be an attendant hypothermia induced by the drug, which can influence both antitumor activity of the drug and have temperature-specific effects on the life-span of animals with leukemia. The article brings up a variable which is not often addressed. The authors suggest that the use of liquid crystal thermography tape may be a useful screen for drugs which produce temperature
changes in the host. In their hands reserpine had both antitumor activity in leukemia L1210 in addition to inducing hypothermia in mice.

A group of articles deal with some recent results of studies with various nitrosourea derivatives; these include use of oral BCNU by Lessner and Vogler, writing for the Southeastern Cancer Study Group, and intravenous BCNU by Rege and Owens, writing for the Acute Leukemia Group B in their studies of advanced lymphoma. Further, a general review of the chloroethyl cyclohexyl nitrosourea derivative (CCNU) is presented by Perloff et al. from Albert Einstein in New York relating their experiences in advanced non-hematologic cancer. These articles reflect the continued usefulness of these compounds in clinical oncology.

A report by Kaung et al. from the VA Lung Cancer Study Group examines its protocols between 1969 and 1972 in which 239 patients were allotted to treatment with local supravoltage radiotherapy, chemotherapy or both. The preliminary results indicated no overall superiority of one regimen over the other. There were also 1307 lung cancer patients with more extensive tumor involvement treated with varying drug regimes, none of which proved superior to the VA Group's past experiences with cyclophosphamide. The analysis of the Group indicated that for the patients with extensive disease, those with initially high performance status seemed to have more favorable prognosis with regard to drug response. These disappointing results are balanced somewhat by a Phase II clinical trial with hexamethylmelamine which demonstrated appreciable antitumor activity in 23 cases of small cell carcinoma of the lung.

Finally, attention should be drawn to an early trial by Creaven et al. from the VA Hospital in Washington, D.C., with the drug ICRF 159. This agent, which can be considered a derivative of EDTA, has activity in human leukemia and may have an important ancillary mechanism of action in preventing metastatic disease in other tumors. Most experience with the agent has been in murine systems.