Adriamycin cardiotoxicity continues to be a dose-limiting obstacle in the optimal use of this broad-spectrum agent in cancer chemotherapy. Two interesting reports in the July issue of Cancer Treatment Reports provide new information on this topic. Greco et al. (National Cancer Institute, Bethesda, Maryland) describe their experience in monitoring left ventricular function by measuring the QKd interval (time from onset of the Q wave to the Korotkoff arterial sound at diastolic pressure in the brachial artery), a dynamic index of cardiac contractility and stroke output. They report significant but transient prolongation of the QKd interval in all patients receiving adriamycin; QKd times were prolonged to two weeks after administration but returned to baseline by the three-week measurement. Failure of the QKd interval to return to baseline values was correlated with congestive cardiac failure in three of the seven cancer patients who received greater than 550 mg./m². This non-invasive technique may be of prognostic utility when it appears clinically indicated that the 550 mg./m² maximum dose should be exceeded. Weiss et al. (Central Oncology Group) document the lack of overt cardiotoxicity when adriamycin is given in a weekly schedule in cumulative doses exceeding 550 mg./m². Citing Central Oncology Group experience in 442 patients, these authors noted no clinically significant cardiac toxicity in 59 patients receiving doses ranging from 550 to 2,500 mg./m², although six patients had cardiac abnormalities attributable to other causes. Thus, dose rate of adriamycin may be an important determinant of cardiotoxicity, as well as the total dose. Confirmatory data on this point are anxiously awaited, since adriamycin in addition to its broad spectrum of activity in advanced cancer, is a potential adjuvant to surgery in a number of neoplasms.

The July issue contains two important reports on the lack of clinical effect of hydrazine sulfate. This compound received considerable publicity in the lay press prior to confirmation of clinical utility. Lerner and Regelson (Pennsylvania Hospital, Philadelphia, Pennsylvania) report no clinical effect in 25 evaluable cancer patients, and Gershonovitch et
al. (Petrov Research Institute of Oncology, Leningrad, USSR) report a minimal objective effect (>50 percent tumor regression) in two of 95 evaluable patients. Over half of their patients reported mood improvement, accompanied in some by dizziness, insomnia or general excitement. Previously, Ochoa et al. (Cancer Chemotherapy Reports 59:1151-1154, 1975) also reported lack of antitumor activity of hydrazine sulfate in 29 evaluable patients, and significant neurotoxicity was encountered in half of the patients. Thus, the weight of clinical evidence has failed to confirm the early enthusiastic reports by Gold (Syracuse Cancer Research Institute, Syracuse, New York). In a letter in the July issue, Gold points out what he considers flaws in the study by Ochoa et al., citing his recent paper (Oncology 32:1-10, 1975) on subjective and objective responses following hydrazine sulfate therapy. While a controversy on this topic may continue, readers may now draw their own conclusions based on the published data.

Several clinical trials reported in the July issue bear mention. Hoge et al. (Oklahoma Medical Research Foundation, Oklahoma City, Oklahoma) report favorable results using ablative endocrine therapy (adrenalectomy/ooophorectomy) followed by cyclophosphamide, vincristine, methotrexate and 5-FU for eight weeks in 39 patients with metastatic breast cancer; 22 complete and 11 partial responses were observed (80 percent overall response rate). The median duration of complete response was more than 16 months. The authors conclude that chemotherapy exerts an additive effect to ablative endocrine surgery, and are now comparing this regimen to additive hormone therapy plus the same chemotherapy in a larger cooperative study.

The ECOG reports a modest antitumor effect of adriamycin in far-advanced lung cancer, noting a 23 percent response rate in oat cell cancer. Since only eight of 140 patients with other histologic types responded, it seems that the usefulness of this agent in this disease is limited.

Using a low-dose combination of bleomycin, adriamycin and vinblastine in 28 patients with metastatic testicular cancer, Kardinal et al. (Western Cancer Study Group) report
only three complete and three partial responses, and "mild" hemopoietic toxicity. This study points up the importance of the dose-response relationship in chemo-sensitive tumors, and the necessity to push active drugs to full, tolerable toxicity.

Eagan and his colleagues (Mayo Clinic, Rochester, Minnesota) report two clinical trials in lung cancer. In one, ICRF-159 was compared to vincristine, bleomycin and adriamycin in 63 patients with non-oat cell bronchogenic carcinoma. Only four partial responses were noted in 52 evaluable patients (primary plus crossover treatment) treated with ICRF-159, as compared to five responses in 36 patients receiving the drug combination. In a second randomized trial in oat cell cancer, the authors compared VP-16-213 with vincristine, cyclophosphamide, methotrexate or vincristine, bleomycin and adriamycin combinations. Seven of 13 previously untreated patients responded to VP-16-213, indicating substantial antitumor activity. The combination treatments produced overall response rates of 68 percent and 44 percent respectively. In view of its activity, the authors are now testing VP-16-213 in combination with adriamycin and/or cyclophosphamide in oat cell cancer.

Finally, the July issue contains two Phase I trials of interest. Vogel et al. (Emory University School of Medicine, Atlanta, Georgia) report on dose and toxicity of 1,2:5,6-dianhydrogalactitol in 28 patients with advanced solid tumors. They recommend a weekly dose of 70 mg./m² for Phase II studies (with 25 percent reduction in patients with compromised hemopoiesis). Objective responses were noted in one patient with malignant melanoma and one with hypernephroma. Nissen et al. (Finsen Institute, Copenhagen, Denmark) studied the tolerance of oral VP-16-213 in 30 patients with advanced cancer. They recommend a dose of 120 mg./m² daily x five employing the oral solution (as opposed to the capsule formulation, which results in erratic absorption). While both hemopoietic and gastrointestinal toxicity were encountered with this formulation, a definite though modest antineoplastic effect was observed.