The June issue of Cancer Chemotherapy Reports notes the recent death of Dr. John P. Glynn, Jr., who during his tenure as Scientific Editor of the Journal had moved the publication forward into the scientific mainstream of cancer journals. Dr. Glynn was responsible for many of the innovations and developments which have marked the past six years of Cancer Chemotherapy Reports. His death at the age of 39 results in the loss of one of cancer's most vigorous investigators.

Several articles in the issue deal with the problem of breast cancer. Sandberg and Goldin, writing from the National Cancer Institute in Bethesda, Maryland, comment on their use of first generation transplants of mammary carcinomas arising spontaneously in mice. The usefulness of the model, with regard to potential relevance to man, is that these first generation transplants are quite slow growing and, therefore, may parallel more closely clinical disease than the usual murine leukemia models. The latter have generation and doubling times of approximately 12 hours, whereas the first generation transplant mammary tumor has a doubling time of almost five days. Such differences are believed to be in part responsible for the notorious resistance of the mouse spontaneous mammary cancer to chemotherapeutic agents. The authors tested some 18 drugs in their system and found several with minimal activity. These included poly IC, L-asparaginase, the cyclohexanol derivative of nitrosourea and phenesterin. When they attempted to relate drug activity in their mammary system to activity in L1210 there was no correlation between these two murine systems with differing doubling times.

Stolfi, et al., from the Catholic Medical Center of Brooklyn and Queens, Inc., New York City, discuss further the use of this spontaneous murine mammary adenocarcinoma mouse model for evaluating therapy of breast cancer. They comment extensively on the immunologic factors governing regression and the role of both resection and chemotherapy in achieving cure rates in what has been, hitherto, a noncurable malignant murine disease.

Phenesterin has been studied in a phase I treatment plan by Ansfield, et al., (University of Wisconsin Medical School, Madison), representing a collaborative effort from several institutions throughout the country. Its clinical trial was conducted and awaited with considerable, positive enthusiasm because of its further demonstrated activity in mammary murine tumors. The authors administered the drug to some 30 patients with advanced breast cancer, all of whom had had prior trials with hormones or cytotoxic agents or both. Only one regression was observed and myelodepression proved to be the major toxic side effect. The
authors comment on their disappointment with regard to the clinical results being somewhat diametrically opposite to the animal data.

Another steroidal compound, 6a-methylpregn-4-ene-3,11,20-trione (NSC17256), is reported on by Ramirez, et al., for the Central Clinical Drug Evaluation Program. This progesterone derivative first achieved considerable notice in chemotherapy when early clinical trials demonstrated approximately a 10 percent sustained response rate with the agent in metastatic malignant melanoma. In a phase II trial the authors studied 407 patients with a variety of tumors. The major tumors studied were melanoma (111 patients) and breast carcinoma (70 patients), and they detected an overall response rate of about five percent. These included complete disappearances of tumor in addition to the more common partial responses, and the authors indicated that additional exploration of the therapeutic potentialities of the drug was in order.

Two papers appear on imidazole carboxamide therapy in cancer. One from the National Cancer Center Research Institute, Tokyo, Japan, by Hoshi, et al., comments on a mercapto derivative of the compound and its use in animal tumors where it has demonstrated activity viewed as superior to 6-mercaptopurine. Kingra, et al., from the Albany Medical College, New York, reported on the use of the dimethyl triazeno derivative in malignant tumors other than human melanoma. It will be recalled that this drug was the initial derivative which elicited clinical interest because of activity against melanoma. Activity against lung cancer and brain tumors was shown in this study.

The report by Cohen, et al., writing for the Eastern Cooperative Oncology Group, concerns the use of radiation with and without the addition of 5-fluorouracil (5-FU) for the treatment of bronchogenic carcinoma. The authors compared the effects of 2,000 rads plus 5-FU, 4,000 rads alone and 2,000 rads alone. Regression in the combined treatment program was equivalent to regression in the group receiving 4,000 rads, while the small dose of radiotherapy was inferior. The authors recommend use of the combination treatment to potentially shorten hospitalization necessitated by prolonged treatment programs which use a 4,000 rad dose.

A major study with the agent L-asparaginase in the treatment of human adult leukemia is reported by Ohnuma, et al., writing for the Acute Leukemia Cooperative Group B. Investigators studied 42 patients with previously treated and resistant leukemia with two differing dose schedules. In only two of 31 patients with acute myelocytic leukemia was a remission obtained, whereas in three of 11 patients with acute lymphocytic leukemia complete marrow response was noted. A variety of toxic effects which are perhaps increasingly well appreciated, such as nausea, vomiting, fever, hepatitis, pancreatitis and renal and cerebral dysfunction, were observed in addition to the more readily appreciated hypersensitivity reactions.

Readers who have followed the discussions appearing in Cancer Chemotherapy Reports on daunomycin (rubidomycin) may be interested in the report by Pittillo and Woolley, from the Southern Research Institute in Birmingham, Alabama, on the biologic activity of adriamycin in microbial systems. Clinicians had anticipated that adriamycin might represent merely an analog of daunomycin with little important difference in mechanism of action or therapeutic efficacy. Such data are, of course, not yet in hand; however, the authors do point out that the two drugs differ in their radiosensitizing effects in some bacterial systems and there are measurable biologic differences between the compounds in regard to their ability to inhibit bacterial growth.