Highlighting Cancer Chemotherapy Reports

A commentary on the December 1971 (Volume 55, Number 4) issue

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The December issue of Cancer Chemotherapy Reports has among its articles several reports of unusual drug toxicity. A reason for calling attention to these unusual reactions to drugs is that, in time, such observations may be usefully employed in the treatment of specific conditions. Background information on this approach was contained in a previously published Commentary by L. M. Cobb (Chester Beatty Research Institute, London, England) on organ-specific chemotherapy (Cancer Chemother. Rep. 54: 375-378, 1970). A more direct parallel is the use of such agents as mitotane (o,p'-DDD) which was observed to produce adrenocortical necrosis and was subsequently proved useful in the treatment of adrenocortical carcinoma. Methotrexate, a notorious abortifacient, is now used successfully in the treatment of choriocarcinoma. Streptozotocin, which produces islet cell malfunction and diabetes mellitus in experimental animals, is evidently useful in the treatment of malignant insulinoma in man.

Pseudourea, an experimental agent with some activity in human acute leukemia, has now been confirmed as one of the few agents producing photosensitization in man. The Writing Committee for the Central Oncology Group amplifies the previous report by Frei, et al. (M. D. Anderson Hospital and Tumor Institute, Houston, Texas) on this phenomenon (Cancer Chemother. Rep. 55: 91-97, 1971). Cerebellar ataxia, occurring during 5-fluorouracil therapy, was not reported until after the drug had been in clinical use for some seven years. Boileau, et al., reporting from the Children's Cancer Research Foundation, Boston, Massachusetts, call attention again to this unusual toxic effect of the drug in five patients, and they observe that in none was there evidence of metastatic tumor to the brain. Therefore, awareness of this drug effect is an important aspect of the differential diagnosis of central nervous system dysfunction occurring during chemotherapy with 5-fluorouracil.

Vocal cord paralysis was thought not to have been previously observed during therapy with vinblastine. Brook and Schreiber, from the Veterans Administration Hospital, Long Beach, California, point out this unusual and unexplained drug effect, which fortunately was reversible within 4-6 weeks of discontinuing standard doses of the drug.

Berenson (Columbus, Georgia) calls attention to his personal experience with an overdose of vincristine, noting that his patient recovered from a dose of 10 mg. of the drug. Toxic reactions included fever, nausea and vomiting, abdominal pain, paresthesias and weakness of the lower extremities which progressed. Neurologic deficit reached a maximum approximately one month
after the drug was given, with a moderate degree of improvement occurring subsequently. Attention is called to another patient who received and recovered from a dose of 25 mg. of vincristine.

Unusual drug toxicity is not the only feature of this month’s issue of Cancer Chemotherapy Reports. In particular, the report by Nissen-Meyer, et al. (Aker sykehus, Oslo, Norway), on an adjuvant breast cancer chemotherapy program from Scandinavia must be rated at least ‘‘G’’ for general consumption. Eleven hospitals in Finland, Norway and Sweden are conducting a controlled clinical trial of chemotherapy as an adjuvant to the conventional primary surgical therapy for operable breast cancer. Cyclophosphamide given intravenously over a 6-day period is shown in this preliminary report to result in drug-treated patients doing better than those receiving surgical treatment only. The report should be studied with interest by physicians in this country who deal with an extremely common clinical cancer for which it is extremely uncommon to find controlled clinical data to guide management. The early results of this study differ somewhat from those published by the National Breast Cancer Project in the United States (Ann. Surg. 168: 337, 1968). The authors suggest that the lack of effect in the American studies may be due to cyclophosphamide now being used in a more potent dose than either the thioTEPA® or 5-fluorouracil doses chosen for the American experience. It will be of interest to follow the more complete results of this program.

Muggia, et al., from the Washington Veterans Administration Hospital-National Cancer Institute, Bethesda, Maryland, describe some early clinical studies with a new podophyllotoxin derivative. Podophyllotoxin is, of course, a constituent of an extract obtained from the roots of the common mandrake plant or May apple. Derivatives of the compound have been useful in ointments in the dermatologist’s armamentarium for decades. The compound had been inactive in the murine leukemia L1210 system; however, since several newer derivatives have demonstrated such activity, the present clinical trials were undertaken. Unfortunately, this mandrake extract did not prove to be magical in its toxic or therapeutic effects in these very early trials. Leukopenia and mild thrombocytopenia demonstrated that other clinical groups have reported more clinically promising results, particularly in malignant glioblastoma and lymphoma. It seems clear that additional studies with the agent or analogs will be carried out in this country.

Keyes, et al., also from the Washington Veterans Administration Hospital-National Cancer Institute group, report on some early experience with the agent dibromodulcitol. The authors described an interesting dichotomy in results on the clinical tolerance to dibromodulcitol in their experience as contrasted to that reported from Hungary. This difference was not explained but points out the need to confirm carefully data derived from overseas studies, even those from Hungary, which is justly famous for its many gifts to this country. Dibromodulcitol has promise, according to the authors, in suitable patients with leukemia and polycythemia vera.

Banerjee and Margulis (Boston University, Boston, Massachusetts) describe an unusual system for screening, that is, testing for active antineoplastic agents. They used the protozoan Stentor coeruleus model for inhibitions of cilia regeneration as an extremely simple and rapid growth-inhibiting measure of a drug’s activity. The authors comment on correlations between their system and other drugs which were picked out em-
ploying more conventional animal or tissue culture screens.

Nitrosoureas are under very intensive clinical study now in the United States, as is no surprise to those following Cancer Chemotherapy Reports. Marsh, et al. (Yale University School of Medicine, New Haven, Connecticut), comment on their experience with BCNU in advanced cancer, noting again the response of resistant Hodgkin’s disease to this drug. An ultimate role for BCNU in the management of clinical cancer seems established, but its relative importance for various tumors and optimal dose scheduling remains to be established.

Writer and Audience

Granted that speeches and articles should not always deal with local particulars, they should always deal with some particulars, if only by way of illustration. Otherwise, writer and audience waste their time in sterile agreement over absolute unknowns. In this world, at any rate, no art or science can long afford to invite assent of this kind to what is unproductive, to what will make no difference in action—including the action of thinking.—Jacques Barzun, So Long As Doctors Have to Think. Bulletin of the New York Academy of Medicine 47: 229-235, 1971. P. 234.