AN IMPORTANT MESSAGE
TREATING CANCER

Clinical studies indicate that Ativan® (lorazepam) Injection can play a significant role in enhancing patient tolerance for and acceptance of chemotherapy. In studies comparing Ativan Injection to other adjunctive agents, patients expressed a strong preference for the regimen including Ativan Injection because of its anxiolytic, amnesic and sedative effects.

The reduction of recall following administration of Ativan Injection was considered by most patients to be not only acceptable, but also desirable. Furthermore, due to its anxiolytic action, Ativan Injection was helpful in relieving the anxiety associated with the stresses of chemotherapy.

NEW ADJUNCTIVE AGENTS NEEDED
A study of 52 mastectomy patients on regimens of cyclophosphamide, methotrexate and 5-FU (CMF) revealed that over one fourth of patients failed to even complete a treatment course of 12 to 18 months, mostly because of the side effects associated with these agents. A recent survey of 56 oncology centers found up to 10% of patients refused further chemotherapy because of actual or feared side effects. Statistics such as these have spurred researchers to seek new adjunctive agents or combinations of existing agents that would increase the tolerability of chemotherapy.

ATIVAN® INJECTION:
A SUPPORTIVE ADJUNCT
In a study involving 18 patients receiving 36 courses of cis-platinum therapy, Ativan Injection was administered prior to therapy. Lack of recall for the chemotherapy infusion, and for the subsequent 8 hours, was reported in 33 of 36 courses of therapy studied. Furthermore, amnesia for the day of chemotherapy was reported in 29 courses. All 18 patients believed the lack of recall was highly desirable.

Dr. John Laszlo and colleagues from Duke Comprehensive Cancer Center, Durham, NC, and Memorial Sloan-Kettering Institute, New York, reported a pilot study involving 32 patients receiving cisplatin with or without other cytotoxic chemotherapy and adjunctive use of Ativan Injection. Thirty patients were evaluated over 45 courses of treatment (two were eliminated for protocol violations).

Dr. Laszlo observed that following lorazepam, recall of the day’s events was reduced for most patients. Post-treatment anxiety was also reduced. Almost all of the patients in the study requested lorazepam (Ativan Injection) pretreatment again for subsequent chemotherapy courses, regardless of incidence or intensity of emetic episodes. From this study, Dr. Laszlo concluded that lorazepam can be an effective agent for these patients.
FOR PHYSICIANS
PATIENTS

A SIGNIFICANT ROLE IN ENHANCING COMPLIANCE IN CHEMOTHERAPY

Clearly, Ativan® (lorazepam) Injection represents an important supportive adjunct in chemotherapy. Patients' ability to tolerate the experience is usually enhanced. Their acceptance of a regimen incorporating Ativan Injection has been excellent. Thus, it is felt that many patients who might otherwise abandon treatment may now be more willing to proceed with Ativan Injection as an adjunct in their chemotherapy regimen.

If outpatients are treated with lorazepam injection, care must be taken on the day of treatment to prevent their undertaking any activity requiring full awareness or coordination.

REFERENCES:

Please see important information on the following page.
**ATIVAN® (lorazepam) injection, a benzodiazepine with anxiolytic and sedative effects, is intended for short-term use. It has the chemical formula C71H71Cl2N5O21S4 and contains lorazepam as the free base.**

**CLINICAL PHARMACOLOGY:** IV or IM administration of recommended dose of 2-4 mg lorazepam injection to adults and children over 12 years old usually results in the control of acute symptoms and a return to sleep. Lorazepam is readily absorbed after oral administration, reaching peak plasma levels within 1-2 hours of oral administration. The duration of action is variable, with some patients experiencing a full recovery within 2-8 hours, while others may require up to 5-7 days for complete recovery. Lorazepam is metabolized in the liver and excreted primarily in the urine.

**PRECAUTIONS:** Lorazepam should not be used in patients with a history of drug or alcohol dependency. It should be used with caution in patients with a history of congenital or acquired angioedema, or a history of respiratory infections. Lorazepam should be used with caution in patients with a history of cardiovascular disease, including congestive heart failure, cardiac arrhythmias, or a history of hypertension.

**INDICATIONS AND USAGE:** Lorazepam injection should be used for the short-term management of anxiety, agitation, and sedation. It is not recommended for chronic use. Lorazepam is primarily used in the preoperative and perioperative periods to reduce anxiety, tension, and drowsiness. It is also used for the treatment of status epilepticus, as a sedative-hypnotic, and for the control of acute agitation in psychiatric patients.

**WARNINGS:** Lorazepam should be used with caution in patients with a history of severe liver disease or hepatic failure. Lorazepam should be used with caution in patients with a history of respiratory depression, including bronchial asthma. Lorazepam should be used with caution in patients with a history of cardiovascular disease, including congestive heart failure, cardiac arrhythmias, or a history of hypertension.

**ADVERSE REACTIONS:** Lorazepam injection is generally well tolerated. The most common adverse reactions are drowsiness, dizziness, and sedation. Other possible reactions include nausea, vomiting, constipation, and urinary retention. Lorazepam injection should be used with caution in patients with a history of urinary retention or constipation.

**DOSE AND ADMINISTRATION:** Lorazepam injection should be administered slowly over a period of 1 to 2 minutes. The initial dose should be 2-4 mg, with a maximum daily dose of 12-16 mg. The dose should be adjusted according to the patient's response and the severity of the condition.

**DRUG INTERACTIONS:** Lorazepam injection should be used with caution in patients taking other sedative-hypnotics, antipsychotics, or other drugs that may cause sedation. Lorazepam injection should be used with caution in patients taking drugs that may interfere with the metabolism of lorazepam, such as cimetidine, diazepam, or other benzodiazepines.

**OVERDOSAGE:** Lorazepam injection should be used with caution in patients with a history of drug or alcohol dependency. Lorazepam injection should be used with caution in patients with a history of respiratory depression, including bronchial asthma. Lorazepam injection should be used with caution in patients with a history of cardiovascular disease, including congestive heart failure, cardiac arrhythmias, or a history of hypertension.

**PREPARATION:** Lorazepam injection should be administered slowly over a period of 1 to 2 minutes. The initial dose should be 2-4 mg, with a maximum daily dose of 12-16 mg. The dose should be adjusted according to the patient's response and the severity of the condition.

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This month Cancer Research extends its cover salute to Dr. Michael B. Shimkin* who has been its Cover Editor for the past 20 years.

Born in Tomsk, Siberia, in 1912, Dr. Shimkin came to San Francisco as a child and in 1937 received the M.D. degree from the University of California. In 1938 he began his distinguished career in cancer research at Harvard University as a Research Fellow of the then newly created National Cancer Institute. From 1947 to 1954 he directed the Laboratory of Experimental Oncology in San Francisco, supported by the University of California and the National Cancer Institute. He then joined the National Cancer Institute in Bethesda as Chief of the Biometry and Epidemiology Branch and, in 1960, became Associate Director for Field Studies. His association with the National Cancer Institute continued until 1963. From 1963 to 1969 he became Chief of Cancer Biology and Professor of Medicine at the Fels Research Institute, Temple University School of Medicine, and then Assistant Vice President for Research at Temple. In 1969, he returned to California to become Coordinator of the Regional Medical Program, Professor of Community Medicine and Oncology, and Associate Dean for Health Manpower, University of California at San Diego, where he is now an Emeritus Professor.

Dr. Shimkin is a Renaissance man in cancer research, having achieved distinction not only in experimental, clinical, and epidemiological studies but also in research administration and the history and philosophy of cancer research. He is a brilliant lecturer and writer for both medical and lay audiences and readers. He has traveled all over the world in connection with international cancer programs and, as an expert on the Soviet Union, has gone to that country many times on scientific missions.

Chemical carcinogenesis was a fledgling field when Dr. Shimkin started his research in it in 1938. He carried out some of the earliest studies on the production of lung tumors in mice by intratracheal doses of polycyclic aromatic hydrocarbons in relation to the effects of age and genetic background. With H. B. Andervont he published an early landmark study of the comparative carcinogenicities of polycyclic aromatic hydrocarbons in the subcutaneous tissue of mice; these and related data were analyzed in detail with W. R. Bryan. During the 1940s he also investigated several aspects of murine mammary carcinogenesis, including the roles of estrogenic substances and the effect of endocrine ablations. Later he investigated the role of endocrine factors in the induction of mammary cancer in the rat with polycyclic aromatic hydrocarbons. One of his major interests has been the induction of lung adenomas in mice as a function of genetic background, carcinogenic stimuli, histopathology, and nongenetic modifying factors.

Dr. Shimkin began his clinical investigations at the Laboratory of Experimental Oncology, University of California-San Francisco. These included early studies on the chemotherapeutic management of lymphoma. During this period he also developed his interest in epidemiological aspects of human cancer. In 1956 he and W. Haenszel analyzed smoking patterns among persons in the United States and showed that they were compatible with the then emerging ideas on smoking as a cause of lung cancer. His epidemiological studies also included analysis of the incidence of lymphomas in the United States, the relationship of schistosomal infection to the development of bladder cancer in middle eastern countries, and factors in the development of breast cancer.

The more than 300 publications by Dr. Shimkin include many important contributions on the history of cancer research. This interest started early in his career. In 1964, he published a seminal work, entitled Science and Cancer, which synthesized for the general public the salient facts about the nature of neoplastic disease and the efforts of science and medicine to control it. Since 1966 he has prepared covers for Cancer Research on many historical aspects of cancer research (see 20-year Cumulative Cover Index, Cancer Res., 45: 6648–6653, 1985). These covers were one of the sources for his book in 1977, entitled "Contrary to Nature," an annotated picture history covering cancer and cancer research from ancient times to the present. In 1981 he published "Some Classics in Experimental Oncology," a reprinting of 50 papers important in the development of experimental cancer research.

Dr. Shimkin has also served the field of cancer research as Editor of the Journal of the National Cancer Institute (1955–1960) and of Cancer Research (1964–1969), and as President of the American Association for Cancer Research in 1973 (see "Upon Man and Beast—Adventures in Cancer Epidemiology: Presidential Address," Cancer Research, 34: 1525–1535, 1974).

The Editors acknowledge with much appreciation the assistance of Dr. James Miller in the preparation of this tribute to Dr. Shimkin.

On this 20th anniversary of our cover themes, we are pleased to have this opportunity to extend our gratitude to Dr. Shimkin for his dedication and invaluable contributions to the journal throughout the years and, in particular, for making the covers of our journal so informative and unique. His broad knowledge of both historical issues and contemporary trends has made Cancer Research covers a distinctive forum for instruction for all members of the cancer research community, but especially for young investigators whose training in their fields depends on a well-informed perspective of the past.

* Photograph of Dr. Shimkin by Ron Mesaros, Topanga, CA.
The Michigan Cancer Foundation (MCF) and Sinai Hospital of Detroit are seeking a clinically-oriented, established investigator to direct a major program in the immunology of cancer. Duties include providing leadership in a clinical oncology service and in the development of a research program. MCF and Sinai Hospital are affiliated with Wayne State University School of Medicine. Send letter of interest and curriculum vitae to:

Dr. Gloria H. Heppner
Michigan Cancer Foundation
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Detroit, MI 48201

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CONCEPTS AND THEORIES
IN CARCINOGENESIS
June 11-13, 1986 - Brugge - Belgium

The Symposium will be a teaching Symposium, aimed at presenting a global as well as critical analysis of current views in the main concepts and theories of carcinogenesis. The possible relevance of this information for studies of human cancer prevention will be stressed. The Symposium is open to all health professionals interested in the understanding of how cancers can arise and how to study their prevention. Active investigators will find there a unique opportunity to have their information updated in fields of carcinogenesis research complementary to their own.

TOPICS: □ Biochemistry of cell proliferation and differentiation □ Normal vs neoplastic tissue behavior □ From the normal cell to cancer: the multistep process □ Tumor / host adaptation - immune mechanisms □ Mechanisms in radiation carcinogenesis □ Mechanisms in chemical carcinogenesis □ Oncogenes □ Viral carcinogenesis □ Genetics and cancer □ Stress, ageing and cancer risk □ Multifactorial aspects in carcinogenesis

FORMAT: Plenary Review Lectures: Each of the topics will be covered by an invited lecture. Poster Session: In addition, a poster session will allow participants to present and discuss current work. Panel Discussion: Recommendations regarding future developments of cancer prevention studies will be discussed at the end of the Symposium.

INFO: ECP - SYMPOSIUM - Dr A.P. MASKENS - Avenue Lambeau, 62 - B-1200 Brussels - Telex: 62173 PRP B

DIRECTOR
The Ohio State University
Cancer Hospital & Research Institute

The Ohio State University invites applications and nominations for the position of Director of The Ohio State University Cancer Hospital and Research Institute. The program will be housed in a 200,000 square foot, 12-story, 160-bed facility to be completed in early 1987. The Director will administer, direct and coordinate all activities of this institute. The Director is responsible for development and execution of a complete cancer program; maintains close working relations with the appropriate departmental chairpersons in all academic matters; is responsible for all medical and research staffing of the facility. The Director reports to the Vice President for Health Services.

Qualifications for this position include an outstanding record of research and scholarly achievement; the candidate should be currently engaged in research. It is preferred that the candidate be an M.D. or M.D./Ph.D. with certification in oncology, if the discipline has certification in the sub specialty. The candidate must qualify for a tenured appointment in one of the academic departments of the university. The candidate should have demonstrated ability in obtaining research and contract funds; be knowledgeable in procedures to attract public and private funds; show clear evidence of national recognition and have demonstrated administrative experience in an academic health center.

Position is available July 1, 1986. Salary is negotiable and commensurate with background and experience. Nominations and letters of application, curriculum vitae, and names, addresses and telephone numbers of 3 references are required. The search committee will begin reading dossiers November 1, 1985 and will continue until a candidate is selected.

The Ohio State University is an equal opportunity/affirmative action employer. Qualified women and minorities are encouraged to apply. Applications and nominations should be addressed to: Arthur G. James, M.D., Chair, Search Committee.

Director, OSU Cancer Hospital & Research Institute
410 W. 10th Avenue
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Columbus, Ohio 43210