ANNOUNCEMENTS

HAEMONETICS RESEARCH INSTITUTE
11TH INTERNATIONAL ADVANCED APHERESIS SEMINAR
Hyatt Regency, Cambridge
Boston, MA USA
April 30–May 1, 1984

For information, contact Janet L. Cumming, Haemonetics Research Institute, 400 Wood Road, Braintree, MA 02184. Telephone: (617) 848-7100 or Telex No. 921 817 Haemonetic Brae.

THE CYTOBIOLOGY OF LEUKAEMIAS AND LYMPHOMAS

An international symposium on The Cytobiology of Leukaemias and Lymphomas will be held in Siena, Italy, May 24–26, 1984, with the main topics Histopathology, Cytology, Cytochemistry, Cytoimmunology, Ultrastructure, Cytogenetics, Cytokinetics, In Vitro Culture Studies, and Mechanisms of Causation and Pathogenesis.

Further information may be obtained from the Scientific Secretaries: Professor D. Quaglino, Istituto di Semeiotica Medica, Universita dell’Aquila, Ospedale G. Mazzini, 64100 Teramo, Italy, or Professor F. G. J. Hayhoe, Department of Haematological Medicine, University of Cambridge Clinical School, Hills Road, Cambridge CB2 2QL, England.

COOLEY’S ANEMIA FOUNDATION, INCORPORATED
Research Grants and Fellowships

The Cooley’s Anemia Foundation, Incorporated, invites applications for research grants up to $25,000 and for fellowships with stipends up to $15,000 in the field of Cooley’s anemia. The deadline for receipt of applications is May 1, 1984. Awards will be made by June 15, 1984, and funding will begin July 1, 1984 for one year with the possibility of renewal for a second year.

For application forms and further information, contact:

Mr. Michael DiFilippo
Executive Director
Cooley’s Anemia Foundation, Incorporated
105 East 22nd Street
Suite 911
New York, NY 10010
Telephone: (212) 598-0911

6TH INTERNATIONAL SYMPOSIUM ON PREVENTION AND DETECTION OF CANCER

Vienna, Austria
November 26–29, 1984

Sponsored by the International Society for Preventive Oncology, World Health Organization, Austrian Cancer Society–Austrian Cancer League, and Association of Clinical Scientists–USA.

The program includes overview lectures, panels, poster sessions, scientific exhibits, and special workshops designed for critical appraisal of current data. Discussions are to concentrate on actions to be taken, and on the implementation of existing knowledge for effective cancer control by primary and secondary prevention. Reports are to present progress in multifactorial etiology of oncogenesis, molecular biology, identification of high risk groups, tumor susceptibility, and clinical and laboratory manifestations of cancer, including tumor markers.
Participants include the clinician, epidemiologist, pathologist, experimental oncologist, immunologist, socioeconomist, educator, and members of the health care team.

Abstracts of presentations are invited by June 15, 1984. Abstracts and program appear in Cancer Detection & Prevention 1984:7(6). Award(s) for outstanding investigation(s) presented by ISPO. The symposium is accredited for 32 CME credit hours. Contact: the International Society for Preventive Oncology, 207 East 85th St., Suite 303, New York, NY 10028, USA. Telephone: 212-534-4991; toll-free in USA, 1 (800) 527-0297; outside Europe, (USA-214)392-3663; in Europe, (AUSTRIA 43-222)52-0544.

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TECHNOLOGICAL INNOVATIONS IN LABORATORY HEMATOLOGY

Chateau Lake Louise
Alberta, Canada
May 30–June 1, 1984

This International Symposium is dedicated to new developments in Hematology Laboratory. Guest faculty who are among the foremost authorities in their field have been invited.

Topics that will be covered are:

- Latest Generation CBC Counters
- 3-Part Differentials
- Automated Differentials
- Clinical Application of Flow Cytometry Systems
- New Directions in Coagulation
- Chromogenic Substrates
- Platelet Function Tests
- Anticoagulant Monitoring
- Role of Computer Systems in Laboratory Hematology

These topics will be discussed in 5 half-day sessions with ample time for discussion. An extensive exhibition relevant to the topics of the Symposium will be held simultaneously.

The Symposium is sponsored by the Foothills Hospital, with acknowledgments to the University of Calgary Faculty of Continuing Education and the Alberta Association of Laboratory Physicians.

Registration fee: $125.00 (not including meals or housing). Further information may be obtained from Dr. Berend Houwen, Chairman Organizing Committee, Foothills Hospital, Room 681D, 1403 29th Street N.W., Calgary, Alberta, Canada T2N 2T9.

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UPDATE IN ONCOLOGY: “TOPICS OF CANCER” SAILING SEMINARS

April 1–7, 1984

A postgraduate educational/sailing course aboard yachts in the US Virgin Islands. Sponsored by the George Washington University Medical Center, Washington, DC. For information, contact Patti Kavanaugh, 2150 Pennsylvania Avenue N.W., Room 406-C, Washington, DC 20037. Telephone: (202) 676-2841.

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CLINICAL HEMATOLOGY AND ONCOLOGY: 1985

Sheraton Harbor Island East Hotel
San Diego, CA
February 18–20, 1985

Sponsored By
Scripps Clinic and Research Foundation
La Jolla, CA

Program Chairman: Ernest Beutler, M.D.—Scripps Clinic and Research Foundation
Faculty

Ernest Beutler, M.D.                   Lawrence A. Harker, M.D.
Dennis A. Carson, M.D.                Alexandra Levine, M.D.
Martin J. Cline, M.D.                 Robert McMillan, M.D.
Lawrence H. Einhorn, M.D.             Samuel Rapaport, M.D.
Mark R. Green, M.D.                   John E. Ultmann, M.D.
Ruth Grobstein, M.D.                  Shobhana Vora, M.D.

Theodore S. Zimmerman, M.D.

Topics

Diagnosis and Treatment of Thromboembolic Disease
Acute Nonlymphocytic Leukemia
Myeloproliferative Disorders
Adjuvant Chemotherapy for Breast Cancer
Monoclonal Antibody Therapy

Registration Fees: $290.00 for the entire course, $110.00 per day, and $90.00 for Residents/Fellows—entire course. “Lunch with the Professor,” scheduled each day, is included in the registration fee.

For additional information, contact Dianne Tissue, Department of Academic Affairs, Box 400S, Scripps Clinic and Research Foundation, 10666 North Torrey Pines Road, La Jolla, CA 92037. Telephone: (619) 457-8556
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<td>10 ml</td>
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<td>145.00</td>
<td>500 ml $4.25 per ml</td>
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<td>100 ml</td>
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ZOVIRAX (acyclovir) selectively stops the virus from replicating and very rarely affects the normal, healthy cell's metabolism. Since the prevention of herpes genitalis infections is presently unattainable, the most effective treatment is early intervention with ZOVIRAX Ointment 5%.

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In its active form, ZOVIRAX is capable of interfering with viral replication by either (1) competitively inhibiting the viral DNA polymerase, or (2) being incorporated into the viral DNA chain and thereby causing chain termination.1 4 (See schematic.) Because virus-specified TK is manyfold more potent in activating acyclovir than is cell-specified TK, acyclovir is highly selective. It inhibits viral replication in infected cells but spares uninfected host cells and their functions.5 6

ZOVIRAX rarely affects normal cell metabolism

As noted above, the key to the effectiveness and safety of ZOVIRAX is the preferential uptake and selective activation of the drug by the virus-infected cell. The virus itself acts as the catalyst in this activation process. Therefore, in the healthy, uninfected cell, ZOVIRAX is virtually nontoxic.

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**Dosage:**

**Primary Treatment:** Zovirax Ointment 5% is contraindicated for patients who develop hypersensitivity or chemical intolerance to the components of the formulation.

**WARNINGS:** Zovirax Ointment 5% is intended for cutaneous use only and should not be used in the eye.

**PRECAUTIONS:**

**General:** The recommended dosage, frequency of applications, and length of treatment should not be exceeded (see DOSAGE AND ADMINISTRATION). There exist no data which demonstrate that the use of Zovirax Ointment 5% will either prevent transmission of infection to other persons or prevent recurrent infections when applied in the absence of signs and symptoms.

**Contraindications:** Zovirax Ointment 5% is contraindicated for patients who develop hypersensitivity or chemical intolerance to the components of the formulation.

**Drug Interactions:** Clinical experience has identified no interactions resulting from topical or systemic administration of other drugs concomitantly with Zovirax Ointment 5%.

**Carcinogenesis, Mutagenesis, Impairment of Fertility:** Acyclovir was tested in lifetime bioassays in rats and mice at single daily doses of 50, 150 and 450 mg/kg/day given by gavage. These studies showed no statistically significant difference in the incidence of benign and malignant tumors produced in drug-treated as compared to control animals, nor did acyclovir induce the occurrence of tumors earlier in drug-treated animals as compared to controls. In 2 in vitro cell transformation assays, used to provide preliminary assessment of potential oncogenicity in advance of these more definitive lifetime bioassays in rodents, conflicting results were obtained. Acyclovir was positive at the highest dose used in one system and the resulting morphologically transformed cells formed tumors when inoculated into immuno-suppressed, syngeneic, weaning mice. Acyclovir was negative in another transformation system.

**No chromosome damage was observed at maximum tolerated parenteral doses of 200 mg/kg acyclovir in rats or Chinese hamsters. Higher doses of 500 and 1000 mg/kg were clastogenic in Chinese hamsters. In addition, no activity was found in a dominant lethal study in mice. In 3 of 13 microbial and mammalian cell assays, no evidence of mutagenicity was observed. In 2 mammalian cell assays (human lymphocytes and L5178Y mouse lymphoma cells in vitro), positive response for mutagenicity and chromosomal damage occurred, but only at concentrations at least 1000 times the plasma levels achieved in man following topical application.

Acyclovir does not impair fertility or reproduction in mice at oral doses up to 450 mg/kg/day or in rats at subcutaneous doses up to 25 mg/kg/day in rabbits given a high dose of acyclovir (50 mg/kg/day, s.c.), there was a statistically significant decrease in implantation efficiency.
How ZOVIRAX® (acyclovir) is activated and works specifically in the infected cell

1) Viral-specific thymidine kinase activates acyclovir

2) Other enzymes continue the conversion of acyclovir to a triphosphate molecule

3) Activated acyclovir competitively inhibits viral DNA polymerase

4) Activated acyclovir can be incorporated into the viral DNA chain thereby stopping viral replication

Pregnancy Teratogenic Effects: Pregnancy Category C. Acyclovir has been shown to cause a statistically significant decrease in implantation efficiency in rabbits, when given at subcutaneous doses providing mean plasma levels of drug 2.2 times those expected from use in patients with normal renal function.

Reproduction studies were not performed in rats. Acyclovir was not teratogenic after subcutaneous administration of up to 50 mg/kg/day during the period of organogenesis in rats and rabbits. Doses up to 45 mg/kg given daily by gavage to mice were not teratogenic. There are, however, no adequate and well-controlled studies in pregnant women. Acyclovir should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers: It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when Zovirax is administered to a nursing woman.

Adverse Reactions: Because ulcerated genital lesions are characteristically tender and sensitive to any contact or manipulation, patients may experience discomfort upon application of ointment. In the controlled clinical trials, mild pain (including transient burning or stinging) was reported by 103 (29.7%) of 364 patients treated with acyclovir and by 115 (31.1%) of 370 patients treated with placebo. Treatment was discontinued in 2 of these patients. Other local reactions among acyclovir-treated patients included pruritus in 15 (4.1%) rash in 6 (1.6%) and vulvitis in 1 (0.3%). Among the placebo-treated patients, pruritus was reported by 17 (4.6%) and rash by 6 (1.6%).

In all studies, there was no significant difference between the drug and placebo group in the rate or type of reported adverse reactions nor were there any differences in abnormal clinical laboratory findings.

Dosage and Administration: Apply sufficient quantity to adequately cover all lesions every 3 hours 6 times per day for 7 days. The dose per application will vary depending upon the total lesion area but should approximate a half-inch ribbon of ointment per 4 square inches of surface area. A finger cot or rubber glove should be used when applying Zovirax to prevent autocontamination of other body sites and transmission of infection to other persons. Therapy should be initiated as early as possible following onset of signs and symptoms.

How Supplied: Zovirax Ointment 5% is supplied in 15 g tubes (NDC 0008-0993-941). Each gram contains 50 mg acyclovir in a polyethylene glycol base. Store at 15°-25°C (59°-77°F) in a dry place.

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