THE CANCER LETTER

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CHEMOPREVENTION CLINICAL TRIALS TO START IN 1982 IF GREENWALD, DRCCA BOARD CAN MOVE FAST ENOUGH

NCI's Div. of Resources, Centers & Community Activities will initiate chemoprevention clinical trials during the 1982 fiscal year, if the division's incoming director, Peter Greenwald, moves quickly enough to establish a chemoprevention staff and develop proposals for concept review by the Board of Scientific Counselors.

DRCCA Acting Director William Terry will leave that position Sept. 1 to resume full time his duties as chief of NCI's intramural immunology program. Greenwald, who heads the New York State Health Dept. Div. of Epidemiology, has been selected by NCI Director Vincent DeVita as DRCCA director. The appointment must be approved by HHS Secretary Richard Schweiker before Greenwald can go to work. He probably will be able to start his new job within a matter of days after the appointment has been made.

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In Brief

USE MORE AD HOC COMMITTEES FOR GRANTS, LOOK AT NUMBER, DISTRIBUTION OF CENTERS: KATTERHAGEN

GALE KATTERHAGEN, member of the National Cancer Advisory Board, suggests that NCI and NCAB consider: (1) making more use of ad hoc committees to review grants. "There is a widening gulf in what is perceived as peer review. Some programs such as nutrition and certain areas of cancer control are examples of where grants have been reviewed by committees with no expertise in those areas. (2) We ought to look hard at some areas such as centers, particularly comprehensive centers. Do we have enough, too many, is the geographic distribution valid? (3) We have difficulty in finding 40,000 patients to enter into clinical trials, out of a pool of 400-500,000. I wonder if our methods are adequate?" . . . **CIS-PLATINUM** low doses have produced objective responses in 11 of 22 patients with squamous cell cancer of the cervix for whom surgery and radiation offered no promise, investigators reported in the Aug. 15 issue of *Cancer.* Of the 11 responding patients, three achieved complete remission. The cooperative study, at Univ. of Mississippi, Univ. of Alabama, UCLA, Wake Forest Univ., and Roswell Park Memorial Institute, concluded that "cis-platinum is clearly an active drug in the therapy of squamous cell carcinoma of the cervix." Authors of the paper were Tate Thigpen, Hugh Shingleton, Howard Homesley, Leo Lagasse, and John Blessing. . . . **GIFTS, PLEDGES** totaling $1.2 million were accepted last week by the Univ. of Texas System Board of Regents to establish two new endowed chairs at M.D. Anderson. One, the Mattie Allen Fair Research Chair, will support research, initially in cancer genetics. The other, the Cicero Brown Chair, will be held in an area of clinical cancer research.

CHEMOPREVENTION CLINICAL TRIALS RECOMMENDATIONS MADE BY BOARD

(Continued from page 1)

Even if Greenwald could start Sept. 1, he would have to move fast to prepare a program for submission to the DRCCA Board, which will meet Oct. 22-23. No grant RFAs or contract RFPs may go out without concept approval by the Board. At the moment, there are no staff members assigned to chemoprevention in the division. Greenwald might get by for a while by taking some DRCCA staff off their present duties, and he might borrow some from other divisions. The long term solution will be to recruit new permanent employees for chemoprevention, but that probably cannot be accomplished before the October Board meeting.

It will be crucial to push through some concept approvals in chemoprevention at that meeting if any significant number of projects is to be started in the 1982 fiscal year. The Board's winter meeting is Jan. 14-15, and that would leave very little time to get the announcements on the street and get proposals in and reviewed in time to be funded with 1982 money.

No definite amount has been earmarked in DRCCA's FY 1982 budget for chemoprevention, but DeVita has said that the program will get whatever it needs and can usefully spend, with clinical trials getting a high priority. Staff estimates have put the figure at $2 million, but that could go up or down depending on the overall NCI appropriation and quality and number of proposals submitted.

Greenwald, who is a member of the division's Board, reported at the last meeting on a chemoprevention workshop sponsored by the Board's Chemoprevention Committee. Board Chairman Stephen Carter heads that committee.

The workshop was held to consider those agents that are potentially available for immediate use in chemoprevention studies—β-carotene, ascorbic acid, α-tocopherol and selenium were considered. In addition, the National Heart, Lung & Blood Institute's experience with large clinical trials was reported and the FDA's perspective on INDs for these agents given.

Greenwald's report:

For each agent, the epidemiology, scientific base for efficacy, toxicity and safety, and clinical efficacy were reviewed. Noted here are highlights and the recommendations for each agent. As the Chemoprevention Committee has not had a chance to review the workshop as a group, some of these comments may be only my personal opinion.

β-Carotene

Forty carbon β-carotene is distinct from 20 carbon retinol (vitamin A). β-carotene in addition to being a retinol precursor has a hormone like action that affects differentiation. Toxicity is also less than retinol, as absorption decreases with larger intakes.

Epidemiologic studies are suggestive of a protective effect against several types of cancer, but inconclusive at present. A key review by Peto et al (*Nature* 290:201-208, March 19, 1981) indicates that 18 of 20 published questionnaire studies reported an inverse association of various cancers with vitamin A, β-carotene rich vegetables, or β-carotene intake. Relative risks were in the order of 1.5 to 2. While there is a consistency in these reports, the limitations of such dietary questionnaires, the use of the same data bases for reports of different cancer sites, the tendency for the literature to select out positive results, and the possibility that greater carotene intake is only a marker for other protective effects of vegetables or avoidance of harmful dietary components (e.g. in meat) should be noted.

Additional epidemiologic data consistent with a protective effect include lower blood retinol levels in cancer patients as compared to controls, and two small studies of blood retinol in stored samples. The latter suggests that persons with higher blood levels had lower cancer risks in later years.

In laboratory animals, β-carotene protects against skin cancer induction by ultraviolet light and perhaps by chemicals. Unlike retinoids, β-carotene studies are scant. Protective effects are claimed but more information is needed for confident interpretation.

β-carotene is thought to be safe, particularly if dose levels are kept below that which causes skin yellowing (e.g. 30 mg on alternate days). Transient gastrointestinal symptoms have been reported and safety of the drug dosage range in pregnancy has not been established.

Recommendations—In making recommendations, workshop participants felt that the question of cancer protection could not be decided without controlled clinical trials, and that waiting for a greater aggregation of indirect evidence might create the dilemma of whether definitive clinical trials would be considered ethical if many people become convinced by the indirect weaker sort of evidence.

Drs. Sporn, Peto and Matthews-Roth made the following recommendations:

1. The consensus is that β-carotene is a safe agent for human administration, with essentially no known significant human toxicity or animal toxicity, at doses that are substantially higher than the 30 mg/-day dose that has been proposed for a human chemoprevention trial.

2. Epidemiology shows a consistent inverse association between human β-carotene intake and cancer risk. As is always the case with observational epidemiological data where the relative risk is not large, the inverse association may be real or may represent an artifact.

3. Some animal studies suggest an anticarcinogenic effect for systemic β-carotene, but the data are

not extensive, and further experimentation is needed.

4. It is well established that β-carotene is an extremely effective agent for quenching singlet oxygen and other activated molecular species that are involved in oxidative damage to biological systems.

5. It is well established that β-carotene is a safe and effective agent for clinical use for ameliorating the symptoms of photosensitivity associated with erythropoietic protoporphyria, by a mechanism that involves quenching of either signlet oxygen and/or free radicals.

6. We therefore recommend that β-carotene be considered for clinical trial for human cancer prevention and urge further expansion of basic research in this area.

Ascorbic Acid

Studies of the potential of vitamins C and E for cancer prevention center on preventing the formation of carcinogenic nitrosamine and nitrosamide compounds from precursor amines or amides in the presence of a nitrosating agent. Ascorbic acid is effective in the aqueous phase and alpha tocopherol in the lipid phase.

Epidemiological studies suggest a benefit of lettuce and other ascorbic acid containing vegetables, which may be specific for the upper gastrointestinal tract. Stomach and esophageal cancers have received the most attention, with pertinent investigations in Colombia, Chile, migrating Japanese, Iran and China. While nitrosamine formation (and its potential inhibition by ascorbic acid) is a plausible mechanism for explaining the high esophageal or stomach cancer incidence in these populations, human carcinogenesis by nitrosamines has not been proven. Additionally, if it does occur, childhood eating patterns, including potential promoting factors such as pickled or highly salted foods, and the development of precursor lesions may be critical. Experimentally, there are convincing animal data in many species. Thus, it is quite possible that ascorbic acid can have a beneficial effect in the long run in preventing upper gastrointestinal tract cancer.

Other actions of ascorbic acid need a basic research buttress.

The safety of ascorbic acid in large doses over long periods of time has been shown in publications on megavitamins and colds. Questions have been raised about gastrointestinal symptoms, renal oxalate stone formation, increased iron absorption and poor tolerance to hypoxic stress. High doses during pregnancy may decrease liver enzymes which metabolize ascorbate, producing a deficiency when the large dose is withdrawn.

Recommendations—Drs. Correa, Mergens, Weisburger and DeCosse made the following recommendations:

1. That the function of these "safe" agents in chemoprevention be regarded as beyond their traditional role as vitamins. For example, in the context of gastrointestinal cancer, it would appear that a dual role could be assigned to the beneficial effect of ascorbic acid: (1) maintenance of organ function; (2) and, the effect of ascorbic acid on chemical and microbial actions which can occur in food and secretions present in the lumen of the gastrointestinal tract.

2. That the application of these agents to prevention of human carcinogenesis will require individualization of agent with tumor. For example, β-carotene and analogs of vitamin A stimulate epithelial differentiation and they may be more useful in the prevention of squamous cancer. Ascorbic acid would be more valuable in the prevention of gastric cancer. β-carotene may be important in the prevention of skin cancer resulting from photosensitivity.

3. That basic investigative and epidemiological work be supported for a better understanding of anticarcinogenic effects of these agents and of the loss of vitamins between food and target tissue. Experimental designs should particularly address the inhibition or reversal of tumor promotion.

4. That cautious human intervention trials be initiated in high risk populations. More than one of these agents may be initiated and a factorial design analysis is preferable. It is not necessary that mechanisms be fully understood before human intervention studies are started although basic studies about mechanisms should be continued. High risk populations should be regarded as varying widely in the intensity and proportion of environmental and genetic contributions to etiology. Hence experimental design must address which kind of cancer, which chemopreventive agent or agents and which conditions will most likely lead to success. It should be recognized that these will be exploratory studies, that there should be no risk to the patient and that results could well affirm the null hypothesis. But it is time to start.

Alpha Tocopherol

Alpha tocopherol is an antioxidant which stabilizes fats, apparently by quenching free radicals. Vegetable oils are the richest dietary sources, and it is abundant in the food supply. It is absorbed with fat via lymph in a process that requires bile. The proportion absorbed decreases with larger intakes. Alpha tocopherol is carried in plasma by nonspecific (low density) β-lipoproteins.

The techniques of thin layer or high pressure liquid chromatography allow ready identification. However, because of interplay of nutrients, prolonged storage is treacherous.

The potential of α-tocopherol for cancer prevention, as with ascorbic acid, is its effectiveness as an antioxidant or nitrosamine blocker. It has been reported to reduce the incidence of dimethylhydrazine-induced colonic tumors in mice.

Little data are available on the descriptive epidemiology of α-tocopherol in relation to cancer occurrence. Reduction of mutagenicity levels of normal human feces by ascorbic acid and α-tocopherol has been demonstrated, and a trial is in progress of their potential for lowering the recurrence rate of colonic polyps (Bruce, Dion et al). There also is a suspected benefit for fibrocystic breast disease (London and Sundaran).

There is no evidence that unusual levels of α-tocopherol are related to any health problem. However, questions about slight raising of plasma cholesterol and prothrombin time, and use during pregnancy should be clarified.

Recommendations—More epidemiological and laboratory research are needed. In view of the safety and potential benefits, inclusion in preventive trials is warranted. Many past claims for medical efficacy of α-tocopherol have not stood the test of controlled experimentation, and may have created an attitude of skepticism for any new potential uses. Dr. Bieri's group will be making further recommendations.

Selenium

Chemical induction of colon cancer in rats can be reduced by addition of selenium to the animals' drinking water. Selenium also can reduce mutagen induced mutation rates in bacterial tests (Jansson et al).

Seafoods and organ meats are rich in selenium. Intake varies in different populations because of soil content and the amount of meat eaten. Blood selenium and the less reliable selenoenzyme glutathione peroxidase activity in red blood cells are assessment methods. Much of the selenium in the body and blood may not be physiologically active (Burk).

High colon, rectal and breast cancer mortality rates in the northeastern United States have been crudely correlated with low soil selenium. Rigorous epidemiological studies of selenium and cancer have not been reported, nor have effects of selenium supplementation on cancer.

Chronic selenosis might result from selenium overdosing through abuse of nutritional supplements. 2400 mg/da may be the lower selenosis level. No more than 350 mg/da could be recommended at this time (Olson).

Recommendations—Dr. Griffin made the following recommendations: It is my opinion that selenium has the most potential for actual chemopreventive trials in humans. Perhaps selenium supplementation could be planned on a specific city or regional basis. I would predict that a significant decrease in the cancer incidence would be apparent within a 5-10 year period. However, implementation of such a plan will require a great deal of study in terms of how much selenium and in what form can be given with absolute safety over extended periods of time. It would be imperative to form an expert evaluation committee. Also, the possibility does exist that important cancer epidemiology figures related to selenium intake may be obtained from studies now in progress within China or other countries. From a recent conversation with Dr. Orville Levander (USDA, Beltsville, Md.), a significant number of people (China, Finland and other countries) are now receiving selenium supplementation.

You had also requested specific areas for research support. Some specific areas are evident from conversations with other members of the "selenium" panel and include:

A. Mechanism(s) of selenium inhibition of carcinogenesis.

B. Stages of carcinogenesis where selenium is most effective.

C. Role of selenium in biological functions other than glutathine peroxidase, i.e., selenium in specific proteins, enzymes, mitochondria, etc.

D. Does exposure to cancer causing agents result in an increased requirement for selenium? If so, the selenium intake and tissue or cellular levels may affect the activation/detoxification of carcinogens, lipidmetabolism with resulting formation and breakdown of H_2O_2 or other peroxides, membrane integrity, heme metabolism, immunological functions and many others.

E. Further confirmation that selenium may enhance DNA repair mechanisms.

F. Establish that selenium may "protect" against radiation effects in tissue culture systems. Dr. Carmia Borek (Columbia Univ.) has indicated that this occurs in her experimental protocols.

G. Further studies involving the effects of selenium in cellular transformation systems as developed by Sachs, Heidelberger, Pienta, DiPaolo and others.

The above list is by no means complete and would require the consensus of many authorities in the fields of carcinogenesis, nutrition, toxicology, etc.

General Comments

1. More epidemiological and laboratory research is needed for all of these agents.

2. A formal gathering and review of data on toxicology and safety should be considered. This should precede clinical trials. This has been done in part by the Food & Drug Administration, and the National Academy of Sciences.

3. Rigorously designed, controlled trials should be judiciously begun for β-carotene, ascorbic acid, α-tocopherol and selenium.

4. These trials should be grant supported. In addition, since larger, perhaps collaborative trials may be needed later, the NCI itself should undertake one or several of these studies. This is crucial to achieve expertness in management of the chemoprevention program over the next decade.

5. The experience of NHLBI should be considered in the design of preventive intervention trials. Case

and control group recruitment, event rates, compliance, statistical power, lag time, response variables, definitions, ethics and organization are among the key methodologic concerns.

6. An IND is needed for a new use of an old drug, including these agents.

NCI REPRIMANDS MDA INVESTIGATORS FOR GIVING DRUGS WITHOUT AN IND

The alleged sins of Marc Straus, Vincent DeVita's failure to make the National Cancer Advisory Board aware of them, and Orrin Hatch's exploitation of the sins and the failure have come to roost in Houston.

Ti Li Loo, the pharmacologist who initiated a study in patients of an experimental drug for which there was no approved IND (*The Cancer Letter,* July 17) has been severely reprimanded by both NCI and his institution, the Univ. of Texas System Cancer Center/M.D. Anderson Hospital & Tumor Institute. Another investigator who collaborated with him has also been reprimanded, and the institution itself has suffered the early termination of an NCI contract.

The recommendations of the NIH committee convened by DeVita to consider the report of the site visit team which investigated the matter became available this week. Recommendations of the committee, concurred in by DeVita and NIH Acting Director Thomas Malone, follow:

- All work under the current contract be terminated except for two ongoing studies which are of high programmatic priority. This work is not anticipated to exceed two months.
- Loo be replaced as principal investigator.
- The government seek reimbursement for funds used to support the unauthorized clinical studies (probably about $4,000).
- Institutional procedures for handling investigational anticancer drugs be modified so that 1) all such studies are under the direction of Gerald Bodey (chief of M.D. Anderson's Chemotherapy Branch); 2) detailed record keeping of receipt and dispensing of investigational anticancer agents be kept by the institution's pharmacy; 3) documents be developed by the university which describe the policies and procedures for the clinical research utilizing investigational drugs, which will ensure compliance in the future with NCI policy and HHS regulations for the protection of human subjects with followup site visits by NCI and the NIH Office of Protection for Research Risks.
- Boh-Seng Yap (the clinician who gave the drug to the patients—Loo is not an M.D. but a PhD pharmacologist) not be granted an FD-1573 (the FDA form which permits a physician to use investigational drugs) for a period of one year. During that period he may use investigational drugs under Bodey's FD-1573. Yap's reinstatement after one year "would be dependent on his activities during the probationary year."
- Loo's infraction be brought to the attention of relevant NIH advisory council or committee should he submit grant or contract proposals during the next two years.
- Loo not be asked to serve on any NIH advisory committees or as a site visitor during that period.

M.D. Anderson had already instituted some of the recommendations and has complied with the rest.

Straus, accused of falsifying data in an Eastern Cooperative Oncology Group study while at Boston Univ. and of administering unauthorized drugs or doses of drugs to patients, was fired by BU. He was hired by New York Medical College and successfully competed for a $300,000 a year, three year program project grant. The only action against him initiated by NCI was forbidding his access to investigational drugs. When the grant, which had been approved in initial review with a priority score of 173, reached the NCAB, DeVita decided not to mention the charges against him, which at that time had not been made public.

Sen. Hatch and some of his committee members, with network TV cameras grinding away, came down hard on DeVita for permitting Straus to be funded in the face of those charges. DeVita's response, that he had felt it would not be appropriate considering that the charges had not been proven and that Straus vigorously denied them, did not impress the senators.

NCI's prompt and severe response to the Loo incident is a message DeVita is sending both to Congress and to all NCI contractors and grantees: The Institute and NIH will deal harshly with any deviations from ethical practices and government regulations. No more being raked over the coals by a congressional committee for not being tough enough.

The actions against Loo and Yap were not as strong as those the Hatch Committee wanted to take against Straus. Both will be permitted to continue to participate in NCI supported research, but only under supervision of others, and Loo is precluded from serving as a principal investigator for two years. The requirement that grant and contract awarding bodies at NIH be informed of his transgression could limit his prospects somewhat.

Factors which helped soften the actions against Loo, Yap and M.D. Anderson included:

—There was no attempt to deceive anyone or hide anything, obviously since the study was submitted for publication (at the AACR meeting last spring).

—Loo had assumed that an IND for the drug (5-methyltetrahydrohomofolate, or MTHHF) existed. "The error therefore appears to be due to inadvertence," the report of the site visit team said. "Dr. Loo assumed on the basis of the time sequence that necessary approvals had been requested and received by March 1980, when this was actually not the case."

—No patients were harmed. The drug was given to

six patients in a radiolabelled study, at doses considerably under that proposed for a phase 1 protocol. (The AACR abstract said four patients received the drug; two others were dropped from the study and not mentioned in the report.)

–Proper informed consent had been obtained in at least five of the six patients. Records for the sixth could not be found.

–It was an isolated incident. The site visit team was unable to find any evidence of any other instance at M.D. Anderson when a study was undertaken prior to approval of an IND application.

The entire incident could be blamed on the long delay between submission by M.D. Anderson to NCI of a protocol for a phase 1 study of MTHHF and approval of the IND by FDA.

Loo had received the drug in 1978 for animal pharmacology studies under the $380,000 a year contract with NCI. Later that year, the phase 1 protocol went to NCI, after approval by M.D. Anderson's institutional review board. It was not approved until December, 1980.

Why the long delay? There were a number of problems with the drug, primarily involving its production and purity. NCI will not approve and pass on to FDA an IND application unless it has an assured supply of the drug, enough at least to complete phase 1 studies.

Loo told the investigators that he had assumed the IND had been approved, as they usually are within a few months after submission.

The contract for animal pharmacology was due to end in July anyway, with recompetition planned under the task order format. NCI had decided, previous to the surfacing of the illegal MTHHF study, to extend the contract for several months while the recompetition was in process. It was the extension which was canceled. M.D. Anderson will not be precluded from competing for a place on the task order list.

3 CONGRESSMEN BACK STRAUS' DEMAND FOR SINGLE PROBE, EVIDENTIARY HEARING

The committee of "Scientists Supporting the Rights of Marc J. Straus, M.D." (*The Cancer Letter*, July 17) has recruited the help of three New York congressmen in its efforts to get HHS to consolidate the FDA and NIH investigations of Straus into one of "scientific peer review."

The three congressmen–Hamilton Fish Jr. and Benjamin Gilman, both Republicans, and Richard Ottinger, a Democrat–wrote HHS Secretary Richard Schweiker:

"Public confidence in clinical scientific research and government oversight of research programs must not be undermined by the absence of speedy investigation and review of allegations of this nature–allegations and charges which have been the subject of broad media coverage and of a Senate hearing, but have yet to be heard by an impartial unitary scientific peer review. The gravity of the charges, with the resulting damage to the professional reputation of Dr. Straus and the integrity of clinical research program procedures in general, make a unitary peer review under the auspices of the department imperative. We urge you to consolidate the FDA and NIH investigations and any hearings planned by these two agencies. One impartial unitary scientific peer review hearing, including experts in oncology, with all relevant documents and testimony presented by all parties involved in the matter, has been requested by Dr. Straus. It is our hope that such a review could lead to a final resolution of this matter."

The NIH probe is headed by William Raub, associate director for extramural research and training, who has said he expects the investigation to be completed by some time in October. NIH is investigating the charge that Straus, when he was principal investigator for the Eastern Cooperative Oncology Group at Boston Univ., falsified data on clinical studies. FDA is investigating charges that patients in Straus' studies received improper doses of drugs.

In a letter to Raub, the committee demanded that the investigation include "full disclosure of relevant documents, and an evidentiary procedure which asks for testimony of his accusers as well. The issues are complex and it will require a full evidentiary proceeding for this case to be resolved fairly. As physicians and scientists, we are adamant that due process not be denied Dr. Straus. An abrogation of Dr. Straus' rights will potentially have a negative impact on the scientific community since any precedents established in resolving this case will impact on any future inquiries of scientific conduct."

The letter to Raub continued, "It is of the utmost importance that this case be resolved as expeditiously and fairly as possible. The damage already inflicted on Dr. Straus has been extreme, and all prior to any findings by any investigatory body. The status of Dr. Straus' current NIH funding was discussed by the U.S. Senate on national television. We are fully aware that Dr. Straus' current grant was funded by the peer review system, based on a meritorious rating. This committee is opposed to any negative action taken against Dr. Straus on the basis of unproved allegations. NIH did not begin its investigation until August 1980, in spite of numerous requests by Dr. Straus from the time allegations were made in 1978, that such a review take place. Dr. Straus should not be penalized for the delay which has occurred in resolving this case. Clearly any delay was through no fault of his. Every scientist must have the right to a fair review of his work and an opportunity for research funding, without prejudice."

NCI CONTRACT AWARDS

Title: Endocrine events at the time of first pregnancy, continuation
Contractor: Emory Univ., $24,937.

Title: Biological characterization studies of animal mammary tumors and human breast cell lines, continuation
Contractor: EG&G Mason Research Institute, $142,213.

NCI ADVISORY GROUP, OTHER CANCER MEETINGS FOR SEPT., OCTOBER, FUTURE

5th Asia Pacific Cancer Conference–Sept. 1-4, Colombo, Sri Lanka. Contact S. Sivayoham, 31 Guildford Crescent, Colombo 7, Sri Lanka.
5th Congress of Radiology–Sept. 2-4, Bratislava, Czechoslovakia. Contact Slovak Medical Society, Mickiewiczova 18/1, 883 22 Bratislava.
International Conference on Malignant Lymphomas–Sept. 2-5, Lugano, Switzerland. Contact F. Cavalli, Serv. Oncologico, Ospedale S. Giovanni, 6500 Bellinzona, Switzerland.
Large Bowel Cancer Review Committee–Sept. 3, Boston Logan Hotel, open 11-11:30 a.m.
Third World Congress on Pain– Sept. 4-11, Edinburgh, Scotland. Contact Center for Ind. Consultancy and Liaison, Edinburgh Univ., 16 George Sq., Edinburgh EH8 9LD, UK.
UICC Clinical Cancer Chemotherapy Course– Sept. 7-11, Colombo, Sri Lanka. Contact S. Sivayoham, Sri Lanka Cancer Society, 37/25 Bullers Lane, Colombo 7, Sri Lanka.
National Cancer Advisory Board Ad Hoc Subcommittee on Nutrition–Sept. 8-9, NIH Bldg 31 Rm 9, 7 p.m. Sept. 8, 8:30 a.m. Sept. 9, open.
Contemporary Issues in Hodgkin's Disease: Biology, Staging & Treatment–Sept. 9-12, San Francisco Hilton Hotel. Contact Lili Zubar, Box 277, University Hospitals, Univ. of Minnesota, Minneapolis 55455.
2nd Annual NCI/EPA/NIOSH Collaborative Workshop: Progress on Joint Environmental & Occupational Cancer Studies–Sept. 9-11, Sheraton Potomac Inn, Rockville, Md., 7 p.m. Sept. 9, 9 a.m. Sept. 10th and 11th.
Bladder Cancer Review Committee–Sept. 14-16, Boston Ramada Inn, open Sept. 14, 8 p.m.-10 p.m., open Sept. 15, 8:30 a.m.-noon.
Soft Tissue Tumor Symposium–Sept. 14-16, New York. Contact Dr. Steven Hajdu, Memorial Sloan-Kettering Cancer Center, 1275 York Ave., New York 10021.
Symposium on Significance of the Non-Involvement of Lymph Nodes in Certain Cancers–Sept. 14-16, Paris. Contact J. Crozemarie, Association pour le Development de la Recherche sur le Cancer, BP3, 94800 Villejuif, France.
Present Status and Future of the Anthracycline Antibiotics in Cancer–Sept. 16-18, New York Univ. Contact Dr. Franco Muggia, NYU Medical Center, 550 First Ave., New York 10016, phone 212-679-3200.
NCI Div. of Cancer Cause & Prevention Board of Scientific Counselors–Sept. 17-18, NIH Bldg 31 Rm 4, 9 a.m. both days, open.
Midwest Cancer Seminar–Sept. 17-19, Madison, Wisc., Concourse Hotel. Sponsored by the Univ. of Wisconsin Clinical Cancer Center. Contact Paul Tracy, MD, Wisconsin Clinical Cancer Center, 1900 Univ. Ave., Madison 53705, phone 608-263-3455. Includes sessions on preventive oncology, new approaches in cancer management, biological response modification, cytotoxic chemotherapy, new concepts in management of bladder cancer, breast cancer, nursing methods for achieving quality of care in oncology, assessment of patient family needs, methods for nursing intervention, techniques to assure continuity of care, and cancer clinical trials update.
Perspectives on Prevention and Treatment of Cancer in the Elderly–Sept. 20-23, Bethesda, Md. Contact Dr. Rosemary Yancik, DRCCA, NCI, Blair Bldg. Rm 632, Bethesda 20205, phone 301-427-8656.
Workshop on Doctor Involvement in Public Education About Cancer–Sept. 20-23, Manchester, UK. Contact R. Davison, Manchester Regional Committee for Cancer Education, Kinnaird Road, Manchester M6O, 9QL, UK.

The Oncology Team: A Diverse But Unified Force– Sept. 21, Fox Chase Cancer Center, Philadelphia. Contact Delaware Valley Chapter, Oncology Nursing Society.
Oral Complications of Cancer Chemotherapy–Sept. 21-22, Baltimore. Contact Univ. of Maryland School of Medicine, 10 S. Pine St., Baltimore 21201.
11th Triennial World Congress of Pathology–Sept. 21-25, Jerusalem. Contact E. Levy, Pathology Dept., Medical Center of the Entral Emek Hospital, Afula, Israel.
Advances in Cancer Chemotherapy–Sept. 21-Oct. 3, Erice, Trapani, Italy. Contact 1st Farmacologia-Cattedra II, Policlinico Feliciuzza, 90127 Palermo, Sicily.
Prostatic Cancer Review Committee–Sept. 23-24, Roswell Park Memorial Institute, open Sept. 24 9 a.m.-adjournment for annual program review.
6th Annual Symposium on Advances in Cancer Treatment Research–Sept. 24-26, Baltimore. Contact Program of Continuing Education, Univ. of Maryland School of Medicine, Baltimore 21201, phone 301-528-3956.
Cancer Research Manpower Review Committee–Sept. 24-25, Bethesda Marriott Hotel, open Sept. 24, 9–10 a.m.
2nd National Seminar on Community Cancer Care–Sept. 25-27, Indianapolis Hyatt Regency Hotel. Contact Office of Continuing Medical Education, Methodist Hospital of Indiana, 1604 N. Capital Ave., Indianapolis 46204.
Progress of Cancer Control 1981: Issues in Screening & Cancer Communications–Sept. 28-29, Roswell Park Memorial Institute. Contact Dr. Curtis Mettlin, RPMI, 666 Elm St., Buffalo 14263, phone 716-845-4406.
NCI Div. of Cancer Treatment Board of Scientific Counselors–Oct. 1-2, NIH Bldg 31 Rm 10, open 8:30 a.m. both days, closed Oct. 1, 7:30 p.m.-adjournment.
Nutrition & Cancer–Oct. 1-2, sponsored by Roswell Park Memorial Institute and American Cancer Society. Contact Gayle Bersani RN, Cancer Control Coordinator, RPMI, 666 Elm St., Buffalo, N.Y. 14263.
NMR Imaging & Cancer: State of the Art Conference–Oct. 1-3, Winston-Salem, N.C. Contact Dr. Francis Mohoney, Program Director, DCT, NCI, Landow Bldg. Rm. C809, Bethesda, Md. 20205, phone 301-496-9360.
National Cancer Advisory Board Subcommittee on Organ Site Programs–Oct. 4, NIH Bldg 31 (room not yet assigned), 7:30 p.m., open.
National Cancer Advisory Board–Oct. 5-7, NIH Bldg 31 Rm 6, open Oct. 5, 8:30 a.m.–3:15 p.m. and Oct. 7, 9 a.m.-adjournment.
NCAB Subcommittee on Planning & Budget–Oct. 5, NIH Bldg 31 Rm 11A10, 7:30 p.m., open.
International Symposium on Health Effects of Tumor Promotion–Oct. 12-15, Cincinnati. Contact Dr. Michael Pereira, USEPA, Health Effects Research Laboratory, 26 West St. Clair St., Cincinnati, Ohio 45268, phone 513-684-7298.
Clinical Trials Committee–Oct. 13, NIH Bldg 31 Rm 7, open 1–1:30 a.m.
Piedmont Oncology Assn. 2nd Annual Conference–Oct. 14, Winston-Salem, N.C. Cosponsored by the Bowman Gray

School of Medicine Oncology Research Center. Simultaneous sessions for oncology nurses and physicians. Physicians contact Dr. Douglas White, nurses Chery Lane RN, both at the center, 300 S. Hawthorne Rd., Winston-Salem 27103.

Southeastern Cancer Research Assn. 9th Annual Meeting–Oct. 15-16, Washington D.C. Contact Dr. Wayne Criss, SECRA, Howard Univ. Cancer Center, Washington D.C. 20060.

New Drugs in Cancer Therapy–Oct. 15-17, Brussels, symposium sponsored by European Organization for Research on Treatment of Cancer and NCI. Contact Dr. M. Rozencweig or Dr. M. Staquet, EORTC Data Center, Institut Jules Bordet, 1 rue Heger-Bordet, B-1000, Brussels, Belgium.

Cancer Control Grant Review Committee–Oct. 19-20, NIH Bldg 31 Rm 10, open Oct. 19, 8:30-9 a.m.

Small Cell Pulmonary Cancers–Oct. 19, Paris. Contact C. Jacquillat, Hospital St. Louis, 2 Place Dr. Fournier, 75475 Paris Cedex 10, France.

UICC European Regional Smoking Control Workshop–Oct. 19-21, Budapest. Contact K. Lapis 1, Inst. of Path & Exp. Cancer Research, Semmelweis Med. Univ., Ulloi ut 26, Budapest VIII, Hungary 1085.

American Cancer Society Third National Conference–Cancer Nursing–Oct. 19-20, Atlanta Hilton Hotel. Contact ACS, 4 West 35th St., New York 10001.

NCI Div. of Resources, Centers & Community Activities Board of Scientific Counselors–Oct. 22-23, NIH Bldg 31 Rm 10, 8:30 a.m. both days, open.

NCI Div. of Cancer Biology & Diagnosis Board of Scientific Counselors–Oct. 22-23, Bethesda Linden Hill Hotel, 9 a.m. both days, all open.

Cancer Care in the Community Hospital–Oct. 24, Our Lady of Lourdes Hospital, Binghamton, N.Y., 8:30 a.m. New York State Cancer Programs Assn. Annual Scientific Program. Presentations will include an address by Guy Robbins, NYSCPA president and director of cancer control at Memorial Sloan-Kettering Cancer Center; Gale Katterhagen, director of oncology at Tacoma General Hospital and member of the NCAB; Peter Wiernik, director of the Baltimore Cancer Research Center; and Lawrence Burke, of NCI's Div. of Resources, Centers & Community Activities. Contact Richard Horner MD, Imogene Bassett Hospital, Cooperstown, N.Y. 13326, phone 607-547-3336.

Fifth Annual Cancer Symposium–Oct. 26-28, Vacation Village Hotel, San Diego, sponsored by Scripps Memorial Hospital Cancer Center. Also, Cancer Symposium for Nurses & Allied Health Care Professionals, Islandia Hyatt House, San Diego. Contact Nomi Feldman, Cancer Symposium Coordinator, 3770 Tansy, San Diego 92121, phone 714-453-6222.

UICC Conference on Clinical Oncology–Oct. 29-31, Lausanne, Switzerland. Also, Conference on Oncological Nursing. Contact Secretary General, PO Box 248, Lausanne 6, Switzerland.

Current Issues in Pediatric Oncology–Oct. 29-30, Hyatt on Union Square, San Francisco. Legal and ethical aspects of treatment for the child or adolescent with cancer. Contact Margaret Stewart, RN, National Program Chairman, Assn. of Pediatric Oncology Nurses, Illinois Cancer Council, 36 South Wabash Ave., Suite 700, Chicago 60603.

Symposium on Abdominal & Extremity Tumors: Diagnosis and Surgical Management–Oct. 30-31, Chapel Hill, N.C. Sponsored by the Clinical Cancer Education Program and Univ. of North Carolina Cancer Research Center. Contact Pam Upchurch, Cancer Research Center, Box 30, MacNider Bldg., Chapel Hill 27514, phone 919-966-3036.

3rd Annual Symposium on Preventive Oncology: Cancer Prevention & Clinical Practice–Oct. 31-Nov. 1, Sheraton Palace Hotel, San Francisco. Contact Univ. of California (San Francisco) Continuing Education in Health Sciences.

FUTURE MEETINGS

Management of Advanced Cancer–Nov. 12-14, Amarillo. Inaugural Symposium of the Don and Sybil Harrington Cancer Center. Focus on problems of patients with cancers for which there are no effective therapies. Theoretical and practical strategies for managing patients with advanced cancer will be discussed. Cosponsored by the Texas Tech Univ. Health Sciences Center. Contact Janie Brown, Office of the Medical Director, Harrington Cancer Center, 1500 Wallace Blvd., Amarillo 79106, phone 806-353-3571.

Seminar for Support Personnel Caring for Leukemia Patients–Nov. 20, Cornell Medical College. Contact Leukemia Society of America Inc., 215 Lexington Ave., New York 10017,

Tumor Cell Heterogeneity: Biologic & Clinical Implications–Dec. 3-4, Johns Hopkins Medical Institutions, Baltimore. Fourth Annual Bristol-Myers Symposium on Cancer Research. U.S. and foregin investigators will review observations leading to the conclusion that cellular heterogeneity is a common characteristic of many cancers. Genetic and epigenetic mechanisms likely responsible for the changing cellular composition of tumors will be discussed. No registration fee, but attendance will be limited. Contact Mrs. Ellie Trowbridge, Symposium Coordinator, Rm 169, Johns Hopkins Oncology Center, 600 N. Wolfe St., Baltimore 21205, phone 301-955-2583.

International Conference on the Modulation and Mediation of Cancer By Vitamins–Feb. 23-26, Arizona Health Sciences Center Auditorium. Sponsored by the Univ. of Arizona Cancer Center. Program will include sessions on general mechanisms, carcinogenesis, biological modification of tumor cells, and clinical studies. Contact Mary Humphrey, Univ. of Arizona Cancer Center, Tucson 85724. Abstracts are welcomed, with a Nov. 1 deadline. Contact Mary Humphrey for abstract forms.

RFP NCI-CP-FS-11030-63

Title: *Support services for a study of cancer following 131-1 therapy for hyperthyroidism*

The announcement of this RFP appeared in ***The Cancer Letter*** July 31. The deadline for submission of proposals has been extended from Sept. 3 to Sept. 10. Also, the requirement that the contractor must have or be willing to establish an operational office within 35 miles of the NIH campus has been deleted.

RFP N01-CP-11021-76

Title: *Preparation of antisera to oncogenic or potentially oncogenic viruses*

The announcement of this RFP appeared in ***The Cancer Letter*** Aug. 7. The deadline for submission of proposals has been extended from approximately Sept. 18 to approximately Oct. 2.

The Cancer Letter _Editor Jerry D. Boyd

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