THE CANCER LETTER
RESEARCH EDUCATION CONTROL

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NUTRITION PROGRAM STARTS TO ZERO IN ON MASS OF DATA, PLAN CONTRACT AND GRANT PROJECT AREAS

One of the paradoxes in the fledgling Diet, Nutrition & Cancer Program is that (1) vast areas of ignorance exist along the entire range of human dietary problems, especially in relation to cancer, although (2) a great deal of information on those subjects has been accumulated. Key tasks in the program as NCI gears up to spend $5 million a year on it are to sort out the respective areas of ignorance and knowledge, attempt to correlate what is known with problems of cancer etiology and treatment, and determine which areas of the unknown should be explored through research grants and contracts.

The Diet, Nutrition & Cancer Program Advisory Committee met for the first time last week and spent two days in an effort to get started on

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In Brief

NO MORE SHIFTS PLANNED FOR TREATMENT PROGRAMS; GROUPS SEEK SURGEON, RADIOLOGIST INCENTIVES

MORE ON NCI reorganization of treatment programs: There will be no more major shifts, at least for now. Director Frank Rauscher feels there should be better coordination between Div. of Cancer Treatment activities and those treatment programs funded with grants still administered by the Div. of Research Resources & Centers. But the major problems with lack of coordination involved the Cooperative Groups, moved from DRR&C to DCT, and previous move from the Div. of Cancer Biology & Diagnosis of intramural clinical activities and the surgery and radiotherapy programs to DCT. There were suggestions that DCB&D's immunotherapy program also go to DCT, but that would have split immunotherapy from the rest of the extensive immunology program, which would not have made much sense. . . . **BIG PROBLEM** in moving Cooperative Groups into multimodality studies will be providing incentives for surgeons and radiotherapists to participate. Physicians were attracted into the Groups because NCI supplied the drugs at no charge. "We'll have to find out what surgeons and radiotherapists need to interest them in the Cooperative Groups," an NCI executive said. Any suggestions? . . . **MEETINGS:** The American Roentgen Ray Society will meet at the Atlanta Marriott Sept. 30-Oct. 3 to hear about new brain scanners and total body scanners. The Society for Pediatric Radiology will meet at the same place Sept. 29. The American Society of Therapeutic Radiologists meets in San Francisco Oct. 9-12 in the Hyatt Regency. The Third International Symposium on Detection & Prevention of Cancer is scheduled for New York City next April 26-May 1. . . . **DON'T OVERLOOK** new NIH review deadlines for grant applications. Review cycles have been changed to coincide with change in the federal fiscal year, to start Oct. 1, 1976. Write to NIH for a copy of the revised review schedule.

WORKSHOPS WILL DEVELOP NUTRITION RFPs, POSSIBLE CREG PROJECT AREAS

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those tasks. After listening to reports on studies ranging from diets of primitive man to the effects of intravenous hyperalimentation on cancer patients, the committee approved proposals for a series of workshops which will lead to development of contract RFPs and possibly cancer research emphasis grant (CREG) projects.

Ten workshops are planned on:

* Anthropology and the definition of natural diet patterns in man.
* Comparative studies in man and animals to define evolutionary patterns of dietary adaptation. Selection of animal models for laboratory studies relevant to man.
* Priorities for acute and chronic studies of dietary alterations in animals that may yield clues in dietary carcinogenesis.
* Priorities for subchronic studies of dietary alterations in man that may yield clues in dietary carcinogenesis.
* Dietary surveys in relation to cancer incidence in man.
* Priorities in the study of host-tumor competition for nutrients, as related to therapy goals.
* Alteration of taste and smell perception in the cancer patient. Modification of receptors and of food characteristics to restore appetite. Definition of basic studies and of clinical trials.
* Behavioral approaches to hyperalimentation in the cancer patient. Definition of basic studies and clinical trials.
* Artificial alimentation. Methods and hardware—formulation of nutrient media. Definition of basic studies and clinical trials.
* Hyperalimentation in specific therapy approaches—chemotherapy, surgery, radiotherapy.

Gio Gori, deputy director of NCI's Div. of Cancer Cause & Prevention who also is DNCP director, brought to the meeting a list of proposed topics for CREG. However, he did not ask the committee for approval of the list, and agreed that they would be reformulated by the workshops. Some of the topics could wind up as contracts instead of in CREG, Gori said. The topics were:

+ Comparative studies to clarify the evolutionary pressures leading to adaptations of dietary, anatomic, digestive and metabolic features in higher animal species. The understanding of this relationship should aim at understanding the natural dietary requirements of man, based on his anatomic, digestive and metabolic features.
+ Studies of the mechanism and results of experimental dietary alterations (proteins, carbohydrates, lipids, fiber, vitamins, minerals, etc.) on physiologic changes—cellular physiology and growth, intestinal flora and metabolites, digestive secretions, hormones, obesity, etc. – that may lead to cancer or that may alert susceptibility or resistance to carcinogenic insults.
+ Metabolic studies of diet alteration in man.
+ Dietary surveys in man in relation to the epidemiology of cancer incidence.
+ Studies of tumor-host competition for available nutrients, with particular regard to therapeutic regimens.
+ Physiology of taste and smell alteration in cancer patients, and approaches to restore normal sensory function by modification of sensory receptors or by modification of food.
+ Alteration of feeding behavior in cancer patients with normal taste and smell perception. Means to restore normal feeding behavior other than through sensory intervention.

Committee members thought that Gori was going to give them an opportunity to make changes, additions and deletions to his workshop list, but they discovered otherwise. Noting that the agenda had only 30 minutes for discussion of the workshops at the end of the meeting, the committee extended that by an hour. But when some members started picking over the recommendations word by word, Gori objected.

"We could be here the rest of the week arguing semantics," Gori said. "I merely submitted this list for your information, and to get your concurrence on going ahead with the workshops. We can expand them or change them as we go along."

"In other words, you just want our blessing to proceed, with these as a guide, and we can send our suggestions to you," a committee member said. Gori agreed.

Gori similarly squelched an effort by committee member William Darby, president of the Nutrition Foundation, to revamp Gori's proposal for distribution of the $5 million earmarked in NCI's 1976 budget for the program.

Gori had proposed that etiology and therapy each have 45% of the budget, with 10% for general support. Darby suggested that the quickest payoff will come in therapy and asked that part of the etiology money be switched to therapy. Gori again demurred, saying that the proposal was very tentative and that no one could determine how funds would be spent until the workshops are completed and contract and grant projects developed.

Under etiology, Gori's proposed distribution would give 10% to normal diet definition, 10% to diet alteration in animals, 5% to diet alteration in man and 20% to epidemiological studies.

Under therapy, he had 10% for basic studies in host/tumor competition for nutrients; 15% for physiopathology of taste and smell modification including behavioral, pharmacologic and food technology remedial approaches; and 20% for hyperalimentation methods, nutrient media and hardware.

General support would include literature surveys, publications and program logistics.

Darby's suggestion that etiology be cut back in favor of therapy drew a sharp reaction from committee member Ernst Wynder, president of the American Health Foundation.

"Prevention is the only way we can make a major impact on survival," Wynder said. He referred to diet studies that show arteriosclerosis "is not an inevitable consequence of aging. Likewise, I believe that cancer is not an inevitable consequence of being born or of aging. In colon cancer, we're talking about 100,000 cases a year. Diet is closely related to colon cancer. As interesting as therpy is, it will not make a major inroad on cancer."

Committee member Stanley Dudrick, Univ. of Texas, suggested that it is too late to prevent cancers that have already started but will not surface for 10 to 20 years. "We have to do something for those people."

"I'll buy that," Wynder said. "But therapy has never wiped out a disease."

Wynder and Darby had clashed earlier when Darby appealed for the committee to go slow in reaching conclusions on relationship of dietary factors with cancer.

"The sources of our food supplies are enormous," Darby said. "Use of agricultural chemicals varies enormously. The growing of animals varies with geography. We are dealing with causes that lie in the remote past. And the potential period of exposure can be 20 to 30 years. We must avoid premature 'Ahas!' We need to look at the entire picture of diet and dietary components before making any recommendations.

Wynder objected. That approach, he said, indicates "we don't want to do anything other than satisfy our intellectual curiosity. From a public health standpoint, if we turn up any significant suspicions, we must take a stand. We'll never unravel all the aspects of this problem, so we'll never take a stand if we take Dr. Darby's statement literally."

Wynder reported to the committee on a variety of epidemiological studies which he said have convinced him that more than half of all cancers are related to nutrition factors. Occupationally-caused tumors are probably no more than 1% of the total, he said; "tobacco is responsible for 40% of cancers in males. Most of the rest are related to nutrition."

The differences in colon, stomach, breast, kidney, pancreas and bladder cancer rates between Japan and the U.S. have to be attributed to dietary differences, a factor especially pointed up by the fact that Japanese migrants to this country by the second generation experience rates similar to the rest of the U.S.

Wynder said cancer rates in Puerto Rico are quite similar to those in Japan. Puerto Rican migrants to the mainland, like the Japanese migrants, also soon pick up the U.S. pattern. He suggested that diet studies in Puerto Rico could supplement those in Japan in helping to pin down the differences responsible for the rate differentials.

Other studies which show positive evidence of dietary relationship to cancer etiology include those of the Jewish population in New York City, Seventh Day Adventists in California, and the population of Utah.

Wynder was not optimistic about the success of investigators in trying to determine the dietary history of cancer patients in the U.S. "You try to take a diet history of a patient here and you'll find he can't remember what he ate yesterday," Wynder said. "I don't want to know what he ate yesterday, but what he ate 10 or 20 years ago." That problem may not be so difficult in Japan and other countries where diets do not vary so greatly, he said.

There are three major dietary factors in relation to cancer, Wynder said— food contaminants, which he said is the least important; specific nutritional deficiencies or imbalances; and specific nutritional excesses or imbalances, which he said is the most important.

Alcolhol consumption has a definite relationship to several cancers, Wynder said, mentioning cancer of the esophagus, larynx and mouth. The high risk drinker is one who consumes seven shots a day and is a smoker, Wynder said.

Wynder discussed the relationship to cancer of fat consumption. "We don't know if the decrease in stomach cancer incidence in the U.S. is due to the increase in fat consumption or to the use of refrigerators in most homes, or to other food developments." He cited a number of suspected associates—fat and/or cholesterol in cancers of the colon, pancreas, kidney and bladder; endocrine relationships to cancer of the breast, prostate and ovary; and carbohydrates in gastric cancers.

"Leukemia is also strongly related to dietary factors, and someone ought to look at the epidemiology of leukemia," Wynder said.

Studies have shown no correlation of colon cancer to constipation, transit time of food through the body or cholesterol levels, Wynder said. He mentioned an animal study "in which we removed the ovaries and fed a normal diet and got no breast cancer. We removed the ovaries and fed a low-fat diet and got no breast cancer. We removed the ovaries and fed a high fat diet and got breast cancer." It made no difference in the high fat diet between those that received lard and those that got corn oil, he said.

"What should we suggest as the prudent diet at least for our own families, if not to the country?" Wynder asked, and then answered—reduce the total calories, reduce the calories from fat, and reduce the cholesterol intake.

S.D. Morrison, of NCI's Div. of Cancer Biology & Diagnosis, discussed host/tumor competition for nutrients. Noting that about two-thirds of those who die of cancer are cachectic at death, he referred to the controversy on the extent to which the wasting is

due to reduced food intake, increased metabolic rate of the host, or preemption of available nutrients by the tumor.

He said there is no convincing evidence in animals of a raised total metabolism of the host. In some human studies, increased total metabolism in the absence of fever has been reported, but there are methodological problems in these studies. There is no question but that the tumor represents a drain, but even with a large tumor the energetic drain is small relative to the cost of the host. Nitrogen drain can be quite large but not so large that it could not be adequately met if food intake were maintained.

In general, Morrison said, the competition for nutrients between host and tumor, in which the host ends up with the short end of the stick, occurs predominantly because of reduced and falling food intake. If there were no deficit in food intake, there would be no substantial adverse competition. However, there may be some specific nutrients for which there is competition that might not be resolved simply by maintaining intake of a normal diet. Also, there may be some idiotrophic demands by the tumor for specific nutrients, deficit of which would not seriously impair the host. That is, the demand of the cancerous organism might be for a significant change in nutrient composition of food as well as for an adequate total intake, either because of specific demands by the tumor or because of change in zone of requirement by the host. There is some evidence, for example, of altered need for zinc, for tryptophan and for vitamin A, and it is possible that failure to meet such altered demands may contribute to the cachexia. However, whether meeting new or altered demands might also restore voluntary food intake is quite obscure. On the other hand, some specific depletions may be more apparent than real. The apparent depletion of sodium is due, at least partly, to retention of sodium by the host, and additional sodium supplementation although increasing bodyweight actively worsens the condition of the host. There are also changes in some blood components that have nutritional relevance, although the changes may not be of nutritional origin, such as hypoalbuminemia and nonparathyroid hypercalcemia.

If it were possible to block or retard or reverse the cachexia (and to the extent that it is now possible to do this as, for example, by parenteral alimentation) is it worth doing? Would it substantially prolong the life of the cancer patient? Morrison asked. When used to improve his condition and reduce his vulnerability to side effects of therapy, would it also accelerate the growth of the tumor and improve its viability and resistance to therapy? This is part of the general notion that the cachexia is an adaptive device of the host to starve the tumor. The notion derives from the early nutritional studies which showed that food restriction generally inhibits tumor growth. It is also, of course, even more effective in depleting the host. The question of whether cachexia modifies the survival time of the cancerous subject has never been explicitly addressed, experimentally. Indirect data indicate that supplying the host with large reserves prior to development of a transplanted tumor does not substantially alter its survival time. The same seems to be true of hyperalimentation, although the nutritional condition of the host until death may be improved by such treatment.

If cachexia is an adaptive response, it seems to be a miserably inefficient one, Morrison said. Similarly, there is little hard information on whether therapy is differentially more or less effective in the cachectic or restored cachectic subject, although the greater vulnerability of the cachectic host to therapy is often asserted. Here it is not really possible to know whether we are robbing Peter to pay Paul. A further reason for reversing the cachexia, if possible, is palliative, and reports from parenteral hyperalimentation indicate that reversal of cachexia is effective in this respect. Rehabilitation after successful therapy does not raise these doubts, but this is a totally different kind of problem in that we are restoring a potentially healthy but debilitated patient with essentially normal feeding responses. Excision or regression of a tumor induces almost immediate cessation of the cachectic process, and, unless depletion has already reached an irreversible stage, voluntary intake rapidly returns to meet metabolic demand.

Dudrick reported on his 10 years of experiments with artificial feeding techniques. "In attempting to apply intravenous hyperalimentation to cancer patients, we initially moved with caution," Dudrick said. "In the first place, sepsis from the catheter seemed a potentially more serious risk because patients with malignancies often have impaired immune mechanisms secondary to radiation therapy or chemotherapy. In the second place, it was feared that intravenous hyperalimentation might in some way stimulate tumor growth. There had been a number of animal studies on the effects of nutrition on tumor growth, and, although the evidence was inconclusive, it was sufficient to indicate circumspection" . . . but "it soon became obvious to us that most of the complications developing after surgery, chemotherapy, or radiotherapy were in part nutritional. As is well known, cancer patients tend to lose weight rapidly as the disease advances, and the loss is aggravated to the extent that appetite and/or gastrointestinal tract function are reduced by therapy.

"In selecting patients for treatment with intravenous feeding, our prime criterion is that the individual, in the judgment of the responsible physician, must be a reasonable candidate for either cure or long-term palliation through surgery, radiation therapy, or chemotherapy. Since we have every expectation that intravenous hyperalimentation, whatever its other effects, will in most cases prolong life considerably, we recognize that to institute it in cases in

which there is no reasonable expectation of response to therapy would simply prolong the patient's suffering. A second criterion is marked malnutrition, which we define as a body weight at least 10% below the patient's optimum, serum albumin below 3.4 gm% and a lymphocyte count 20% or less of normal.

"Thus far, we have treated some 800 patients with a wide variety of oncologic diseases, including tumors of the gonads, colon, small bowel and lung. From the nutritional standpoint, the treatment has been a success. Nearly all of the patients regained the weight they had lost, and, in the rest, the weight loss was either stopped or minimized. From the therapeutic stnadpoint, the results are less clear-cut. In the group undergoing chemotherapy, about 35% have shown a positive response, defined as a reduction in tumor volume of at least 50% for a minimum of 29 days. Although precise comparisons are always difficult in such cases, it is believed that this is somewhat in excess of normal expectation, which might lie in the 25 to 30% range. However, it should be noted that some clinicians have reported responses without intravenous hyperalimentation comparable to those we have observed.

"Perhaps more to the point, there is certainly no evidence that the response rate has been reduced, i.e., that improving nutrition also stimulates tumor growth, as had originally been feared. . . .

"Therapeutic results have been more obvious in several subgroups of the patients in whom intravenous hyperalimentation has made possible certain modifications in treatment," Dudrick continued. "One group consisted of 10 individuals suffering from metastatic carcinoma of the colon. All were malnourished by our standards and were therefore given intravenous feeding for 7 days before treatment with 5-fluorouracil (5-FU). Initially, we were quite concerned that intravenous hyperalimentation might abolish the GI signs of 5-FU toxicity, which are normally the first to appear, leaving as the only guide to dosage the fall in white cells which is potentially much more serious. However, the first symptoms of toxicity were still diarrhea and stomatitis, but they were usually extremely mild, resolving within 24 hours after the 5-FU was discontinued. The drug was given intravenously in doses of 15 mg per kg of body weight per day, diluted in 50 ml of 5% dextrose solution and administered as a 1-hour infusion. The dose was repeated until signs of toxicity appeared. By this means, it was possible to give an average of 7 gm of the drug in 8.3 days—large doses for any patient and doubly so for this group, most of whom would have been judged unable to tolerate 5-FU at all without intravenous hyperalimentation. The response to therapy in these 10 patients was 40%, which, although markedly better than normal expectation for patients of this type (perhaps 20%), was still not very impressive in overall terms, because each patient eventually died from his disease and the study group was small. The fact is, however, that 5-FU is not very effective for intestinal tumors, but it is the best drug available for routine clinical use at this time.

"Another innovation in chemotherapy made possible by intravenous hyperalimentation has involved a series of individuals with testicular tumors or squamous cell carcinomas of the lung treated with a combination of chemotherapeutic drugs including vinblastine and bleomycin. As with most chemotherapeutic agents, the perennial problem with these drugs is toxicity, especially of the GI tract, as a result of which the patient loses weight after treatment even more rapidly than he did before treatment. The usual procedure has been to give a course of chemotherapy in the hospital and then send the patient home to recover his weight and strength, a process that often requires a minimum of a month and sometimes as much as eight weeks. The individuals in this group were given intravenous hyperalimentation before treatment and also during and after treatment. As a result, they lost little or no weight and also recovered from their GI symptoms much more quickly. Thus oral feeding could be resumed often in 3 to 5 days after treatment. The hematopoietic side effects by contrast were not minimized by intravenous hyperalimentation. In a sense this is fortunate because if these effects of the drug had been abolished, the tumor response would probably have been abolished as well. Thus, before instituting a second course of treatment, the chemotherapist still has to wait for leukocyte counts to return to normal, but this requires only about two weeks as contrasted to the four to eight weeks the patients previously needed in order to return to a normal nutritional state. The effect has been to permit treatments to be more closely spaced, and it is hoped that the result will be an increase in the tumor response to these drugs.

"As for the threat of sepsis—the basis of our initial reservations with respect to treating cancer patients with indwelling catheters—our experience has been good. The average period of intravenous hyperalimentation has been 26 days and in one case as long as 104 days. We have not changed catheters routinely in the absence of signs of infection but have regularly cultured them on removal. The rate of contamination, chiefly with *Candida albicans* and *Staphyloccocus epidermis,* has been only 2.2%, which is about the same as the incidence in noncancer patients.

"In the course of gaining experience with total parenteral nutrition in cancer patients, interesting and potentially significant observations have been made. For example, there is an impressive reduction in stress ulceration of the stomach and/or duodenum among patients on intravenous hyperalimentation. At M.D. Anderson we and others had observed a rather high rate of stress ulceration in patients undergoing intensive oncologic therapy. With intravenous hyperalimentation, supplemented where necessary with antacids, such ulcers are now almost nonexistent, the

probable reason being the healthier state of the gastroduodenal mucosa.

"The most elusive, and at the same time most fascinating, goal concerns the possible use of dietary therapy in cancer. Is there, one wonders, some special proportion of amino acids, or some modification of certain amino acids, which will nourish the body but starve the tumor? Thus far, neither we nor, so far as we know, anyone else is near an answer. By using intravenous hyperalimentation as a tool, we at least know that if an answer ever emerges, we will possess the means to implement it."

Willaim DeWys, Northwestern, discussed problems in modification of feeding behavior in cancer patients.

"In anorectic cancer patients, it is possible to identify a number of specific problems for which specific therapy may be directed," DeWys said. "Many patients may have abnormalities in taste sensation, and these patients may be benefitted by suggestions for changes in their diet. The complaint of reduced sense of taste or reduced interest in eating may be correlated with an elevation of the taste threshold for sucrose. Patients with this taste abnormality may be able to improve their caloric intake by increasing the seasoning of their food. In patients who complain of a dislike for meat or a sense that meat does not taste well to them, an abnormal lowering of the taste threshold for bitter taste has been observed. For these patients, suggestions as to substitutions of the protein source in their diet may be worthwhile. Patients with this taste abnormality will experience the greatest dislike for beef or pork but may still be able to eat poultry or fish. If the abnormality is more severe they may also develop a dislike for poultry or fish but may still be able to eat cheese and eggs as a protein source. An occasional patient will discover for himself these possible changes in his diet, but most patients require the suggestion of the medical care team in order to make these changes in their diet.

"At some point in the course of their disease, many patients with cancer will have pain, and in a significant number of these patients the pain sensations may interfere with their eating behavior," DeWys noted. "Adequate pain relief with analgesics will result in improvement of their caloric intake, Nausea may be a component of the anorexia of malignancy, and judicious use of antiemetics may have a beneficial effect on the eating behavior of these patients. Many patients will develop a depressive reaction as a response to learning about their diagnosis or observing the adverse effects of their disease, and this will interfere with their eating behavior. Emotional support and antidepressive medications may result in improvement in eating behavior.

"Patients who have experienced some type of mechanical interference with their eating or digestion, such as bowel obstruction, may develop a conditioned aversion to eating. If the patient experiences abdominal pain, nausea, and vomiting after eating he may be conditioned to avoid eating. Even after the obstructive abnormality is corrected surgically, the patient's conditioned aversion may persist and behavioral modification therapy may be necessary to return this patient to a normal eating behavior.

"In addition to those specific problems, it appears that a nonspecific approach to modification of eating behavior may be worthwhile in the cancer patient. This approach is based on the principles of behavioral modification, which include educating the patient as to the importance of improved caloric intake, providing the patient with limited, potentially achievable goals, and measuring and providing feedback to the patient. The goal that we have usually suggested is maintenance of the patient's current weight and activity status. Setting higher goals will result in patient frustration and lack of interest in further following the program. We measure the patient's weight and also make an objective scoring of his performance status and provide feedback to the patient to encourage further efforts.

"The details of the plan for modification of eating behavior include maintenance of a diary of daily food intake and adherence to specific techniques of mealtime and snack eating. The diary of daily food intake serves as a measure of the patient's eating activity and also provides a tool in educating the patient, allowing one to point out the deficiencies in caloric intake. The techniques of mealtime eating which seem important include serving food family style, attempting to increase the caloric content of the foods eaten, and allowing the patient a leisurely pace of eating. Serving the food family style allows the patient to select and choose appropriate portions from the several foods offered. This approach is an important difference between the patient's eating at home and in the hospital, and a significantly better eating behavior has been noted when patients are out of the hospital as compared with hospitalized patients.

"Specific behaviors which may stimulate mealtime and snack eating are also discussed with the patient. It is suggested that the patient have an adequate supply of snack foods in his home and that all leftovers be stored in attractive see-through containers so that the patient has visual stimulae to encourage his eating activity. The patient should be allowed to suggest freely items for the family shopping list and if possible to participate in food shopping. The taking of meals should be associated with pleasant surroundings and activities, and one should vigorously discourage the family from trying to coerce the patient into eating, since this results in an unpleasant mealtime milieu and may further interfere with the patient's eating behavior."

Additional reports presented at the DNCP Advisory Committee meeting and at a previous workshop will appear next week in ***The Cancer Letter.***

NCI ADVISORY GROUP MEETINGS FOR SEPTEMBER

Temporary Committee for the Review of Data on the Carcinogenicity of Cyclamate—Sept. 4, Bldg 31 Room 10, 9 a.m., open all day.
Committee on Cancer Immunobiology—Sept. 4, Bldg 10 Room 4B14, open 2—2:30 p.m.
Cancer Control Intervention Programs Review Committee—Sept. 4, Bldg 31 Room 9, open 8:30—9 a.m.
Workshop for Contractors in the Cervical Cytology Screening Program—Sept. 5, Bldg 31 Room 8, 9 a.m.—5 p.m., all open.
National Cancer Advisory Board Subcommittee on Environmental Carcinogenesis—Sept. 5, Bldg 31 Room 7, 9:30 a.m., all open.
Committee on Cytology Automation—Sept. 8-9, Bldg 31 Room 8, open 9—10 a.m. both days.
Breast Cancer Treatment Committee—Sept. 8-9, Bldg 31 Room 9, open Sept. 8 9 a.m.—5 p.m.
Tobacco Working Group—Sept. 9-10, Bldg 31 Room 6, 9 a.m. both days, all open.
Committee on Cancer Immunodiagnosis—Sept. 9, Bldg 10 Room 4B14, open 1—1:30 p.m.
President's Cancer Panel—Sept. 11, Univ. of Wisconsin (Madison), McArdle Laboratory for Cancer Research, Bowman Room, 10:30 a.m., all open.
Cooperative Group Chairmen—Sept. 16, Bldg 31 Room 11A10, 9 a.m.—5 p.m., all open.
Breast Cancer Diagnosis Committee—Sept. 17, Landow Bldg Room C418, open 9—10:30 a.m.
Cancer Clinical Investigation Review Committee—Sept. 22-24, Bldg 31 Room 6, open Sept. 22 8:30—10:30 a.m., Sept. 23 9 a.m.—12.
Diagnostic Radiology Committee—Sept. 24, Bldg 31 Room 9, open 8:30—10:30 a.m.
Clinical Cancer Education Committee—Sept. 25-26, Bldg 31 Room 5, open Sept. 25 8:30—9:30 a.m.
Committee on Cancer Immunotherapy—Sept. 25, Bldg 10 Room 4B14, open 1—1:30 p.m.
President's Biomedical Research Review Panel—Sept. 29-30, Bldg 31 Room 6, 9 a.m.—5 p.m. both days, all open.
Biometry and Epidemiology Contract Review Committee—Sept. 30-Oct. 1, Landow Bldg Room C418, open Sept. 30 7:30—11 p.m.

RFPs AVAILABLE

Requests for proposal described here pertain to contracts planned for award by the National Cancer Institute, unless otherwise noted. Write to the Contracting Officer or Contract Specialist for copies of the RFP. Some listings will show the phone number of the Contract Specialist, who will respond to questions about the RFP. Contract Sections for the Cause & Prevention and Biology & Diagnosis Divisions are located at: NCI, Landow Bldg. NIH, Bethesda, Md. 20014; for the Treatment and Control Divisions at NCI, Blair Bldg., 8300 Colesville Rd., Silver Spring, Md. 20910. All requests for copies of RFPs should cite the RFP number. The deadline date shown for each listing is the final day for receipt of the completed proposal unless otherwise indicated.

RFP NCI-CB-63927-39

Title: *Development of topical chemotherapeutic agents for mycosis fungoides*
Deadline: *Nov. 4*

NCI is interested in awarding a contract to evaluate existing cancer chemotherapeutic agents for use in the treatment of mycosis fungoides when applied topically. The project will consist of two phases: first, patch testing to determine relative effectiveness of approximately 30 existing cancer drugs on lesions of the disease, and second, clinical trials of the most promising drugs, applied widely and for extended periods, for effectiveness and safety.

Contracting Officer: Harold Simpson
Biology & Diagnosis
301-496-5565

RFP NCI-CB-64000-34

Title: *Studies and investigations on endocrine therapy plus chemotherapy in patients with breast cancer*
Deadline: *Dec. 1*

NCI is interested in establishing a contract with organizations having the capabilities to carry out a research and development program in conducting clinical studies which evaluate combining non-hormonal therapy with endocrine ablative therapy or with hormone additive therapy in patients with advanced breast cancer.

These studies and investigations shall be performed on at least 50 patients per year who are relapsing after treatment of primary breast cancer or whose primary cancer is too extensive for local treatment. NCI will be receptive to collaborative ventures where several institutions combine their patients in a common protocol.

It is desirable that the measurement of estrophilic receptor protein in available cancer tissue be included in the protocol. Organizations should be able to: (1) devise a protocol in which the sequentially or simultaneously combined therapies are utilized in a controlled fashion and (2) provide follow-up data about response to treatment, duration of response, and side-effects of treatment.

Contracting Officer: P.J. Webb
Biology & Diagnosis
301-496-5565

RFP NO1-CP-55731-62

Title: *Animal pathology support*
Deadline: *Oct. 2*

Existing classifications and reporting of spontaneous and experimental tumors in the Carcinogenesis Program are not satisfactory. There is a lack of accuracy and standardization of tumor diagnoses which are important end-points in carcinogenesis studies and, as a result, inadequate input into the Registry of Experimental Cancers. In many cases, the significance to tissue reactions to chemicals and other agents under test and the histogenesis of certain experimental tumors are obscure.

The goal of the Tumor Pathology Section of the Carcinogenesis Program is to develop a highly competent effort which will support the extramural and intramural program activities as follows:

Provide diagnostic pathology criteria, evaluation, standarization and monitoring.

Expand the Registry of Experimental Cancers, and develop definition of tumor types and nomenclature which can serve as a national reference center for animal tumor pathology. Also, develop suitable methods of coding and input of pathology data into the Registry.

Study tumor histogenesis and determine morphologic criteria for the predictability of tumor development in response to carcinogens.

Determine the comparability and relevance of experimentally induced tumors to human cancer.

Provide pathology services to the Carcinogenesis Program in the collection and preparation of animal tissue specimens.

Provide residency experience in comparative tumor pathology particularly as it relates to carcinogenesis.

Task 1 – Diagnostic

The contractor shall, under direction of the project officer:

1. Provide professional and technical pathology support to the carcinogenesis intramural and extramural programs. This includes, as necessary, tissue processing for light and electron microscopy, slide preparation and staining, and histopathologic and electron microscopic diagnoses. The pathologists will serve as consultants to the Tumor Pathology Section and participate, as requested, in advisory panels, workshops, seminars and site visits.

2. Assist, as requested, in pathologic evaluation and presentation of results of Carcinogenesis experiments in the intramural and collaborative programs.

3. Provide technical and professional supportive service to the extent necessary in the event of inadequate pathology capabilities by contractors due to loss of staff, overcommitment, or other difficulty until deficiencies can be corrected.

4. Provide training in gross necropsy and histology procedures to technical personnel as required to improve and support techniques in the contract program.

5. Utilize consultants as needed and at the project officer's request.

Task 2 – Investigative

The contractor shall:

1. Provide investigative and experimental pathology support to the intramural and extramural carcinogenesis programs. This will include interpretation, definition and classifications of tumors and related lesions through the use of special stains, histochemical, electron microscopic studies, transplantation and other procedures as necessary. The pathologists will assist in the selection and coding of lesions for entry into the Registry of Experimental Cancers, serve as consultants to the Tumor Pathology Section and participate, as requested in advisory panels, workshops, seminars and site visits.

2. Evaluate pathology results in various stages of experimentation to gain insight into the histogenesis of relevant lesions. This will include the study of possible preneoplastic lesions and their morphologic and biologic evolution in order to establish more accurate criteria for tumor predictability.

3. Evaluate pathology results from the comparative standpoint to determine the comparability and relevance of experimental tumors and related lesions in various organ systems to human counterparts.

4. Provide pathology experience and training to veterinarians and physicians in comparative and experimental tumor pathology. This will involve seminars, conferences, gross necropsy techniques and interpretation, histopathology and methods of tissue preparation under the supervision of qualified veterinary and medical pathologists. Animals and tissues under evaluation in the NCI Carcinogenesis Program as well as teaching material available at the applicants' institution will be utilized.

5. Utilize consultants as needed and at the project officer's request.

Offerors may respond to the entire workscope or to only one Task. More than one award may result from this RFP.

Under Task 1 – Diagnostic, the estimated level of effort is pathologists, 2 man years; histopathology technicians, 4 man years; appropriate clerical help. Under Task 2 – Investigative, the estimated level of effort is 1 man year each for pathologist, data technician, histopathology technician, pathology resident.

Contract Specialist: Dorothy Sirk
Cause & Prevention
301-496-6361

CONTRACT AWARDS

Title: Evaluation of engineering and biological operations of a NCL cytoscreener

Contractor: Univ. of Utah, $111,521.

Title: Determination of optimal frequency of screening strategies

Contractor: Boston Univ., $234,000.

SOLE SOURCE NEGOTIATIONS

Proposals are listed here for information purposes only. RFPs are not available.

Title: Cell biology facilities and tumor immunology

Contractor: Meloy Laboratories Inc.

The Cancer Newsletter—*Editor* JERRY D. BOYD

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