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FISHER, BONADONNA STUDIES STILL FUEL DEVITA'S OPTIMISM; CARBONE LISTS SIX BASIC RESEARCH NEEDS

When the reports from the Fisher and Bonadonna studies first came in showing dramatic increases in disease free intervals for breast cancer patients who received L-PAM or CMF after surgery, pessimists (or realists) in and out of the two programs warned that results were only

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In Brief

NCI-LITTON NEGOTIATIONS ON FREDERICK CONTINUE; STAFFS NOT WORRIED ABOUT POSSIBLE GAO PROBE

NCI NEGOTIATIONS with Litton Bionetics for renewal of the $25-30 million a year contract for operation of Frederick Cancer Research Center are still going on. The complete proposal is due for final NCI and NIH review early in September. Meanwhile, NCI and Litton staff at Frederick are awaiting possible decision by the Government Accounting Office on whether a full scale investigation by the congressional agency will be conducted. They feel that the intensive peer review and annual audits since the contract was awarded in 1972, plus constant monitoring by two full time NCI contract officers and the NCI scientific staff in residence mean GAO will find few if any of the problems that turned up in the investigation of the Eppley contract. "But if they look hard enough they can always find something," said one staff member. . . . **WATER SHORTAGE** in Maryland communities adjacent to Washington forced NIH to close up last week, which is why most phone calls went unanswered. A fire in the plant that pumps water out of the Potomac reduced the flow to a trickle. NIH and other large installations which use substantial amounts of water were cut off, forcing NIH to close down its air conditioning in the midst of a record heat wave. Only a handful of NCI staff members stuck it out in their sweatbox offices. . . . **MICHAEL SHIMKIN**, professor at the Univ. of California School of Medicine in La Jolla and former NCI executive, has finished writing *Contrary to Nature—A History of Cancer Research from Greco-Romans to Rauscher.* NCI, which financed the work, feels Shimkin has done a superb job. It will be available from the Government Printing Office in a few weeks. Shimkin is also writing a series of articles on the history of NCI. . . . **DAVID BALTIMORE**, Nobel Prize winner, on the "fragility" of basic research: "The fragility comes in with a stationary NCI budget, When a new idea comes along, NCI will have to support it at the expense of something else. The easiest place to go, the most vulnerable target, is basic research." Sidney Salmon, Univ. of Arizona, responded: "Basic research and investigator initiated research are frequently considered synonymous. I'm involved with investigator initiated clinical research, which is equally fragile. The 30% funding (of approved investigator initiated grants) also applies to clinical research."

CARBONE ASKS LAB, CLINICAL SCIENTISTS TO WORK TOGETHER; LISTS RESEARCH NEEDS

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preliminary. "The recurrence curves and ultimately the survival curves may flatten out and we won't see any significant differences," they said.

Others, like James Holland, hailed the studies as a major breakthrough in cancer treatment, and Holland urged that CMF adjuvant therapy be used in general practice, while clinical research with other combinations of drugs and modalities continue.

It seemed at times during the past year that the pessimists were right. After two more years, the recurrence curves did flatten out. In the case of CMF, which in the Bonadonna report of 1975 showed significant improvement in disease free intervals for post as well as premenopausal patients, the results two years later showed almost no difference between the older women receiving adjuvant therapy and those with surgery alone.

Physicians around the country, heeding Holland's advice, have widely used CMF for patients with positive axillary nodes. Has that been a mistake?

Not, according to eternal optimist Vincent DeVita, if it doesn't lock in physicians to CMF when better regimens come along. Moreover, the director of NCI's Div. of Cancer Treatment is convinced that the Fisher and Bonadonna results still offer reason for optimism.

"The Bonadonna results now are very good," DeVita recently told ***The Cancer Letter.*** "The only problem is that he (Gianni Bonadonna) talks about it too much."

He explained that results in various subsets of patients on Bonadonna's study may change from month to month. Bonadonna is in great demand as a speaker at scientific and various public meetings "and it's hard for him to say no," DeVita said. The result is a seeming fluctuation in the results as Bonadonna accurately reports the statistics as they stand at a particular moment. "People tend to focus on one subset, and then on the changes," DeVita said. "But taken together, they are consistent."

The real benefit from improved therapy, of course, is in increased survival. DeVita feels that Bonadonna's postmenopausal patients are just now starting to reach the point where increases in survival will start to show up in the data. "There's no question that there is a significant difference in survival for premenopausal patients," DeVita said.

Bonadonna's postmenopausal patients with four or more positive nodes have shown a significant improvement in the recurrence rate over controls. This has not resulted yet in significant survival improvement, but DeVita is convinced that it will.

Postmenopausal patients with one to three positive nodes have not demonstrated any significant difference yet in recurrence over controls treated with surgery alone.

There is still a "very significant difference" in recurrence when the data on all of Bonadonna's patients, pre and postmenopausal, are pooled, DeVita said.

Bernard Fisher, who heads the National Surgical Adjuvant Breast Project which did the L-PAM study, "doesn't report his data too often," DeVita said, and thus his studies are not subject to the seeming fluctuations that beset Bonadonna's findings.

L-PAM never did show much improvement for older patients, but it did have a striking difference for premenopausal women in disease free intervals. The first reports showed best results for patients with four or more positive nodes; now, better results are turning up for patients with one to three positive nodes, simply because controls with lesser nodal involvement (and presumably less disseminated disease) took longer to recur.

Holland, head of the Dept. of Neoplastic Disease at Mount Sinai Hospital and chairman of the Cancer & Leukemia Cooperative Group, is standing by his earlier advice, published as an editorial in the "New England Journal of Medicine" in February, 1976. He feels the Bonadonna work "was a first class study."

Paul Carbone, former NCI clinical scientist and chairman of the Breast Cancer Task Force Treatment Committee who is now professor and chairman of the Dept. of Human Oncology at Wisconsin Clinical Cancer Center, drew on his experience in breast cancer research in developing a treatise on the relationship of clinical trials and tumor biology. In his Rosenthal Foundation Award lecture delivered at the American Assn. for Cancer Research annual meeting, Carbone suggested six research topics for basic scientists to explore. He called it "a shopping list of important research problems that would be extremely helpful to the clinical investigator in attempting to treat cancer patients." They were:

- Develop methods to determine the metastatic potential of a specific cancer. "The key question is how can we determine the biologic potential of the cancer which appears to be localized in the breast? . . . Is a specific tumor more likely to have widespread metastatic potential or is the tumor destined to be localized? This would involve a detailed study of examination of the tumor itself as well as methods to evaluate effectively host resistance. Measurements of tumor factors or host factors alone may not be enough. A strong host protective potential may overcome a tumor propensity to metastasize."
- The need for information on the apparent "normal" tissue in the same breast that has a cancer. "We need to know the biological behavior of the precancerous lesions in the breast, particularly whether these lesions that we recognize as cancer in situ will develop into overt clinical cancers."

Carbone said that clinical trials now underway by

NSABP in which only the single cancer lump in the breast is removed and the remaining part of the breast is not treated or is treated by high dose radiotherapy may provide some answers. "Cancer of the breast may be multifocal with about 40% of the breasts with one cancer having other cancers or precancerous lesions in the same breast. Thus breast cancer may be a tissue disease and that the inciting carcinogenic factor or factors may persist in the host or give to anomalies that will give rise to other distinct malignancies. The clinical cancer lump may be a biological accident and lesions may have disappeared or new ones appear subsequently. . . . The rate of development of cancers in the same breast or opposite breast will be most interesting to observe (in the NSABP trials). Early ipsilateral failures would be interpretable as inadequate treatment. Late recurrences are highly likely to be new cancers. If the radiated breast does not develop cancer whereas the opposite untreated breast continues to develop second cancers, this would be an indication that the initiating carcinogenic phenomenon occurred early in the patient's life and may not be persisting. Another important lesson from this study is the ability of radiotherapy to control preclinical cancer. Another important aspect of these trials would be the differences in rates of cancer development in the segmental mastectomy group without x-ray treatment as compared to the radiated segmental mastectomy breast. These trials are extremely important biologically and illustrate the back flow in information clinic to lab."

- Develop a better understanding of the role of local lymph nodes in controlling cancer cell growth. "Why do some cancers that have spread to the local lymph nodes appear to remain static or disappear whereas others develop a lethal potential?"

Carbone pointed out that in the trials of radical mastectomy vs. total mastectomy vs. radiotherapy plus total mastectomy, 39% of the patients had histologically proven cancer in the axillary lymph nodes in the radical mastectomy group. Patients randomized to the other two arms came from the same overall mix of patients, and Carbone assumed that the same percentage of axillary node involvement must have been present in those groups. "After four years of followup, the survival of the three groups is comparable. If these figures persist then one could deduce that the impact of local lymph nodes as immunologically beneficial does not exist. Removal of the lymph nodes or sterilization with high dose radiotherapy does not have an adverse effect on survival. Thus attempts in the lab to define the effect of local lymph nodes on containing tumor growth would seem relevant and important."

- "My fourth request for basic scientists would be to study the differences between premenopausal and postmenopausal human breast cancer. We know that the epidemiologic factors relative to age incidence indicates that there is a different slope of incidence (age related) for breast cancer in women less than 50 as compared to women over 50."

Carbone referred to differences found by Bonadonna and Fisher in results with pre and postmenopausal patients. "We know the chemotherapy can effect the hormonal output of the ovaries. On the other hand prophylactic oopherectomy per se does not prolong recurrence in patients with early breast cancer. Are there other effects? Studies by Davis et al in patients receiving adjuvant chemotherapy with L-PAM or a four drug combination CMFV do reveal that levels of circulating estrogens and FSH are affected by chemotherapy in premenopausal patients. In addition, they will report that there is a significant decrease in plasma prolactin response following TRH stimulation. Prolactin appears to be very important in rat tumors. Thus there is an effect of chemotherapy on both pituitary and ovarian function. Is it prolactin or are there other hormonal effects? Moreover in patients with recurrent disease several studies have revealed that chemotherapy combined with oopherectomy results in improved survival and disease free survival.

"The effect in premenopausal patients may be a combined chemotherapy hormone effect. This should suggest that one might combine chemotherapy with hormonal therapy in postmenopausal patients."

Carbone said he feels the value of adjuvant therapy is "not any less likely if the results with L-PAM or CMF turn out to be only temporary. A negative study would indicate that the specific type of systemic therapy tested might be relatively ineffective. One must use systemic therapy along with effective local treatment to improve survival. What is disappointing is that if a relatively potent and toxic treatment like CMF is not effective then chances of finding a more tolerable and effective treatment appear less promising. Possible approaches include use of adriamycin containing combinations or combining chemotherapy with immunotherapy or hormonal treatments."

- Development of better tumor cell markers of cell numbers. "We need to be able to follow more quantitatively the changes in tumor growth rates during treatment and after therapy manuevers. A sensitive indicator of tumor cell number would be extremely important in deciding how intensive the adjunctive therapy should be as well as how long it should be used.

"Research in the treatment of cancer would be immeasurably improved if we could define some biochemical or immunochemical product of tumor cells that correlates with tumor cell numbers. Oncofetalantigens CEA, AFP are helpful but are not specific or universal enough to be the immediate solution. In patients with choriocarcinoma the HCG is a very useful parameter to follow. In patients with multiple myeloma immunoglobulins are practical

nature of the contract was such that it was necessary to make up an ad hoc committee to review it, since none of the existing chartered committees included the necessary expertise.

Solomon pointed out that the proposal was broken up and various parts sent only to those committee members competent to review them; some parts went to only one reviewer. "There were nine standard chartered committees in 1973," Solomon said. "The proposal parts could have been sent to various members of those committees and accomplished the same thing."

What all this meant, Solomon said, "was that NCI deviated from the normal routine."

An ad hoc committee was used again in 1974, but by then the chartered committees had been abolished and NCI was in the process of establishing new ones. "They had no choice except to go to ad hoc committees," Solomon said. "We're not going to make a big point out of that."

The contract is up for renewal this year, and the proposal this time will be reviewed by a fullfledged, chartered committee which has all the disciplines needed.

The contract expired June 30, and NCI extended it to Sept. 30 while the new proposal is being reviewed. Meanwhile, NCI has asked the HEW regional auditor in Kansas City to audit Eppley's accounting system. Also, Congressman David Obey, who initiated the GAO investigation, released a letter last week from NCI informing Eppley that payment of $237,650 for renovation of its animal breeding facility will be withheld until questions raised by GAO have been resolved.

The Cancer Letter report of June 24 noted that GAO did not plan to include in its report any reference to an alleged conflict of interest posed by the fact that Eppley Director Philippe Shubik is a member of the National Cancer Advisory Board and had been chairman of its Subcommittee on Environmental Carcinogenesis. This was an issue first raised by Obey, and in a news release on the GAO findings, Obey contended that GAO intended to point out that "an appearance of a potential conflict of interest" existed.

Obey aide Scott Lilly insisted last week that GAO had verbally informed Obey that the conflict of interest issue would be dealt with in the report. "We only put in our news release what GAO told us," Lilly said.

Solomon told ***The Cancer Letter,*** "As of now, there will be no discussion in the report of an appearance of a conflict of interest. But we are concerned about whether or not Eppley received favorable treatment, whether there was favoritism in awarding the contract."

Members of NIH technical review committees may present more of a conflict of interest than NCAB members, Solomon said. "Virtually all NCI technical indicators of tumor cells, but as yet we are not able to quantitate blood levels with tumor cell numbers in breast cancer. Studies by Tormey and coworkers have examined a variety of tumor markers in patients with breast cancer that appear promising."

- Interdisciplinary research efforts should be continued, enlarged and refined. "Basic research need not be restricted to the laboratory. Good clinical research is good tumor biology. . . . I feel that biological control of cancer growth is an accomplishable feat. As we develop more sensitive indicators of tumor cell numbers, more specific methods of diagnosis, we may be able to appreciate minimal volumes of tumors. Cancers may be diagnosable in a state where only a few thousand cells may be present. These few cells scattered in a 50 or 70 kg adult will not be visible on the x-ray or palpable by the surgeon. We are already able to diagnose lung cancer with cytology and despite intensive searches with fiberoptic encoscopic equipment no primary can be found. Cytocidal chemotherapy may be applied in these clinical situations.

"However, it would be more exciting if we could cause these small malignancies to differentiate and disappear by reverting back to normal end stage non dividing cells. Vitamin A analogues are being contemplated for this use since they can reverse metaplastic epidermoid cells.

"The challenge to both clinicians and basic scientists is to do good research. Hopefully there will be an interchange to the benefit of both. The basic scientists and the clinician working together become a powerful team. . . . Good clinical research is like good laboratory research, asking important basic questions. I feel that together we will prevent or cure cancer. Nothing is gained by interfraternal battling. The problem should not be laboratory or clinical research, but rather good biological research, clinical and laboratory," Carbone concluded.

GAO REPORT TO FOCUS ON "WEAKNESSES" IN EPPLEY AWARD; MORE PROBES COMING

The General Accounting Office report on its investigation of NCI's contract with Eppley Institute will focus on "weaknesses" in the process in which NCI awarded the contract in 1973 and 1974. The report also will include discussion of missing animals, inadequate record keeping on staff time, equipment and supply control, and allegedly unauthorized projects (***The Cancer Letter,*** June 24).

Matt Solomon, who heads the office GAO maintains at NIH, told ***The Cancer Letter*** that the "weaknesses" included the use of an ad hoc committee instead of a chartered committee to review Eppley's contract proposal in 1973; that no guidelines were given to the reviewers on how to designate priorities; that NCI staff had no way to determine how strongly reviewers felt about particular points.

NCI has maintained that the multidisciplinary

review committees have members who have contracts with NCI and whose contracts are reviewed by the committees on which they serve."

Solomon acknowledged that the people most qualified to do cancer research are also those most qualified to review research proposals and said he was not suggesting that the peer review system should be dropped or even substantially modified. "If the system is fraught with conflict of interest or self interest by committee members, obviously some changes would be necessary. We want to make sure that the system works as well as it can."

The draft of GAO's report will go to NCI and Eppley by the end of July, and they will have 30 days to make their comments which will be in the final report which probably will be issued in September.

Meanwhile, Solomon's four-man staff will be kept busy working on new investigations of NCI requested by Congress:

- Henry Waxman (D.-Calif.), a member of the Fountain Intergovernmental Operations Subcommittee which has its own investigation underway, has asked GAO to look at these aspects of NCI's activities—contract administration and whether the Eppley situation is typical; whether the reorganization of the Carcinogenesis Program has been an improvement and does NCI have a problem filling vacancies in the program; how the chemical bioassay backlog was built up, and can NCI be reasonably expected to work it down; and how advisory committees and study groups impact the Carcinogenesis Program.
- Sen. Robert Dole (R.-Kan.) has asked GAO to investigate the programs and functions of the institute, including review of methods used in cancer research, and whether NCI intends to push research in nutrition.
- Obey indicated he may ask GAO to look at other major contracts, probably the Litton Bionetics contract for operation of Frederick Cancer Research Center and the Tracor-JITCO prime contract for carcinogenesis testing.

PROFLAVINE BIOASSAY "INCONCLUSIVE" DUE TO HIGH INCIDENCE IN CONTROLS

Availability of a report on animal tests of proflavine for carcinogenesis was announced by NCI in the *Federal Register* July 12.

The compound was fed to rats and mice for approximately two years. According to a summary of the report included in the announcement, "The observed incidence of hepatocellular carcinoma in female mice was 4/50(8%) in the control group, 20/49 (41%) in the low-dose group, and 22/50 (44%) in the high-dose group. In male mice, the observed incidence of hepatocellular carcinoma was 20/49 (41%) in the control group, 28/49 (57%) in the low-dose group, and 30/50 /60%) in the high-dose group.

"Five malignant neoplasms of the intestinal tract, consisting of three leiomyosarcomas of the small intestine, a sarcoma near the colon area, and an adenocarcinoma of the small intestine were observed in five of the high-dose male rats. None were observed in other treatment or control groups."

Because of the unusually high tumor incidence in control animals and in treated female mice, results are considered inconclusive by NCI.

The tests were part of the Institute's Carcinogenesis Bioassay Program. Copies of the report are available from the Office of Cancer Communications, NCI, Bethesda, Md. 20014.

NEW SACCHARIN STUDIES CONVINCE FDA IT IS A CARCINOGEN; COMMENTS ASKED

The Food & Drug Administration has extended the time for comments on its proposal to ban the use of saccharin as a food additive to Aug. 31 and has specifically asked members of the scientific community for comments on two new epidemiological studies which FDA said support its earlier finding that saccharin is a carcinogen.

One of the two studies "indicates a positive dose and duration related correlation between saccharin use and cancer of the bladder in human males," FDA said. "This potentially significant finding appears to be consistent with the results of the three animal feeding studies which show that saccharin is a carcinogen and on which the commissioner relied in proposing to restrict the use of saccharin in food, drugs and cosmetics."

FDA proposed to permit the sale of saccharin only as an over the counter single ingredient drug. This would permit those who require it for health reasons, such as diabetics, to obtain it. Of course, anyone else can purchase over the counter drugs, non prescription drugs, but FDA reasoned that the consumption would be reduced to a fraction of the present use by forbidding its use in processed foods.

"This proposal was based primarily on three long term animal toxicity studies with saccharin conducted by the Wisconsin Alumni Research Foundation, FDA, and the Health Protection Branch of the government of Canada," FDA said. "These three studies each indicated that saccharin causes cancer of the bladder in laboratory animals. The Canadian study, the most recent of the three, laid to rest speculation that the increase in cancerous tumors noted in the two earlier studies was attributable to an impurity in the saccharin tested, orthotoluenesulfonamide.

"On the basis of these findings, the commissioner concluded that saccharin could not be considered safe for human or animal consumption as a food additive, or as an ingredient in cosmetics; it should not be an ingredient in any drugs for human use unless a persuasive showing could be made that its use was essential, e.g., to make medications intended for diabetics palatable. The commissioner also concluded

that the unequivocal findings from the Canadian carcinogenicity study triggered the application of the Delaney clause of the Food Additives Amendment of 1958, which forbids the approval of any food additive 'if it is found to induce cancer when ingested by man or animal, or if it is found, after tests which are appropriate for the evaluation of the safety of food additives, to induce cancer in man or animal.'

"Since the publication of the commissioner's proposal, a panel of expert scientists assembled by the Office of Technology Assessment (OTA) has examined all of the pertinent data on the safety of saccharin, including the Canadian study. The panel concluded, unanimously, that the Canadian study has been well conducted and its results properly assessed, that it demonstrates unequivocally that saccharin is a carcinogen, albeit perhaps weaker than some other cancer-causing compounds, and that it confirms the results of earlier animal studies. The OTA panel also concluded that the then-reported epidemiological studies of the effect of cancer in humans were not sufficiently sensitive to detect an increase of bladder cancer attributable to saccharin consumption of the magnitude suggested by extrapolation of risk from the animal studies, and therefore did not supply a basis for discounting the risk to humans.

"In recent weeks, the commissioner has been advised about two additional epidemiological studies that relate to the effects of saccharin consumption on humans. One study was directed toward the examination of smoking, occupational exposure and other factors in the epidemiologic pattern of bladder cancer in humans, and incidentally assembled some limited data that have been described as suggesting no positive association between bladder cancer and saccharin use. The other study, a retrospective case-control study that included more than 600 individuals with bladder cancer and a like number of controls, reports a positive dose- and duration-related correlation between saccharin use and bladder cancer in human males. This study in particular has renewed and heightened the commissioner's concern about the safety of long-term saccharin consumption. The commissioner desires to receive comments on and evaluations of the two studies from members of the scientific and medical communities. The commissioner believes that a short additional delay in the issuance of final regulations produced by this notice is required, for several reasons:

"1. The delay will not significantly increase the risk of cancer for any individual who now consumes saccharin. That risk, although a matter for serious concern, appears to be attributable to prolonged consumption of saccharin and to be dose related. During the additional two months required to permit scientific evaluation of the new studies the risk to any saccharin user is not likely to increase measurably.

"2. From the beginning of this administrative proceeding, the commissioner has regarded it as essential that the debate about the correctness of the agency's proposed action and the wisdom of the laws on which it rests be based on reliable scientific evidence, and that all of the data supporting the action be subject to the scrutiny of the scientific community. Thus he welcomed the attentive examination provided by the expert panel of the Office of Technology Assessment. The commissioner believes that the evidence provided by the two new epidemiological studies should be subject to the same kind of external evaluation before it becomes a basis for regulatory action.

"3. The new report of human risk from saccharin consumption raises questions about the advisability of the agency's proposal to permit marketing of saccharin as a single ingredient over-the-counter drug. A further period for comment will permit this issue to be fully addressed in light of the new information.

"4. Finally, the commissioner believes that providing an additional period for the submission of comments and the continuation of discussion of the issue should permit wider public understanding of the new evidence regarding human risk and better appreciation of the propriety of the actions the agency has proposed."

The new Canadian study was coordinated by the Epidemiology Unit of the National Cancer Institute of Canada in cooperation with the Univ. of British Columbia, Dalhouse Univ. of Halifax and Memorial Univ. of St. Johns, Newfoundland.

The second new study was by Ernst Wynder and R. Goldsmith, American Health Foundation. It is scheduled for publication in the September issue of *Cancer.*

In the new Canadian study, data from 480 matched pairs of males showed a bladder cancer risk ratio of 1.6 for users of artificial sweeteners (principally saccharin) vs. nonusers. This means that there is an estimated 60% increase in the risk of bladder cancer in males. The risk ratio of 1.6 is statistically significant.

Wynder and Goldsmith found that 13 of 132 males with bladder cancer used artificial sweeteners as compared with 16 of 124 matched controls and concluded that "no association of bladder cancer with artificial sweetener was found."

FDA tended to discount the Wynder-Goldsmith conclusion because it was primarily concerned with tobacco and occupational exposure and only "incidentally" assembled "limited" data on saccharin.

Comments may be sent to Hearing Clerk, (HFC-20), FDA, Rm 4-65, 5600 Fishers Ln., Rockville, Md. 20857.

Meanwhile, Congress is moving toward imposing a delay in the saccharin ban. The House Health Subcommittee this week approved a bill that would prevent FDA from taking action for 18 months and require the Institute of Medicine of the National Academy of Sciences to assess the evidence against sac-

charin. The Senate Health Subcommittee has already approved a similar bill.

The House bill also would ask the Academy to report on the overall human application of animal tests.

TRAVEL GRANTS AVAILABLE TO U.S. SCIENTISTS FOR UICC CONGRESS IN 1978

The USA National Committee for the International Union Against Cancer (UICC) is sponsoring a travel grant program to benefit U.S. scientists who could not attend the XII International Cancer Congress in Buenos Aires next year without such assistance.

There are two categories of travel awards that will be available.

1. Invited participants of conferences and symposia.
2. Presentors of proffered papers.

The number of grants in category 2 will be limited. Those eligible for awards in category 2 are qualified scientists who are citizens or permanent residents of the United States. Each applicant will be judged on the merit of his contribution to the Congress, considering his training, experience, and potential, as well as a reasonable representation of age groups. The application must be approved by an appropriate official of the applicant's institution.

Final approval of the travel award cannot be made until the USA National Committee receives official verification of the acceptance of the paper by the Cancer Congress program committee.

Both categories of grants will ordinarily be limited to economy roundtrip air fare plus $150. Deadline for receipt of applications is Feb. 1, 1978. Requests for application forms should be addressed to:

USA National Committee for the UICC
Division of Medical Sciences
National Research Council
2101 Constitution Avenue, N.W.
Washington, D.C. 20418.

UPTON HEARS LECTURE ON PROBLEMS HE'LL FACE; DUE TO START JULY 25

Arthur Upton made his first semiofficial appearance as NCI director—"semi" because the White House has yet to officially announce his appointment—this week at the meeting of the President's Cancer Panel.

After Panel Chairman Benno Schmidt spent two hours expounding on the problems he feels the new director will have to tackle, it occurred to some that Upton might decide he didn't want the job after all.

"Yes, I still want it," Upton laughed. "If the job didn't have the challenges those problems represent, it wouldn't be worth having."

Upton is spending two days a week at NCI, until he takes over July 25. At least, July 25 is the target date, but White House spokesmen will not confirm that the appointment will be made by then.

The problems Schmidt covered were the same ones he had mentioned at the Fountain Subcommittee hearings (*The Cancer Letter*, July 1).

CONTRACT AWARDS

Title: Develop and evaluate new methods for obtaining monodisperse and preparations, and to provide vaginal cell samples, continuation
Contractor: State Univ. of New York (Albany), $143,100.

Title: Investigation of a slit scan technique as a basis for an automated pre-screening system for cancer detection in cytology, continuation
Contractor: Univ. of Rochester, $368,741.

Title: Epidemiology of medullary and lobular breast cancer, continuation
Contractor: Memorial Sloan-Kettering Cancer Center, $65,000.

Title: Epidemiologic characteristics of pre- and post-menopausal breast cancer, continuation
Contractor: Duke Univ., $174,800.

Title: Studies and investigations on therapy of patients with stage II and III carcinoma of the breast, continuation
Contractor: Evanston Hospital, $99,900.

Title: A comparative study of xeromammography versus film mammography, continuation
Contractor: Stella & Charles Guttman Institute, $35,612.

Title: Comprehensive cancer center communications network
Contractor: Illinois Cancer Council, $133,500.

Title: Definition of epidemiologic characteristics of pre- and post-menopausal breast cancer, continuation
Contractor: Univ. of California (Berkeley), $81,700.

Title: Combined study of the possible association of dietary factors and non-contraceptive exogenous estrogens with breast cancer, continuation
Contractor: Univ. of Hawaii, $100,000.

Title: Surgery plus systemic treatment of breast cancer, continuation
Contractor: Univ. of Pittsburgh, $499,000.

Title: Investigation of possible correlations between morphological and epidemiological characteristics of breast cancer, continuation
Contractor: Univ. of Texas System Cancer Center, $40,000.

Title: Immunological studies of human breast cancer, continuation
Contractor: Albert Einstein College of Medicine, $110,738.

Title: Studies and investigations on therapy of patients with stage II and III carcinoma of the breast, continuation
Contractor: UCLA, $223,000.

Title: Epidemiological studies in the etiology of cancer in veterans, continuation
Contractor: National Academy of Sciences, $91,945.

Title: Study of oncogenic herpesviruses in primates, continuation
Contractor: Harvard College, $23,627.

Title: Studies to determine viral involvement of feline mammary carcinoma, continuation
Contractor: Sloan-Kettering Institute, $159,100.

Title: Research on transformation of differentiating cells, continuation
Contractor: Univ. of California (Berkeley), $55,000.

Title: Cellular immunity studies to herpes simplex associated antigens, continuation
Contractor: Johns Hopkins Univ., $45,780.

Title: Studies of latent virus infection and transmission, continuation
Contractor: Southwest Foundation, $403,170.

Title: Purification and characterization of viruses, continuation
Contractor: Electro-nucleonics Laboratories Inc., $559,692.

Title: Research on Hodgkins Disease and other malignant lymphomas, continuation
Contractor: Stanford Univ., $972,900.

Title: Operation of holding facility for small laboratory animals, continuation
Contractor: Litton Bionetics, $221,179.

Title: Prototype network demonstration project in head and neck cancer, renewals
Contractors: Univ. of Arkansas Medical Center, $293,559, and Hahnemann Medical College, $196,426.

Title: Demonstration of cancer rehabilitation facilities and/or departments
Contractors: Roswell Park Memorial Institute, $366,837; and Univ. of Pittsburgh, $347,631.

Title: Breast Cancer Detection Demonstration Project, renewals
Contractors: Univ. of Southern California, $371,590; Univ. of Michigan, $379,334; Medical College of Wisconsin, $246,599; and Univ. of Kansas Medical Center, $296,670.

Title: Mammography training program, renewal
Contractor: New York Medical Center, $77,904.

Title: Clinical oncology program
Contractors: Methodist Hospital of Indiana, $282,993; Allentown Hospital Assn., $232,295; and Southwest Texas Methodist Hospital, $237,152.

Title: Specific and non-specific immunotherapy as an adjunct to chemotherapy in skeletal and soft tissue sarcomas
Contractor: UCLA, $167,177.

Title: Immunotherapy of squamous cell carcinoma of the lung treated by resection or radiotherapy
Contractor: Long Island Jewish-Hillside Medical Center, $101,430.

Title: Phase I study of mycobacterium phlei in advanced lung cancer, hypernephroma and malignant melanoma
Contractor: Univ. of Minnesota, $79,596.

Title: Evaluation of immunotherapy with tumor preparations in man (active specific immunotherapy)
Contractor: Sloan-Kettering Institute, $127,845.

Title: Adjuvant tumor specific active immunotherapy of squamous cell carcinoma of the lung
Contractor: Health Research Inc., $114,101.

Title: Studies of immune stimulants in patients receiving radiation therapy
Contractor: Emory Univ., $172,806.

Title: Preparation and distribution of rabbit serum complement
Contractor: Jackson Laboratory, $72,721.

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