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ARTHUR UPTON WILL BE NEW NCI DIRECTOR; COLLEAGUES CONVINCED HE'LL BE STRONG LEADER

The long wait for a new NCI director is nearly over. Arthur Upton, professor of pathology at State Univ. of New York (Stony Brook), is President Carter's choice to head NCI and the National Cancer Program.

The White House had not made the appointment official by *The*

(Continued on page 2)

In Brief

MORE MONEY FOR FEWER GRANTS? OR SPREAD IT AROUND, RHOADS ASKS; AACR TO TAKE STANDS

JONATHAN RHOADS, chairman of the National Cancer Advisory Board, in discussion on the 1978 and 1979 budgets: "Shall we pay grants on an all or none basis? Or pay part (that is, reduce amounts and spread the money over more grants), perhaps determined by priority? If we cut off groups completely, they tend to disband. If we give them partial funding, they can keep part of the groups together. It's amazing how often a group can do all essential parts of a study with less funds than requested" . . . . **LAURENCE ROCKEFELLER**, NCAB member: "How can we do significant research in environmental carcinogenesis when the primary environmental causes of cancer are excessive smoking, drinking, eating—eating too much in general, the wrong things in particular?" . . . **GUY NEWELL**, acting NCI director: "There is a $500,000 reserve (in the 1978 budget) in RO1 (traditional grant) funds for environmental carcinogenesis related grants" . . . . **DENMAN HAMMOND**, NCAB member: "On my campus (Univ. of Southern California) there is a feeling that despite the fact NCI is funding only 30% of approved RO1s, other NIH institutes are funding even less." Newell replied that the overall NIH funding level is 35%, and NCI's is 33%, including competing renewals. . . . **HAROLD AMOS**, NCAB member: "One thing we have to say is that our problem is a dilemma of success. We are achieving what Congress asked us to. If we stop where we are, we won't exploit those successes. We have to demand an extended budget" . . . . **REGIONAL NURSES** conference is scheduled for June 15-16 by the Delaware Cancer Network in Wilmington at the Sheraton Brandywine Inn. Topics are immunology and use of immunotherapy in treatment of cancer. Contact Joanne Tully, senior nurse coordinator, 302-428-2112. . . . **AACR TO TAKE** positions on issues related to cancer and cancer research, AACR President Gordon Zubrod reported at the association's annual business meeting. "The policy committee recommended that the association consider discussion and formulation of statements," Zubrod said. "The board felt that there should be an opportunity at our annual meeting for broad discussion of public issues." Members generally agreed that AACR had a responsibility to develop public discussion of the scientific issues on such topics as recombinant DNA research and laetrile among others.

UPTON CAN MAKE 'TOUGH DECISIONS;' ADVISED CARTER ON NUCLEAR ENERGY

(Continued from page 1)

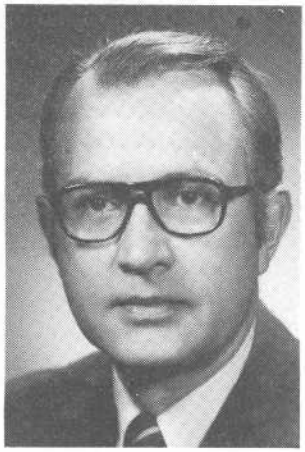
Arthur Upton

Cancer Letter press time this week, but the announcement is expected momentarily.

Upton, 54, is one of the country's leading experimental pathologists, as is his nearest competitor for the NCI directorship, Arnold Brown of the Mayo Clinic. Upton is generally considered the world's leading experimental pathologist in radiation damage and radiation carcinogenesis.

Upton has been a member of the Board of Scientific Counselors for NCI's Div. of Cancer Biology & Diagnosis since 1973 and is the Board's present chairman. One of that Board's primary duties is to review and monitor the research carried on by the division's intramural scientists, a factor which should ease some of the apprehension of NCI staff that an "outsider" at the helm might not have the same rapport with NCI scientists that Frank Rauscher had. Rauscher came up through the ranks as an NCI scientist.

"The people in DCB&D know Upton and respect him," one NCI executive told *The Cancer Letter*. "Those in the other divisions don't know him as well, but they will find him to be a fair and reasonable man."



Arnold Brown

NCI staff members who know Upton agree that he can "make the tough decisions, and can make them stick." He had better, because there will be plenty of them for him to make.

Upton is articulate, poised, and will be able to deal effectively with Congress and the public, his friends believe. "He's not a neophyte in dealing with people in high places," said one. In fact, one of the high places where his advice was sought and given recently was the White House. The President called Upton in to help formulate the policy on nuclear energy, when the decision was made to encourage development of existing systems and delay research on the fast-breeder reactor.

The fact that Upton had met Carter and dealt with him may have influenced the President's decision to select him over Brown.

Positions of leadership held by Upton include president of the American Assn. for Cancer Research, 1963-64; president of the American Society for Experimental Pathology, 1967-68; president of the Radiation Research Society, 1965-66.

Upton was a member of NCI's Carcinogenesis Advisory Panel in 1972-73 and currently serves on the following groups:

Nuclear Energy Policy Study Group of the Ford Foundation; Environmental Protection Agency's Pesticide Policy Advisory Committee; World Health Organization International Agency for Research on Cancer Scientific Council (and current chairman); U.S.-Japan Radiation Effects Research Foundation Scientific Council; National Center for Toxicological Research Scientific Advisory Board; Scientific Advisory Group of the U.S.-Japan Cooperative Cancer Research Program; International Commission on Radiological Protection; Federation of American Societies for Experimental Biology Life Sciences Research Office Advisory Committee; Argonne National Laboratory Advisory Committee for the Center on Human Radiobiology; National Academy of Sciences-National Research Council Committee on the Biological Effects of Ionizing Radiation; Steering Committee of the Los Alamos Meson Physics Facilities; and the National Council for Radiation Protection and Measurements.

Upton received his pathology training in the distinguished Univ. of Michigan pathology department. A native of Ann Arbor, he received his BA and MD degrees there. He went to Oak Ridge National Laboratory in 1951 and was chief of the Pathology-Physiology Section of the Biology Division from 1954-69. His mentor there was Jacob Furth, perhaps the greatest experimental pathologist of his time.

He left Oak Ridge to become professor of pathology and chairman of the department of pathology at Stony Brook in 1969. He was dean of the School of Basic Health Sciences for five years, and gave that up two years ago to return to his work as a professor. Since 1969 he also has been attending pathologist at the Brookhaven National Laboratory Medical Dept.

With all that background in pathology and carcinogenesis, Upton might be considered as one who would be inclined to favor an emphasis on environmental carcinogenesis research. "He certainly will support sound initiatives in that area, but I'm confident he will want a balanced program," one of his colleagues said.

Upton will be appointed to the Public Health Service as a commissioned officer, which with the medical officer stipend will give him a salary of around $52,000, somewhat more than he would receive in the top civilian grade the position carries. He also will receive retirement credits which will be supplemented by credits he earned as an officer in the Air Force reserve for 15 years. He served in the Army from 1943 to 1946.

Both Brown and Upton were recommended to HEW Secretary Joseph Califano by the search committee appointed by Califano to find candidates for the job. Both were considered highly qualified; qualifications aside, the selection of Upton has to be considered a put down for the President's Cancer Panel and its chairman, Benno Schmidt.

The law which created the Panel (the National Cancer Act of 1971) expressly directs the Panel to recommend prospects for NCI director to the President when a vacancy occurs. That authority does not forbid the secretary from seeking other advice, but the fact that he did does not demonstrate a high degree of confidence in the Panel.

The Panel, largely at Schmidt's urging, recommended Brown to President Ford last October when Rauscher announced his resignation. After Ford lost the election, Brown said he didn't want the appointment unless it was cleared with President-elect Carter. This Schmidt attempted to do, without success. Schmidt tried again after the inauguration, and after considerable delay, Califano came up with his request for a search committee to consider other candidates.

Schmidt insisted he never regarded the decision to establish a search committee a put down for himself or the Panel, especially since he was named to the committee. He has assured NCI staff and Cancer Program advocates that he feels he can work with Califano (and the President), has confidence that Califano will support the program and will turn out to be a strong and effective secretary.

SCHMIDT'S INFLUENCE IN FOR ANOTHER TEST; SHINGLETON NOMINATED TO PANEL

Another test of Schmidt's influence with the Democratic Administration is shaping up over the selection of someone to fill the spot on the President's Cancer Panel now held by R. Lee Clark.

Clark, president of the Univ. of Texas System Cancer Center and current president of the American Cancer Society, has been on the Panel since its inception. His term expired in February, however, and Schmidt has recommended the appointment go to William Shingleton, director of the Duke Univ. Comprehensive Cancer Center.

Schmidt, as were all other members of the Panel to date, was an appointee of the Republican Administrations. Although biomedical research is not supposed to be involved with or affected by partisan politics, a body created by Congress to advise the President can't be considered nonpolitical.

Former Presidents Nixon and Ford accepted most of Schmidt's recommendations for appointments to the Panel and the National Cancer Advisory Board. Nixon named Frank Rauscher NCI director in 1972 on Schmidt's recommendation.

The extent of Schmidt's influence and that of the Panel in the present Administration remains a question.

OBEY ATTACKS EPPLEY, SHUBIK, NCI, ASKS FOR COMPLETE GAO REPORT

Congressman David Obey (D.-Wisc.) has unleashed his strongest attack yet on the Univ. of Nebraska's Eppley Institute and its director, Philippe Shubik. After nipping away for more than a year at Eppley with innuendoes and dark hints of misdeeds, Obey this week said, "If what the General Accounting Office has apparently found in reviewing the Eppley contract (with NCI) is an indication of how other contracts and research efforts at the Cancer Institute have been administered, I think the Congress has no choice but to consider a complete overhaul of the institute."

Obey last year asked GAO, the agency that watches over operations of the Executive Branch for Congress, to investigate the Eppley contract. NCI's Div. of Cancer Cause & Prevention contracts with Eppley, presently at a cost of about $3 million a year, for carcinogenesis research and bioassays. David Clayson is the principal investigator, but Obey's target has been Shubik.

Obey said this week that he was "disturbed by both oral reports and copies of official documents" he has received from GAO as a result of its investigation. Among those findings which have been reported orally, Obey said, are:

—"At no time since 1973 has the Eppley contract been awarded or renewed in a manner consistent with HEW or NCI's own guidelines or standard procedures.

—"The Eppley Institute continued to receive ever increasing sums of money from the Cancer Institute despite strongly negative comments by a number of outside reviewers.

—"Efforts by the Cancer Institute to monitor the Eppley contract were lax and in some cases non-existent.

—"Approximately 12 projects were conducted by the Eppley Institute with the use of federal funds which were never contained in a contract nor officially approved by Cancer Institute personnel.

—"The Eppley Institute is closely affiliated with an industrial research facility which performs research on industrial chemicals for major U.S. corporations at the same time the Institute performs research for the government on such chemicals. There have been instances where equipment, test animals and other research materials paid for with federal money have been used in performing tests for corporations without reimbursement to the government.

—"Approximately 50,000 test animals bred under the government contract and valued at approximately $1.75 a piece are unaccounted for (the Eppley Institute contends the animals were destroyed).

—"There has been and continues to be an appearance of a potential conflict of interest in the awarding of the Eppley contract. Dr. Philippe Shubik, director of the Eppley Institute, serves on the National

Cancer Advisory Board which is appointed by the President and oversees the operations of the Cancer Institute. Dr. Shubik serves as well as chairman of the National Cancer Advisory Board's Subcommittee on Environmental Cancer and is therefore the member of the board most directly responsible for overseeing the operations of the division of the Cancer Institute which awards and administers the Eppley contract."

Obey said that he felt that NCI was "already taking steps to rectify some of the shortcomings" found by GAO but that he was "concerned that at least some of the problems found in the awarding and monitoring of the Eppley contract may also be present in other NCI research projects."

Obey said that he would be formally preparing a request for a GAO investigation of at least two other major NCI contractors in the next few weeks.

Obey asked GAO for a full report on the investigation and requested a report" as soon as possible which covers at least the following aspects of the contract with the Eppley Institute:

"1. What actions have been taken by NCI in awarding and monitoring the contract since 1973?

"2. Are contractor controls over the use of funds and property adequate?

"3. Have various personnel matters pertaining to the professional staff at the Eppley Institute been handled in an effective and proper manner?

"4. What work has been done under the contract since 1973 and can its usefulness be determined?

"Comments on the report by NCI and Eppley Institute officials should be solicited and included in the report along with any conclusions or recommendations you may wish to offer."

Here's how the project summary describes the work being done under the contract:

"The NCI carcinogenesis area is committed to scrutinize possible environmental hazards and directs a major part of its programs to this goal. Included is testing in various materials for carcinogenicity, and fundamental studies in carcinogenesis. Selection of compounds for testing is jointly determined by NCI and the Eppley Institute, and testing capacity has been made available from time to time for compounds requiring urgent national attention.

"More fundamental studies are principally related to improving screening and testing methodologies but also include research in mechanisms of action and in the chemistry and pharmacology of metabolized carcinogens and related compounds. The effort continues to provide advanced training in a field in short supply of competent investigators, and is permitting inclusion of several graduate students within the activities of the group."

Gio Gori, DCCP deputy director, is project officer for the contract.

NCI will respond to comments and criticisms in the GAO report and the response will be included in the final report. Whether or not GAO views the alleged shortcomings as Obey does remains to be seen. Obey's criticisms may come up at the hearings scheduled next week by Congressman L.H. Fountain's Government Operations Subcommittee on Intergovernmental Relations (see following article). DCCP Director James Peters will attend that hearing and might have the opportunity to respond to Obey's charges then.

NCI's response to the seven specific charges made by Obey probably will be along the following lines:

- Improper review. NCI insists the review was conducted entirely within the scope of government regulations and according to its own practices. Obey made the point at the appropriations hearings on NCI's budget earlier this year that the Eppley contract was not reviewed in 1973 by a standing committee. Peters tried to explain then that because of the multidisciplinary nature of the contract, it was necessary to put together an ad hoc committee for the review, since no standing committee then was available that was qualified to review it. The ad hoc group did not meet but members reviewed those portions of the proposal which fit their areas of expertise. Reviewers included such highly respected scientists as Norton Nelson of New York Univ. and Bernard Weinstein of Columbia Univ. A standing multidisciplinary review committee has been chartered and will review the contract this year.
- Negative comments by some reviewers. Some reviewers did recommend some cuts totaling from $50-70,000 which did not amount to much out of a $3 million contract. Some reviewers were less enthusiastic about the project than others. But the consensus of the reviewers was to support the proposal. In almost every review of a contract or grant proposal, reviewers will criticize various aspects of it but frequently will end up giving it an overall high priority score.
- Inadequate monitoring. NCI contends that Eppley has been site visited at least as frequently as any other organization with a contract of that size, if not more so. Clayson submits reports at least once a year, and those reports are scrutinized by Gori and his staff.
- Projects conducted by Eppley which were not spelled out in the contract or authorized by NCI staff. NCI feels that research contracts should not limit investigators to specific tasks, that NCI should not try to dictate every move. Flexibility permits scientists to follow new leads that may surface. Two examples of this in the Eppley project led to development of the hamster pancreatic cancer model and the hamster cheekpouch model (which permits investigators to observe tumor blood supply in a living animal).
- Use of resources paid for by NCI in work done at Eppley for industry, and the fact that Eppley tests chemicals for industry that it also tests for NCI. NCI feels that since Clayson's operation is in a facility

physically separated from the one that does work for industry and that since Eppley maintains a tight accounting system for the government contract, prospects for conflict of interest are minimized. If some equipment or animals purchased with government funds are used for the other work, NCI agrees that reimbursement should be made.

• 50,000 test animals unaccounted for. With a breeding program that has produced hundreds of thousands, perhaps millions, of animals, 50,000 that had to be destroyed at one time or another over the period of the contract does not seem excessive. "There's no way you can schedule breeding to have precisely the number of animals you need at precisely the right time," an NCI executive said. All organizations with large bioassay programs have surplus animals, including NIH and NCI's big operation at Frederick Cancer Research Center. Surplus animals at NIH and Frederick are offered first to anyone at NIH, then elsewhere in the government, finally to anyone who can use them. Those not distributed for testing (rats, mice, hamsters usually) are sent to the Patuxent Wildlife Refuge where they are fed to wild game.

• Shubik's conflict of interest as an NCAB member and chairman of the Board's Subcommittee on Environmental Carcinogenesis. At the appropriations hearing, Obey contended that a conflict of interest existed largely because, he said, the subcommittee had oversight responsibility for DCCP, where of course the Eppley contract originated and is administered. Peters tried then to explain that it did not have that responsibility, and that it in fact had a very limited charge from the Board, but apparently Obey was not listening.

The subcommittee was appointed by NCAB Chairman Jonathan Rhoads with Shubik as chairman and charge with two tasks: To develop criteria for assessing the evidence for the carcinogenicity of chemicals, and to develop suggestions for enhancing research on environmental carcinogenesis. At that time, Shubik was the only Board member with a high degree of expertise in the field of carcinogenesis. Other members of the subcommittee were William Baker, Edward Burger Jr., Irving London, and William Powers. The subcommittee employed a number of consultants, all highly respected in environmental carcinogenesis.

The subcommittee worked for nearly a year to develop the criteria, a concise, 10-page document that has become a useful tool for investigators and the regulatory agencies. The subcommittee also made a number of recommendations to the Board, including requests for stepped up funding of environmental carcinogenesis research, establishment of centers for such research, creation of an NIH study section specifically to handle grant proposals in that field, and support for training more epidemiologists.

At no time did the subcommittee attempt to review or develop policy for DCCP, nor did it engage in any review of DCCP intramural operations or exercise any oversight of DCCP activities and personnel.

When Obey pressed Peters on the subcommittee's role in overseeing his division, Peters explained that subcommittee was established with two specific charges. "I do not believe that the degree of their overseeing the direct operations of the Carcinogenesis Program is that great," Peters said.

"Well, nevertheless, it would be helpful for you or anyone else working in that area if you had good relations and good communications with Dr. Shubik, would it not?" Obey insisted.

"With all members of the Board," Peters answered.

Why Obey has singled out Shubik as a target for conflict of interest charges is a mystery. Nearly every scientific member of the Board, the President's Cancer Panel, and the various advisory committees could be subject to such charges. Rhoads is affiliated with the Univ. of Pennsylvania, which has a large number of NCI grants and contracts. Denman Hammond was chairman of the Board's Subcommittee on Centers & Construction, and is director of the Univ. of Southern California-Los Angeles County Comprehensive Cancer Center, recipient of many large NCI grants and contracts. Panel member Paul Marks heads the Cancer Program at Columbia Univ., which is seeking Board and NCI recognition as a comprehensive cancer center. There are many other examples.

NIH and NCI handle the conflict of interest matter by insisting that any member of ad advisory group with an interest in a proposal the group is considering, either directly or through his institution, be absent when that consideration is taking place. Marks, for example, did not attend any part of the Board's meeting last month when Columbia's request for comprehensive status was discussed.

Shubik no longer is chairman of the subcommittee, having been replaced by Henry Pitot of the McArdle Laboratory, affiliated with the Univ. of Wisconsin. Pitot is one of the newer members of the Board with a strong scientific background in environmental carcinogenesis. Others are Bruce Ames, Univ. of California; Gerald Wogan, Massachusetts Institute of Technology, and David Hogness, Stanford.

McArdle's affiliation with the Univ. of Wisconsin is not unlike that of Eppley's with Nebraska. McArdle and the rest of the cancer research complex that make up the Univ. of Wisconsin Comprehensive Cancer Center have a large number of NCI grants and contracts. And, although McArdle as an institution does not contract directly with industry for research, a number of individuals and groups at McArdle and elsewhere at the university do consulting work for industry and perform drug tests for pharmaceutical manufacturers.

NCI executives do not feel there is any conflict of interest at McArdle, nor do they feel there is any at Eppley. Some are wondering why Obey is going after

an organization in another state while ignoring a similar operation on his own home ground.

Shubik said he was "shocked" by Obey's statements. GAO investigators and Eppley staff members met following completion of the audit last month. "They were very pleasant, and told us there were no gross discrepancies," Shubik said. "We went over every detail, and frankly I was surprised our records were so good."

FOUNTAIN DOESN'T EXPECT 'INSTANT BREAKTHROUGH' BUT PLANS HEARINGS

Congressman L.H. Fountain, chairman of the House Government Operations Committee Subcommittee on Intergovernmental Relations, will hold three days of hearings next week on NCI and the National Cancer Program.

The hearings will start at 9:30 a.m. each day, June 14-16, in Room 2247 of the Rayburn Building.

Witnesses the first day will be Dorothy Rice, director of HEW's National Center for Health Statistics; Irvin Irwin, director of biostatistics at Roswell Park Memorial Institute; Sidney Wolfe, medical director of the Health Research Group; Howard Temin, Nobel laureate from the Univ. of Wisconsin; Solomon Garb, director of the American Medical Center at Denver and chairman of the Citizens Committee Against Cancer; and James Holland, professor and chairman of the Dept. of Neoplastic Disease at Mt. Sinai Hospital.

Appearing on the following two days will be R. Lee Clark, president of the Univ. of Texas System Cancer Center and president of the American Cancer Society; Benno Schmidt, chairman of the President's Cancer Panel; Donald Fredrickson, director of NIH, and Guy Newell, acting director of NCI.

The hearings will conclude at noon each day.

A spokesman for Fountain said that the hearings are intended to be a review of the Cancer Program since passage of the National Cancer Act of 1971.

"The legislative history of the Act shows that it was intended to result in conquering cancer," the spokesman said. "Congressman Fountain doesn't expect instant breakthroughs, he knows it's a long term project and in fact that we may never conquer cancer. But he thinks it is appropriate now to take a look at how the program is being administered, where we are, what the prospects are, has there been bad judgment in determining priorities, could we do better."

NEW SUBCOMMITTEE CHAIRMEN NAMED

Chairman Jonathan Rhoads of the National Cancer Advisory Board reorganized the Board's various subcommittees and appointed new chairmen to most of them. Most extensive reorganization involved the Subcommittee on Centers & Construction, chaired by Denman Hammond. That was divided into two groups, Hammond heading the Subcommittee on Construction and William Shingleton chairman of the Subcommittee on Centers.

Harold Amos and Hammond were named co-chairmen of the Subcommittee on Special Actions for Grants, with Amos responsible for basic research and Hammond for clinical research. Other subcommittee chairmen are Frederick Seitz, Planning & Budget; William Powers, National Organ Site Programs, and Henry Pitot, Environmental Carcinogenesis.

ABSTRACTS OF 'MOST NEWSWORTHY' PAPERS PRESENTED AT AACR MEETING

The Program Committee for the 68th annual meeting of the American Assn. for Cancer Research selected 17 papers it considered to be "most newsworthy." Abstracts from those papers, in the fields of virology, experimental chemistry and carcinogenesis, were published in the May 27 and June 3 issues of *The Cancer Letter.* Abstracts of the papers in clinical investigation and clinical chemotherapy follow:

CLINICAL INVESTIGATION/CLINICAL CHEMOTHERAPY

PROGESTERONE RECEPTORS – A NEW APPROACH TO RECURRENT ENDOMETRIAL CANCER – Clarence Ehrlich, Peter Young, Robert Cleary, Indiana Univ. Medical Center

This study was designed to determine if specific cytoplasmic progesterone receptors could predict a response of endometrial cancer to progestin therapy. Using a dextran-coated charcoal assay we have studied specific progesterone receptors in endometria and various gynecologic neoplasms from 100 patients. Using our criteria 97% of normal endometria, 80% of endometrial polyps and 92% of endometrial hyperplasias had high progesterone receptor activity. Endometrial adenocarcinomas retain specific progesterone receptors but as cancers become more anaplastic fewer retain high progesterone receptor activity. We found that 85% of Grade I, 62.5% of Grade II, and 50% of Grade III endometrial adenocarcinomas retained high progesterone receptor activity.

High progesterone receptor activity in recurrent endometrial adenocarcinomas appeared to be predictive of a response to progestin treatment. All 3 endometrial adenocarcinomas with high progesterone receptor activity responded objectively to progestin therapy while only 1 of 9 endometrial adenocarcinomas with low progesterone receptor activity responded to progestins.

INTENSIVE REHABILITATIVE SUPPORT OF THE PATIENT WITH ADVANCED CANCER THROUGH HOME HEALTH CARE – J.W. Yates, F.P. McKegney, G. Visco and G.S. Brown, University of Vermont

Sixty patients receiving palliative radiation and/or chemotherapy have been allocated to three patient groups for the evaluation of supportive interventions: I Clinic visit, II Clinic and periodic home visit by Social Worker Evaluator (SWE) and III Clinic and home visits by SWE and Nurse Practitioner (NP). A multidisciplinary team approach to inpatient and the transfer of much of this expertise to NP through didactic and patient discussions has been accomplished. Patients' assessments of mental and physical status are accomplished using Cantril's Self-Anchoring scale technique. Global evaluator assessment of patient performance has been quantitated with techniques including Karnofsky scoring.

In normal individuals, measurements of satisfaction in activity domains which demonstrate positive correlations include: family life, health, and nonworking activities. The interposition of severe illness does not appear to diminish satisfaction in these areas except where physical debility causes reduction in activity. As seen in a well population, assessments by outpatients consistently appear more positive or

optimistic than would be expected. Preliminary data suggest the Karnofsky score may be a reasonable measure of rehabilitative benefit. Early results from the first 60 patients suggest home NP intervention is beneficial.

CANDIDA INFECTIONS: CLINICAL AND PATHOLOGIC CORRELATIONS IN 168 CONSECUTIVE AUTOPSY PROVEN CASES IN CANCER PATIENTS — H.D. Brereton, D. Ihde, A.S. Levine, R.C. Young, NIH

The clinical underestimation of serious Candida infections is dramatically illustrated here where Candidiasis was the sole cause of death in 13 (8%), a major cause of death in 44 (26%) or a contributing major cause of death in 37 (22%), but was suspected at admission in only 6 (3%) and felt likely enough during the last hospital stay to warrant IV amphotericin in only 20 (13%). Most patients had hematologic/lymphoid cancers and were being treated with steroids and/or one/more chemotherapeutic agents. Blood cultures were not diagnostically sufficient being + in only 21 (12%), but a clinical profile of high risk factors included fever on IV antibiotics, low PMN level, abnormal LFTs, abnormal creatinine, low gamma globulin and the presence of other infections.

Organ involvement included the esophagus 108 /64%), lung 56 (33%) which was often associated with disseminated Candidiasis but limited to the lung in 9 cases, stomach 52 (31%), large bowel 46 (27%), small bowel 44 (26%), kidney 39 (23%), liver 34 (20%), heart 23 (14%) which was usually a myocarditis and not a valvulitis, and CNS 18 (11%).

Thus, in this series serious Candida infections were consistently underestimated, and the clinician must rely on a composite of high risk factors rather than fungal cultures to institute definitive therapy.

METHOD FOR DETERMINATION OF HORMONE-DEPENDENCE OF HUMAN BREAST CANCER CELLS — J. Post, R.J. Sklarew, and J. Hoffman, New York Univ. Research Service, Goldwater Memorial Hospital

Although 55% of patients with estrogen receptors respond to hormonal manipulation the course in individual patients does not correlate with receptor conc. The stimulatory effect of estrogen upon cell proliferation in vitro could provide a more direct demonstration of hormone dependency and circumvent these uncertainties. The use of ^{3}HTdR autoradiography permits the identification of stimulated and resistant cells in mixed cell populations. In 3 day cultures of human breast cancer cells (MCF-7), after 24 hrs. of ^{3}HTdR the labeling index increases from 45.9% to 77.3% in the presence of 17-β-Estradiol (10^{-7}M) while the S-time remains ~13 hrs. After Nafoxidine (10^{-6}M)/24 hrs., the index falls to 32.4%. After 18 hrs. of Colcemid+estradiol the mitotic index is 6X higher than in controls. While estrogen stimulates MCF-7 cells to enter S, the population is heterogeneous in its responsiveness. On the other hand, a subline of BT-20 is not stimulated by estrogen. This approach provides direct demonstration of hormone effects on cancer cell proliferation. It has been adapted to measuring hormone-dependency in suspensions of enzyme-dissociated human breast cancer cells from surgical specimens. Differences in response have been found which may be useful clinically in decision-making with regard to hormonal manipulation.

A RANDOMIZED STUDY OF RADIATION THERAPY (RT) VS RT AND CHEMOTHERAPY (CT) IN STAGE IA-IIIB HODGKIN'S DISEASE — J.A. Grasso, A. Panahon, J.H. Kaufman, M. Friedman, R. Moore, L. Stutzman, Roswell Park Memorial Institute

Between February 1971 and June 1975 101 patients with Stage IA-IIIB Hodgkin's disease have received RT: involved field — Stage I all cell types and Stage IIA nodular sclerosis (NS) and lymphocyte predominant (LP); total nodal radiation — all other stages. After RT patients were randomized for 1) 6 months of post radiation CT with chlorambucil, vincristine, vinblastine, procarbazine and prednisone or 2) no chemotherapy. The 3 year relapse free (R) and survival (S) rates were 57% and 89% for the RT only group compared to 85% ($p<0.01$) and 94% for the RT + CT group. The 3 year R and S percentages in the RT and RT + CT groups by stage and cell types were:

	IIA		IIIA		L.P.		N.S.		M.C.	
RT	62	91	37	92	66	100	60	90	44	67
RT + CT	100	100	100	100	80	91	93	96	78	79
p			<0.05				<0.01			

At 3 years the R & S for "A" patients treated with RT was 53 and 90% compared to 91 ($p<.001$) and 98% with RT + CT. The comparable data for "B" patients was: RT 65 and 70%; RT + CT 70 and 60%. While there were no significant differences in survival, remission duration was significantly increased with the addition of post RT chemotherapy.

LONG-TERM FOLLOWUP EVALUATION OF CONPADRI-I ADJUVANT CHEMOTHERAPY IN OSTEOSARCOMA — W.W. Sutow, M.M. Romsdahl, P.G. Dyment, A.E. Frias, Southwest Oncology Group

CONPADRI-I adjuvant chemotherapy (cyclophosphamide, oncovin, phenylalanine mustard, adriamycin) in nonmetastatic osteosarcoma was initiated in 1971. This permits evaluation of long-term followup results in 18 patients treated before July, 1972 (Group A) and in 19 patients treated from July, 1973 through December, 1973 (Group B).

Ten of 18 in group A remain NED, 50 to 73 months from diagnosis. Nine of 19 in group B are NED 28 to 56 months from diagnosis. No group A patient developed metastases after 12 months. No group B patient had metastases after 14 months. Chemotherapy was discontinued in all patients after the first 55 weeks from start to adjuvant program.

The results suggest that CONPADRI-I has achieved disease control in the surviving patients, not merely a delay in the onset of metastases. This experience may have important implications in respect to evaluation of effect of chemotherapy on the cure rate of osteosarcoma.

CLINICAL TRIAL OF CIS-DIAMMINE DICHLOROPLATINUM (CIS PT II) IN OSTEOGENIC SARCOMA — J. Ochs, A. Freeman, H. Douglass, Roswell Park Memorial Institute, and L. Sinks, Vince Lombardi Cancer Research Center

Cis Pt (II) is a potent new antineoplastic agent which behaves like an alkylating agent. Initial trials showed efficacy in testicular tumors. Dose limiting toxicity was primarily renal and auditory.

Because Cis Pt (II) was effective in undifferentiated tumors and because heavy metals such as lead are laid down in bone, we investigated the use of Cis Pt (II) in far advanced osteogenic sarcoma. Eight patients with metastatic osteogenic sarcoma no longer responsive to either high dose Methotrexate and/or Adriamycin (ADR) after surgical removal of primary site were treated with various drug schedules of Cis Pt (II). Toxicity included: 7/8 with nausea and vomiting, 6/8 with elevated BUN and/or creatinine, 2/8 with elevated transaminase and 1/8 with significantly depressed white count and platelets. Maximum cumulative dosage was 660 mg/m^2. All laboratory parameters returned to normal values. Cis Pt (II) is an effective agent in the treatment of metastatic osteogenic sarcoma and may have promise as an adjuvant agent in the primary treatment of osteogenic sarcoma.

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, citing the RFP number. Some listings will show the phone number of the Contract Specialist, who will respond to questions. Listings identify the respective sections of the Research Contracts Branch which are issuing the RFPs. Their addresses, all followed by NIH, Bethesda, Md. 20014, are:

Biology & Diagnosis Section — Landow Building
Viral Oncology & Field Studies Section — Landow Building
Control & Rehabilitation Section — Blair Building
Carcinogenesis Section — Blair Building
Treatment Section — Blair Building
Office of the Director Section — Blair Building
Deadline date shown for each listing is the final day for receipt of the completed proposal unless otherwise indicated.

RFP NO1-CP-75921-69

Title: *Evaluation of calorie/nitrogen ratio of oral solutions used in feeding cancer patients*

Deadline: *July 22*

The purpose of this project is to determine the optimal calorie/nitrogen ratio in oral solutions for patients with head and neck and upper gastrointestinal tract cancers. These particular cancer patients are emphasized as they might rely on the use of oral solutions because of frequent problems with oral food intake. Determining the optimal calorie/nitrogen ratio is emphasized as both adequate calorie and protein intake are paramount to subverting malnutrition and to contributing to anabolic process to metabolism.

This project will be a randomized, prospective clinical trial. Each participating institution will be required to incorporate common procedures into its experimental protocol. This common protocol must be approved by the project officer before patients are admitted to the study.

Offerors should address their proposal in terms of their specific capabilities such as their experience in treating certain tumor types, administration of oral solutions, evaluation of nutritional status, availability of an adequate study population, and access to pertinent laboratory facilities.

Contracting Officer: L.M. Waring
Carcinogenesis
301-427-7575

CANCELLATION

Title: *Administrative support services for the Div. of Cancer Biology & Diagnosis*

NCI announced the cancellation of RFP NCI-CB-74172-39 that appeared in ***The Cancer Letter*** May 27, 1977. Reason for cancellation was that "it is in the best interest of the government, because there are deficiencies in the workscope."

CONTRACT AWARDS

Title: Continuation of pathological history of the mammary gland in pseudohermaphroditic rats and mice
Contractor: City of Hope National Medical Center, $92,700.

Title: Continuation of Control of DNA synthesis in the mammary gland
Contractor: Stanford Univ., $90,000.

Title: Continuation of Study effector molecule binding to mammary cell surfaces
Contractor: Stanford Univ., $115,000.

Title: Continuation of An evaluation of surgical adjuvant chemotherapy utilizing 5-FU, cytoxan and prednisone
Contractor: Mayo Foundation, $94,850.

Title: Continuation of Study of the role of the stroma in the growth of neoplastic and preneoplastic lesions of the mammary gland
Contractor: Baylor College of Medicine, $87,500.

Title: Detection of circulating antigen-antibody complexes in cancer
Contractor: Scripps Clinic & Research Foundation, $86,524.

Title: Immunodiagnosis of carcinoma of the gastrointestinal tract
Contractor: Scripps Clinic & Research Foundation, $121,885.

Title: Preparation of reagent antisera and antigens
Contractor: National Jewish Hospital & Research Center, Denver, $70,831.

Title: Isolation and characterization of human peripheral blood monocytes
Contractor: Univ. of Colorado Medical Center, $51,528.

Title: Development and implementation of at-home rehabilitation programs
Contractor: The Cancer Center Inc., Cleveland, $270,919.

Title: Continuation of Therapy of patients with gastric carcinoma
Contractor: Univ. of Southern California, $170,616.

Title: System planning support services for the National Cancer Plan.
Contractor: JRB Associates, $300,980.

Title: Continuation of study of patients with ovarian carcinoma
Contractor: Mount Sinai School of Medicine, $49,492.

Title: Continuation of Study to develop a method of predicting response to adrenalectomy
Contractor: Univ. of Chicago, $100,000.

Title: Continuation of Microcirculation/molecular transport in mammary cancer
Contractor: Univ. of Arizona, $100,000.

Title: Continuation of Differentiation of mammary epithelial cells
Contractor: Washington State Univ., $53,600.

Title: Immunological markers applicable to cytology automation
Contractor: Univ. of Miami, $240,902.

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