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Accrual Picking Up, Still "Nothing To Write Home About;" Unfunded MDs "Subsidize Entire Program"

Tal Pomeroy, an oncologist in private practice in Santa Cruz, CA, had been listening to a recitation of the dismal record of patient accrual by so many clinical trials in the U.S. and the reasons why, at a forum sponsored by the Clinical

(Continued to page 2)

In Brief

Coltman, Loeb Lead ASCO, AACR; Young, Busch Presidents Elect; Renilda Hilkemeyer Honored

NEW LEADERS of the American Society of Clinical Oncology and American Assn. for Cancer Research took over at the annual meetings last week in New Orleans: Charles Coltman is the new ASCO president and Robert Young of NCI is the president elect. Lawrence Loeb is the new AACR president and Harris Busch is the president elect. B.J. Kennedy and Enrico Mihich are the outgoing presidents of ASCO and AACR, respectively. John Yarbro was elected secretary treasurer of ASCO, replacing Stephen Schimpff, and Thomas King was elected treasurer of AACR. Robert Handschumacher has been secretary treasurer of AACR, but a bylaws change conferred the secretary position onto the executive director, Margaret Foti. New ASCO directors are John Glick and Stephen Jones; new AACR directors are Bernard Fisher, J.A. Levy, Sandra Waldman and Stuart Yuspa. . . . **JAMES COX**, chairman of the Radiation Therapy Oncology Group, took exception to comments by Bruce Chabner, director of NCI's Div. of Cancer Treatment, to the effect that patients in certain major U.S. cities have limited access to clinical trials (**The Cancer Letter**, May 20). Cities named by Chabner included Milwaukee and St. Louis. "The Medical College of Wisconsin in Milwaukee and Washington Univ. in St. Louis are two of the most important, in terms of scientific input and patient accrual) members of ROTG," Cox wrote. Chabner's comments were made during a discussion on patient accrual and the high priority intergroup studies involving the multimodal cooperative groups; they did not encompass the specialty and pediatric groups. . . . **RENILDA HILKEMEYER**, who as director of nursing at M.D. Anderson for 22 years established oncology nursing as a separate specialty, received an honorary doctor of public service degree from St. Louis Univ. last month. . . . **ROGER PRIORE**, director of biomethematics at Roswell Park Memorial Institute, has been appointed director of management information systems.

Harold Rusch, McArdle Founder, Dies At 79 . . . Page 5

DCE Board Approves Reissuing Epidemiology Small Grants PA . . . Page 7

RFAs Available . . . Page 6

More CCOPs, CGOPs Would Help; Cooperative Group Accrual Increasing

(Continued from page 1)
Practice Committee of the American Society of Clinical Oncology, meeting last week in New Orleans.

Bruce Chabner and Robert Wittes of NCI, Charles Coltman, chairman of the Southwest Oncology Group, and Gary Ratkin, chairman of the Clinical Practices Committee, had recounted the long and familiar list of why so many physicians do not participate in clinical trials, along with other "hurdles to clinical trials accrual," (Chabner's words).

At other times during the ASCO meeting, NCI Director Vincent DeVita, along with Chabner, director of the Div. of Cancer Treatment; Wittes, director of the Cancer Therapy Evaluation Program; Coltman and others went over the same ground.

The issue of adequate funding for clinical trials was not one of the primary concerns. If accrual can be stepped up, "we will be faced with the problem of finding the money for it," DeVita said at a press conference. "I would like to have that problem."

The inference was, as DeVita, Chabner and Wittes have been saying for months, that the problem is structural, philosophical, cultural, or whatever, and that money was not the root of this evil.

Tal Pomeroy's situation, as he described it during discussions at the Clinical Practice Committee forum, indicates if money isn't the only answer, it could certainly help.

Pomeroy said that he had been entering about 40 patients a year through an NCI supported Community Clinical Oncology Program. That CCOP did not make it through last year's recompetition, leaving Santa Cruz oncologists and cancer patients without easy access to clinical trials.

"The nearest place we could go is at Davis, 180 miles away," Pomery said. "But when I called them, they said they didn't have enough money to take us. I called NCI and SWOG, but no one had any answers."

Someone from SWOG had an answer this time. "Call me," Coltman quickly responded. "My number is 512/366-9300. I'll fix that. The Univ. of California at Davis will be thrilled to work with you."

Wittes told Pomery, "You and people like you are to be congratulated for participating even when you aren't funded. You're subsidizing the entire program."

Pomeroy's situation undoubtedly exists everywhere a CCOP is unfunded--those from CCOP 1 who did not score well enough to be funded in CCOP 2, and the new ones who are in the same situation. Each one represents a group of physicians anxious to participate in clinical trials. Some money spent to fund some of those CCOPs, either through that program, the Cooperative Group Outreach Program, or through the new mechanism CTEP has developed to bring nonaffiliated physicians into the high priority clinical trials, could have a major impact on overall accrual.

Coltman told ASCO members at the forum that 43 percent of SWOG's patients are entered by physicians in private practice, either through CCOP or CGOP. He noted that skeptics of those programs had questioned whether community physicians could do as well as their academic colleagues in quality control.

Community MDs Hold Their Own

SWOG has looked at that issue several ways, and Coltman had previously reported that the community centers more than held their own in treatment outcome. Last week, he compared SWOG member institutions with CCOPs and CGOPs on the percent of eligible patients entered on research protocols and on the percent evaluable:

--Members, 94 percent of the eligible patients entered, 94 percent evaluable.

--CCOPs, 96 percent entered, 97 percent evaluable.

--CGOPs, 94 percent entered, 97 percent evaluable.

Patient characteristics were comparable, and the results did not depend on a different patient mix, Coltman said. "The fact is that community physicians did better."

Coltman noted that SWOG has formed a urologic cancer group that is ready to go, awaiting funding from NCI. He also mentioned the "RFA" SWOG put out to nonmember physicians, inviting their participation in the high priority trials (**The Clinical Cancer Letter**, March, 1988). "We were stunned by the response," with applications from 178. But only 37 new groups, with an annual accrual of 2,350 patients, were accepted.

Participation is limited to experienced investigators, but Coltman said that lack of money prevented acceptance of many more.

"All we need is the cash. When we get the cash, we'll increase accrual to all the cooperative groups," Coltman said.

Coltman is the new president of ASCO, and he said he "personnally has committed" his

year in that job to an effort to enhance clinical trials participation by ASCO members.

Chabner noted that only 25,000 patients a year are being entered on cooperative group protocols.

That is less than three percent of new cases, and means that the average trial requires three to five years for accrual, and five to 10 years to complete. At present rates, the five high priority trials are not likely to be completed in less than seven years, some from 10 to 15 years, Chabner said.

Chabner listed as "hurdles to clinical trials accrual:"

--The failure by many cancer centers to participate in cooperative group trials. "There is no incentive for them, but that is being redefined," he said, alluding to development of guidelines for the new comprehensive center grants.

--Lack of understanding by the public of the potential risks and benefits of participating in clinical trials.

--Physician unwillingness to participate.

--Limited access for minority patients to trials.

Ratkin had his own list of impediments:

*Many physicians feel that trials are not appropriate for the practice of oncology, and they question whether they are important enough.

*Trials are difficult and time consuming.

*Some physicians believe that some trials are unethical.

*Negative economic factors include physician and nurse time; insurance reimbursement denials; the Medicare prospective payment system (applying now only to hospitalized patients).

*Reluctance of insurers to cover clinical trials in medical malpractice policies.

"We need a national effort to better educate private insurers," Ratkin said.

"Objections to participation are multifactoral and come at you from many directions," Wittes said. Among these are that many physicians have a "philosophical aversion" to clinical trials. They are convinced that individualized therapy precludes it.

Other issues are randomizing vs. expectations of private patients; and the quality of the scientific questions being asked in the studies.

"The issue is, is the question worth answering?" Wittes said. "If yes, and people shrink from doing their part in finding answers to problems, then they become part of the problem themselves."

Wittes said the response to SWOG's RFA proves that there is "a large potential reserve of clinical trials participants among physicians who do not now participate."

NCI will expect participation in the high priority trials "by all elements of the NCI supported network, provided they have no other trial of comparable importance," Wittes said.

Wittes has had "preliminary contact" with HMOs on participating in clinical trials. "We had a clearcut expression of interest from two, and tentative interest from others. The for profit organizations particularly are interested, "because they feel it could give them a leg up on their competition."

Wittes said he has heard from the oncology community that the most important effort NCI can make in enhancing accrual is a publicity campaign designed to convince physicians and the public of the value of clinical trials. The Office of Cancer Communications has put together such a program and is in the process of implementing it.

Wittes said he has "no reason to be optimistic" about insurance coverage for patient care costs in clinical trials. "That's a disaster waiting to happen."

The issue is more complicated than denial of reimbursement for investigational treatment, Wittes said. Reversal of the traditional practice of paying for any physician prescribed use of a drug approved by the FDA, regardless of the approved indication, "is an act of desperation" by insurance companies struggling to hold down their premiums.

The Health Care Finance Administration has even gone so far as to deny reimbursement for a labeled indication of a marketed drug on the basis that it is more expensive than another drug, Wittes noted.

Chabner emphasized that "all clinical trials are based on some scientific evidence that a new therapy might be better than the standard treatment." Patients entering clinical trials are assured that they will receive either the best known treatment, or treatment for which there is scientific evidence that it may be even better.

Coltman was questioned about the respondents to SWOG's RFA who were not accepted. "That leaves 4,000 patients on the table," the questioner asked. He said he was one of the physicians not accepted, and that SWOG's letter informing of that did not offer

any alternatives for participation. Coltman disagreed, and said his letter invited those physicians to participate through CGOP.

Carl Pinsky, chief medical officer of NCI's Biological Response Modifiers Program, chaired the forum.

Bernard Fisher joined Coltman, DeVita and Wittes at a press conference called to discuss clinical trials.

Fisher is chairman of the National Surgical Adjuvant Breast & Bowel Project. Coltman called NSABP "the most successful patient accrual machine in the nation," and asked Fisher how he does it.

"That's because we've been at it the longest, since 1958," Fisher said. He used the occasion to plead with the press "to forget the soap box stories and tell the public about clinical trials, where we test the best known therapy against what could be better."

Wittes carried on his comments about problems with reimbursement. NCI money going into clinical trials includes very little for patient care, he pointed out. Patients receive the best clinical care when they are entered in clinical trials, "so there is no reason insurance companies should not cover it. But there is an increasing tendency to deny claims which in the past they have paid."

DeVita said that reimbursement policies are encouraging patients "to go on standard treatment, where the insurers will reimburse. That is detrimental to patients, and will cost the insurance companies more. It makes sense economically to do it the right way."

Asked about the impact of the DRG method of reimbursement for Medicare and Medicade patients, Wittes said, "We were concerned initially, but there is no data that the prospective payment system as such is a major problem now. Most clinical trials now involve outpatients (who are not subject to DRG limits)."

Wittes continued, "We're facing unprecedented opportunities. We have never been so rich in opportunities as we are now, in the common epithelial cancers, breast, colon, rectal, prostate."

On a question about the impact of budget cutting, Wittes said that the clinical trials program has not had a budget cut, although it also has not had the increases it could use. "We never have as much money as we need or could use profitably. We need to improve getting patients on trials. If we do, we'll find a way to pay for it, out of a budget of more than one and a half billion dollars."

DeVita responded to a question on whether Biotherapeutics Inc., the for profit company which offers experimental treatments to appropriate patients for fees ranging up to $30,000, competes with NCI for patients.

"There are lots of patients out there," DeVita said. "There is no shortage. Biotherapeutics is doing it a little differently. What they are doing is taking therapy that seems to be working and selling it. My feeling is that we ought to be making that therapy available to everyone. Biotherapeutics is exploiting the slowness of the system."

One of the major topics for between session discussions at ASCO was NCI's action in sending out a nationwide "alert" about the apparent value of treatment for node negative breast cancer. Many clinicians said they had had immediate responses from patients concerned about whether they should be receiving adjuvant chemo or hormonal therapy.

Asked why he did it, DeVita said, "The Institute did it, not me." He said the PDQ Editorial Board, the National Cancer Advisory Board and most of his senior staff all agreed. Also, cooperative group leaders involved in the node negative trial had agreed it should be stopped because it "was not ethical to continue," with a no treatment arm. "We felt the women and their physicians should have that information."

DeVita brought up the clinical trials issue at last month's NCAB meeting, as he had said he would continue to do until the situation improved.

And some of the information he presented indicated that it has improved to some extent:

<>Annual accrual rate for the high priority trials has increased from 564 to 1,008 patients, up by 178 percent, despite closing of the node negative trial.

<>Overall annual accrual, based on the first three months of this year, is up 15 percent (from 12,394 to 14,268 patients per year).

<>Eight cooperative groups have increased accrual while only two had decreases in 1988 over 1987, based on accrual during the first six months of last year and the first quarter of this year.

Here's the breakdown on those figures by group, from 1987 to 1988:

Pediatric Oncology Group led all others, increasing by 69 percent. POG was followed NSABP, 58 percent; North Central Cancer Treatment Group, 45 percent; SWOG, 38

percent; Gynecologic Oncology Group, 36 percent; Lung Cancer Study Group, 33 percent; Radiation Therapy Oncology Group, 29 percent; and Childrens Cancer Study Group, 11.2 percent.

Eastern Cooperative Oncology Group declined by 9.2 percent and Cancer & Leukemia Group B by 5 percent. Dropping the node negative breast cancer trial, originally an ECOG study, cut into its projected accrual. CALGB just lost some of its member institutions as a result of peer review, which may have affected its projections.

DeVita again expressed criticism of cancer centers in general for "not playing a major role in clinical trials, over and above their participation with the cooperative groups." He insisted that clinical trials should be a requirement in the new guidelines being developed for comprehensive centers.

"I'm in a lot of trouble. This is not a popular issue," DeVita told the NCAB. "My colleagues in the groups have asked me to quiet down. But we are failing to make progress in some cancers. I need to deal with this by bringing it to the NCAB publicly. It's a defensive strategy.

"The good news is that we are switching over in the terms of award (in the cooperative agreements supporting the groups), modifying them to terminate studies that are not accruing."

DeVita also repeated criticism of centers which have not provided their clinical protocols to NCI for use in PDQ.

"Use of PDQ is increasing at a pretty good rate," Devita said. "Hours of usage are up by 43 percent. We've added EORTC protocols. Europe is using PDQ, and it is now a worldwide system. An external advisory board (chaired by NCAB member Helene Brown) is helping modify the system for use by lay persons.

"PDQ has every clinical protocol funded by the government, and everyone in Europe, but unfortunately some centers still have not submitted theirs." He named the centers as Johns Hopkins, Mayo Clinic, Univ. of Miami, Univ. of Pennsylvania, Wayne State Univ., Columbia Univ. and Illinois Cancer Council.

"The people in those cities are not being well served," DeVita said. He added that Mayo is not participating "because Dr. (Charles) Moertel (former director of the Mayo Cancer Center) believes PDQ inhibits clinical trials, that it encourages physicians to treat with those protocols themselves."

Harold Rusch, Cancer Research Pioneer And McArdle Founder, Dies At 79

Harold Rusch, 79, a major figure in cancer research for nearly a half century and founder of the Univ. of Wisconsin's McArdle Laboratory for Cancer Research, died May 26 at home in Madison after a prolonged fight against prostate cancer.

Rusch founded McArdle in 1946 and served as its director until 1972. It was one of the first facilities in the country to comprehensively study the fundamental biological and biochemical activities of cancer cells. Rusch recruited outstanding scientists, and under his leadership they built McArdle into one of the most prestigious cancer research institutions in the world.

In 1972, Rusch became the first director of the UW Clinical Cancer Center, a position he held until retirement in 1972. He also chaired the UW Medical School departments of oncology (1948-72) and human oncology (1972-78). Upon retirement, he was named emeritus professor of human oncology.

Rusch pioneered the identification of wavelengths of sunlight responsible for causing skin cancer in 1941. Also in the early 1940s, he showed that overeating resulting in obesity increases the risk of cancer by reducing activity of adrenal glands. Rusch was particularly interested in the concept that cancer does not occur as the result of a single event, but rather as a series of biochemical changes, an approach which became the basis for establishing McArdle as one of the world's preeminent cancer research centers.

"Dr. Rusch was an outstanding individual who served his state, country, university and profession well," said Paul Carbone, director of the UW Clinical Cancer Center. "His efforts will be long remembered."

"Few individuals have had a greater influence on cancer research in the United States than Harold Rusch," said Henry Pitot, McArdle director. "He has trained more than 1,000 individuals presently involved in basic and applied research on cancer and its prevention, diagnosis and treatment. Dr. Rusch was a humble, unassuming, forthright person who always placed the needs of his colleagues and students above his own."

Rusch played an important role in development of the National Cancer Act of 1971. He served on the Yarborough Panel of Consultants which drafted recommendations incorporated into the Act. Rusch, with Lee Clark and Benno

Schmidt, insisted on including language encouraging development of cancer centers, one of the more significant elements of that landmark legislation.

The Act created the National Cancer Advisory Board, and President Nixon appointed Rusch as one of the first members. He was first chairman of the Board's Centers Committee and helped write the initial requirements ("characteristics," they were called) for consideration as a comprehensive cancer center. The UW Clinical Cancer Center and McArdle Laboratory were one of the first recognized as a comprehensive center by NCI.

Rusch recently received a letter of appreciation from President Reagan for his "achievements as a pioneer in cancer medicine" whose influence and work has inspired physicians, stimulated researchers and above all benefitted patients "not only in Wisconsins but throughout our country and the world."

Rusch belonged to numerous professional medical societies and served on many national and international committees involving cancer research and therapy. Among his many appointments to scientific editorial boards, he was editor in chief of "Cancer Research," published by the American Assn. for Cancer Research, from 1950-65.

He was elected as a fellow to the American Academy of Arts and Sciences in 1959 and to various medical fraternities. He is listed in most of the "Who's Who" directories in education, science and medicine.

Between 1936 and 1978, Rusch had 178 research articles published in scientific journals.

A Wausau native, he graduated from Wausau High School in 1926. He received his BA from UW (Madison) in 1931 and his MD, also from UW (Madison) two years later.

Rusch is survived by his second wife, Louise Turner Van Wart Rusch, daughter Carolyn Schlotthauer, grandchildren Kristina and William Schlotthauer, brother William Rusch and two nieces. His first wife, Lenore Robinson, died in 1978, and his other daughter, Judith Ann Tyler, in 1976.

A memorial service will be held June 12 at 1 p.m. at the Alumni Lounge of the Wisconsin Center in Madison. Memorial contributions may be made to the McArdle Laboratory, Univ. of Wisconsin, Madison 53706, or the UW Clinical Cancer Center, Madison 53792, to establish a fellowship commemorating Rusch's life and service.

RFAs Available

RFA 88-CA-13
Title: Animal models for human papillomavirus associated neoplastic diseases
Application receipt date: Sept. 15
Letter of intent receipt date: Aug. 15

The Biological Carcinogenesis Branch of NCI's Div. of Cancer Etiology invites grant applications to study the host response mechanisms that mediate the regression of human papillomavirus (HPV) associated neoplastic lesions using either established animal models or new animal models of HPV associated diseases.

HPVs are strongly associated with a variety of human anogenital neoplasms, e.g., cervical dysplasias and carcinomas, and are a probable etiological factor in their development. Studies in animal models leading to the development of prototype vaccines to prevent initial HPV infections or to induce the regression of established HPV lesions are encouraged. Basic studies on the mechanism of progression of genital warts and other initially benign papillomavirus lesions to dysplasia and possible carcinoma using animal models are also welcome.

The major emphasis of the research to be funded under this RFA is the promotion of basic studies on the host response mechanisms that mediate the regression of HPV associated neoplastic lesions using either appropriate known animal models or new animal models. Studies on the mechanism of progression of the initial HPV infection to dysplasia and carcinoma using animal models are also encouraged. The scope of this RFA includes both animal papillomaviruses and human papillomaviruses infections in animals.

Collaborative projects which include molecular, cellular, immunological and pathological aspects are strongly encouraged. Examples of pertinent studies (which are not all inclusive) are (1) identifiction and chracterization of experimentally useful animal papillomavirus host systems whose disease pattern is similar to the progression/regression profile seen in neoplastic human disease; (2) identifiction and characterization of animal models that can be infected with human papillomaviruses; (3) characterization of the mechanisms of progression/regression of HPV lesions to dysplasia and carcinoma with particular emphasis on molecular processes and the participation of the humoral and cellular immune responses; (4) identification of specific viral or cellular antigens (epitopes) which mediate the most immune response; (5) development of specific antibodies or the establishment of cytotoxic T-lymphocyte lines specific for HPV associated dysplastic or carcinomatous cells; (6) development of prototype animal/human vaccines which can protect animal models from viral challenge or can induce the regression of estabalished lesions in these models; (7) development of procedures to facilitate the regression of dysplastic or malignant lesions via immunotherapeutic or chemotherapeutic approaches.

Approximately $1 million in total costs per year for five years will be committed to specifically fund applications submitted in response to this RFA. It is anticipated that five to six awards will be made. This funding level is dependent on the receipt of a sufficient number of applications of high scientific merit. The total project period for applications should not exceed five years. The earliest feasible starting date for the awards will be April 1, 1989. Nonprofit and for profit institutions are eligible to apply. Foreign and domestic institutions are eligible.

Complete copies of the RFA and additional information may be obtained from, and letters of intent should be sent to, Dr. Alan Schreier, Program Director, DNA Virus Studies II, Biological Carcinogenesis Branch, DCE, NCI, Executive Plaza North, Rm 540, Bethesda, MD 20892, phone 301/496-1953.

DCE Board Approves Reissuing Epidemiology Small Grants PA

Reissuance of the Epidemiology & Biostatistics Program's small grants program announcement for epidemilogy received concept approval from the Div. of Cancer Etiology Board of Scientific Counselors at its meeting last month.

DCE staff members feel the small grants can be very useful in stimulating epidemiologic research. The program as it had been established had some limitations, however, and the number of applications had dwindled. Some modifications were recommended, including doubling the money available for individual awards.

The Board approved that recommendation, and went along with other changes based on experience in the initial program.

The Board also approved recompetition of the Epidemiology Program's contract for radiation dosimetry for epidemiologic studies.

Also receiving concept approval last month were a noncompetitive renewal and a supplement, including:

--$285,000 supplement to the interagency agreement with the Small Business Administration for the mortality study of workers exposed to acrylonitrile. This involves a 17 month extension required because of the unexpected size of the study population. Entire cost of the project will be about $1.5 million.

--Three year extension of the interagency agreement with the Dept. of Energy for studies of radiation induced chromosome damage in humans. Cost of the extension was estimated at $390,000.

Descriptions of the competitive concepts follow (other concepts approved by the Board appeared in last week's issue of **The Cancer Letter**; concepts for AIDS related research and support appeared in **AIDS update** May 23):

Small grants program for epidemiology. Reissuance of a program announcement.

In 1984, epidemiologist members of the DCE Board requested assistance in improving continuity of research support support for extramural investigators, and this was the topic of a workshop in March 1985. One of the several recommendations was the establishment of a small grants program. Following approval by the NCI Executive Committee and the DCE BSC, the program announcement was issued in December 1985. Eligible applicants were those planning a complex epidemiologic investigation; those developing or validating a laboratory procedure for use in cancer epidemiologic research; and those in need of rapid funding for innovative cancer epidemiologic research. Rapid turnaround was recognized as an important objective.

The program has now completed six cycles and is a valuable adjunct to other funding programs. Of 68 applications received, 54 (79%) were approved by special review committees; 19 were approved for funding by the NCI Executive Committee and 18 (26%) have been funded. Among the 18 funded applications, 10 support dissertation projects; of the remaining eight, four are awarded to individuals at the assistant professor level, two grantees are at the associate professor level, and two are senior investigators. Thus, the program provides startup funding for young investigators and is attracting bright doctoral students to cancer investigations. Recently, young investigator awards have been converted to five year FIRST awards that fare poorly in epidemiologic review. The small grants have increasing potential as a recruitment incentive and to underwrite modest studies by junior faculty. A need also exists for increased support of highly exploratory work in rapidly evolving areas, such as AIDS research.

However, there are some problems. The first two cycles following the announcement resulted in 24 and 17 applications. With each succeeding cycle, the number fell, so that only four were received last October. The time which has elapsed since the announcement is partly responsible for the decline. However, another factor is the current limit of $25,000 for each individual award, which requires that extensive institutional resources be available to underwrite many of the actual costs of the projects.

A frequent criticism by reviewers is the inadequate amount of data which can be collected, leading to diminished enthusiasm. A fourth source of difficulty has been that pilot/feasbility studies are often inadequately described by applicants. In proposals to develop a laboratory procedure, the strengths of laboratory and epidemiologic collaborators have been poorly balanced. Investigators with interesting ideas need more shared knowledge of both the laboratory and epidemiologic constraints peculiar to the procedure and its use. Often, the requisite skills do not exist within the same institution.

This is a short term award, not to exceed three years, intended to provide support for pilot projects, testing of new techniques, or innovative or highly exploratory projects which could provide the basis for more extended research.

Investigators are eligible to apply for a small grant to support research on a topic relevant to cancer etiology if they are interest in planning a complex epidemiologic investigation; developing or validating a laboratory or statistical procedure for the ultimate purpose of applying it in cancer epidemiologic research; carrying out an innovative epidemiologic research project, not integral to ongoing supported research, or highly exploratory research in rapidly evolving areas (such as cancer related AIDS research), for which rapid funding is justified--the availability of special personnel for limited time periods is considered to be a valid factor in evaluating the need for rapid funding.

Added to that list in the new announcement will be these activities:

--The analysis of previously collected data, particularly when combining data from multiple studies is contemplated for worthwhile purposes, such as examining consistency or strength of observed associations.

--Resolving methodologic problems, such as documenting the accuracy of a customary procedure or evaluating the effect of cancer, its diagnosis and/or treatment on risk factor estimates derived from case control studies.

The award will provide a maximum of $25,000 in direct costs per year (the previous announcement limited the total award to $25,000). These funds may be used for personnel (added to this announcement), supplies, small equipment and travel required by the project. Salary support for the principal investigator will be allowed in unusual instances when clearly justified. The

normal duration of support is two years, but applications may be made for up to three years if the total direct costs are $50,000 or less. Projects concerned with multidisciplinary collaboration, such as the development or validation of a laboratory procedure for use in epidemiologic research may request modest costs for a period of intensive orientation for one or more collaborating investigators to facilitate transfer of new techniques when it is clearly justified by complexity of the task and details of the orientation are included in the proposal. NCI expects to make approximately five awards from each review cycle.

Instructions to applicants will be modified to emphasize the need for pilot and feasibility studies to incorporate evaluable endpoints and specify formal decision criteria.

Genrose Copley is the program director.

DCE Director Richard Adamson explained that the division would like to expand the award period for the small grants program beyond its current three year period. He pointed out that the money to fund the grants does not come from the RO1 and PO1 pool, but is set aside for the small grants program. The small grants "don't count against the number of grants we have to fund," he said, adding that DCE would like to make the small grants program more flexible.

Noting that the original purpose of the program was to fund young investigators, DCE Board Member Thomas London asked, "Is that happening?"

"It is happening," Copley replied. Approximately 50 percent of the grants awarded have supported dissertation research, she said. The program is also intended to provide clinical funding for the development of better laboratory tests and procedures, but NCI has not had as much success in that field.

Radiation dosimetry for epidemiologic studies. Recompetition of a contract held by Univ. of Texas M.D. Anderson Cancer Center. Total estimated cost for the five year award is $990,000, with $195,000 the first year (FY89).

The accurate estimation of radiation dose to specific organs following exposure is an essential part of our program of radiation studies. A comprehensive approach to radiation dosimetry permits the accurate quantification of risks and a better evaluation of dose response relationships. Since 1979, radiation physicists at M.D. Anderson Hospital have collaborated with NCI on radiation dosimetry for epidemiologic studies. Radiation doses have been estimated from measurements made on patients during treatment, from dosimetry experiments that reconstruct exposure situations on anthropomorphic phantoms, and from computer simulations using Monte Carlo techniques which have been developed by Oak Ridge National Laboratory. Data from completed studies indicate a high degree of consistency of measurements made using these different resources. In addition to dosimentry measurements required for full scale investigations,' this contract provides preliminary estimates of organ doses for planning new studies.

Projects requiring continued or additional dosimetry support include young girls receiving repeated spinal x-rays to monitor scoliosis during the growth spurt, women treated with radiotherapy for cancer of the uterine corpus, women treated with radiotherapy for breast cancer, children treated with radiotherapy for retinoblastoma, women given radiation for benign gynecological disorders, women receiving radiotherapy for infertility, persons irradiated for peptic ulcer, children irradiated for tinea capitis and other benign disorders of the head and neck, patients treated with radioactive iodine for hyperthyroidism, children receiving multiple chest fluoroscopies during cardiac catherization, children in the UK irradiated for childhood cancer, and patients treated for cancer with neutrons. Contract funds would be used to support personnel, including the principal investigator, a computer programmer, a medical abstractor and two radiologic physics technicians. In addition, materials and dosimetry supplies, such as thermoluminescent dosimeters, would be purchased as necessary.

The contractor will provide the support necessary to make measurements on patients, anthropomorphic phantoms, or water phantoms in order to reconstruct radiation doses to specific organs following medical exposures. The contractor will (1) determine the manner in which physical dosimetry can be best applied to the epidemiologic studies of interest; (2) coordinate dosimetry data collected or prepared by other medical physicists who are participating in the the Branch's studies; (3) compare measured doses with calculated organ doses to validate consistency and accuracy of simulation models (measurements will be made to allow a separation of organ doses into the contribution from (a) head leakage and collimator scatter, and (b) scatter within the patient from the useful beam); and 94) continue dosimetry of neutron distributions from betatrons and other high energy linear accelerators as well as from primary neutron sources.

John Boice and Charles Mays are the project officers.

The concept was approved with two abstentions. DCE Board Member George Casarett raised a number of concerns about the project.

"I have some apprehensions about the program," he said, specifically asking how investigators would account for previous radiation exposure.

Concept presentor Ruth Kleinerman said subjects would be screened for any significant recent diagnostic radiation such as upper GIs, lower GIs, or myelograms, and by looking at the patient's average bone marrow dose.

"I appreciate the need and desire to get data from human chromosomes," Casarett said, but asserted that the studies "aren't designed to gain needed information on dose response relationships or mechanism studies. These studies involve rather diffuse (applications) of chromosome studies" and fail to include data on lymph nodes. While it will be easy to present the data obtained from the studies, he warned that it will be "very difficult to interpret without something done to fill these holes."

Board member Roy Shore said he was supportive of what the studies were trying to accomplish, and that the technology to be used would attempt to assess factors that no one has previously tried to do, such as "the effect of dose fractionation, factors of partial body radiation, especially neutralizing radiation of interest."

Adamson told the board that DCE will conduct a site visit in the fall and can examine some of these questions at that time. "I recommend that we go ahead, but charge that we look at these questions in the fall."

BSC Chairman Hilary Koprowski asked what would be done if the site visit team recommended changes in the program. DCE could either change the program, or stop it, if the board wanted to, Adamson replied.

Board member Moyses Szklo characterized the program as an exciting opportunity. "As an epidemiologist, I would be excited about it."

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