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COLORECTAL, LUNG CANCER SCREENING TECHNIQUES SHOW NO MORTALITY IMPROVEMENT, CONFERENCES FIND

Consensus conferences convened by NCI's Div. of Cancer Control & Rehabilitation to assess the state of the art in screening for lung and colorectal cancer have concluded that methods in use or under test for early detection of those diseases have not yet demonstrated any reduction in mortality in screened populations.

Participants in both conferences agreed that until benefits have been

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In Brief

ROBERT MILLER TO HEAD INTERNATIONAL AFFAIRS OFFICE; PITOT: NO BASIS FOR 20% ESTIMATE

ROBERT MILLER, chief of NCI's Clinical Epidemiology Branch, will head the Office of International Affairs, the job held by Gregory O'Conor before he became director of the Div. of Cancer Cause & Prevention. Miller will continue as Clinical Epidemiology chief. . . . HENRY PITOT, director of McArdle Laboratory, on the NCI-OSHA report that estimates occupational exposures are associated with at least 20% of cancers: "If you just state the 20% with reservations, the reservations won't be heard. My colleagues in the lab agree that the old figure of 1 to 5% probably is not correct, but there is no basis for 20%." . . . NATIONAL CANCER Advisory Board did not get around to consideration at its November meeting of the proposal by former Board member David Hogness to establish a review mechanism to speed followup of information coming out of basic research. It will be on the agenda for the Board's January meeting. . . . NEW PUBLICATIONS: "Health Through Nutrition, A Comprehensive Guide for the Cancer Patient," and "Up & Around, Rehabilitation Exercises for Cancer Patients," published by Alchemy Books, 681 Market St Rm 755, San Francisco 94105. Ernest & Isadora Rosenbaum, Carol Stitt and Harry Drasin are authors of "Health Through Nutrition," $5.95; the Rosenbaums, Francine Manuel, Judith Bray and Arthur Cerf wrote "Up & Around," $3. "Asbestos & Health" and "Smoking & Health," annotated bibliographies of public and professioanl education materials, free from Cancer Information Clearinghouse, NCI, 7910 Woodmont Ave., Suite 1300, Bethesda, Md. 20014. "Endocrine Control in Neoplasia," edited by Rameshwar Sharma and Wayne Criss, $36; "Hormones, Receptors & Breast Cancer," edited by William McGuire, $27; "Lung Cancer Progress in Therapeutic Research," edited by Franco Muggia and Marcel Rozencweig, $45; and "Platelets, A Multidisciplinary Approach," edited by Giovanni de Gaetano and Silvio Garattini, $36; all from Raven Press, 1140 Ave. of the Americas, New York 10036; "The Breast Cancer Digest, A Guide to Progress in Medical Care, Emotional Support & Educational Programs," available free from Robert Denniston, NCI, Bldg 31 Rm 4B39, Bethesda 20014.

CONFERENCES SUGGEST NO MASS SCREENING PROGRAMS FOR COLORECTAL, LUNG CANCER

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demonstrated, no mass screening demonstration programs should be undertaken. They recommended that existing studies should be continued and suggested that additional clinical investigations would be helpful in determining more definitively the value of various screening methods.

The conference on colorectal cancer covered all methods of screening and early detection but was primarily concerned with testing of occult blood in the stool as a screening technique. A number of studies was reviewed, including the results of clinical trials of occult blood testing for colonic neoplasms conducted in the U.S. and Germany. Proctosigmoidoscopy as a screening tool was not discussed in detail; participants felt that physician utilization has been low as a consequence of poor patient and physician acceptance of rigid sigmoidoscopy.

The conference recommended the following studies to clarify the role of flexible sigmoidoscopy:

1. Comparison of the value of flexible sigmoidoscopy with that of rigid sigmoidoscopy in a total program of detection of asymptomatic colonic neoplasms.

2. The evaluation of the possibility of training general internists and paraprofessionals to use flexible sigmoidoscopes adequately.

3. Comparison of the relative value of several different lengths of the flexible sigmoidoscope.

4. Comparison of the value of flexible sigmoidoscopy plus air contrast barium enema with that of endoscopy of the total colon (colonoscopy). The combination of flexible sigmoidoscopy and air contrast barium enema is considerably less expensive and may be more generally available. If the two are equally effective, the less expensive flexible sigmoidoscopy and air contrast barium enema could be an alternative approach.

The following recommendations were made for high risk groups:

1. The organization of cooperative studies to establish the proper surveillance procedures for high risk groups. Currently, there are no available data on the choice of surveillance methods for the followup of these patients. High risk groups include persons with inflammatory bowel disease (both ulcerative and granulomatous colitis), persons with various familial polyposis syndromes, persons with a strong family history of site specific cancer of the colon, persons in cancer families where colon cancer, endometrial cancer, and breast cancer seem to be clustered, and patients who have had a previous adenoma or colon cancer removed. Cooperative studies in high risk groups may be of value in the evaluation of diagnostic procedures and the effects of diet on the prevention of cancer.

2. The development of risk profiles and registries of those at high risk. Various centers need to pool and exchange information about profiles and to perform identifying tests requiring skills not available at every center.

3. The investigation of dye scattering techniques and other methods to identify dysplastic lesions. This should reduce the need for multiple biopsies in patients with ulcerative colitis.

4. The development of innovative approaches to identify persons in the general population who are at high risk for colon cancer but not included in the known high risk groups above.

Research to identify immunologic and biochemical markers in colonic washings, blood, and urine should be strongly encouraged.

The conference steering committee commented that:

"There are insufficient data to indicate that screening for colorectal cancer by stool occult blood testing reduces mortality from the disease in screened populations participating in clinical trials. More time is needed for the ongoing clinical trials to collect enough additional data for assessment of survival benefit, risk possibilities, and economic feasibility. Although it is recognized that decisions must sometimes be based on incomplete evidence, caution is advised in the development of recommendations about mass screening programs for colorectal cancer at this time. This caution is based on the absence of a clear demonstration of (a) improved survival rates in screened individuals with colon cancer or (b) a net margin of benefit to health in comparison with the costs and risks entailed in the further study of all positive occult blood reactions by barium enema and/or endoscopy.

"Until more knowledge of the benefits and risks of screening for this cancer site is available, mass screening demonstrations should not be initiated.

"Additional clinical investigations are strongly urged before occult blood testing can be endorsed for general use. However, because the method is commercially available for unregulated use by practicing physicians or other health care service providers, the following guidelines for professional use are recommended:

"1. A statement that benefit/cost/risk indices cannot be determined at this time.

"2. A statement that in the light of present information, the uncontrolled application of the method outside of special evaluation studies may not represent a wise use of health care resources and may not be of benefit to the recipients.

"3. Where used the technique should be limited to asymptomatic men and women over the age of 40 unless there are additional personal or familial risk factors.

"4. Where used the procedure should include:

"—A meat-free high fiber diet. (No consensus was

reached on the number of days prior to the first test.)

"—Storage of specimens for less than 4 days before testing.

"—No rehydration of slides when using Hemoccult II slides.

"—The recording of all results as positive or negative. Doubtful readings should be recorded as negative and trace readings as positive.

"—The handling of a single positive slide as if all slides are positive.

"5. At present all positive tests should be followed by complete examination of the colon by radiological and/or endoscopic means.

"6. Expertise and facilities for diagnosis and treatment should be readily available for followup.

"7. Fecal occult blood testing should not be used at present as a substitute for proctosigmoidoscopy or as a basis for clinical decisions in patients with symptoms of colorectal cancer.

"The major controlled clinical research trials which are evaluating colorectal cancer screening using occult blood testing should be continued. These are (1) the evaluation of occult blood testing performed annually in a study group as a part of the patient examination at the Preventive Medicine Institute—Strang Clinic in collaboration with the Memorial Sloan-Kettering Cancer Center; and (2) an evaluation of occult blood testing in combination with a diagnostic protocol in a control group, an annual screening group and a biennial (every two years) screening group at the Univ. of Minnesota.

"Because the definitive diagnosis of colorectal cancer must be geared to the proper interpretation of the pathology, including all the histologic variations in adenomas and the premalignant and malignant changes that may occur within them, the development of a uniform interpretation and nomenclature is needed. Workshops for this purpose may be useful.

"Professional organizations should educate the radiological, medical and surgical communities regarding the importance of an air contrast study in addition to the standard barium enema in the radiological examination of the patient suspected of having a colonic neoplasm or a small polypoid lesion.

"Professional organizations should encourage the assumption of responsibility by physicians for adequate cleansing of the colon in preparation for barium examinations. The risk and expense of this examination are not justified in poorly prepared patients."

The summary report of the lung cancer screening conference:

Lung cancer now accounts for about 14% of all cancer cases and 22% of all cancer deaths; men are affected about four times more frequently than women, but incidence in women is increasing more rapidly than in men. Cigarette smoking is the predominant cause in both sexes, but increased risk of lung cancer has also been reported in asbestos workers, coke oven workers, uranium miners, workers in certain metal smelting and refining plants, and in some branches of the chemical industry. In most instances that have been studied, cigarette smoking increased the risk of lung cancer among such workers. Generally, incidence has been found to be proportional to the dose or duration of exposure to the carcinogen. Variations in individual susceptibility, possibly due to genetic effects, immune factors, or other respiratory diseases, appear to play a role in lung cancer risk.

The pathogenesis of lung cancer has been deduced from histological studies of bronchial tissue from patients dying from lung cancer, and from smokers, ex-smokers, non-smokers and those without pulmonary disease who have died from other causes. Progressively increasing frequency of hyperplasia and of atypical cells has been found in the bronchial epithelium in proportion to the duration and amount of cigarette smoking. Although the frequency of these abnormal changes was greatest near the bifurcation of the major bronchi, they were also found throughout the tracheobronchial tree. All stages from slight hyperplasia to carcinoma-in-situ and invasive cancer were observed. The bronchial epithelium of ex-smokers showed histological evidence of reversibility of premalignant lesions after cessation of smoking. However, a basis for correlating the abnormalities of cells shed into the sputum with the various premalignant lesions that were detected histologically has not been clearly established.

In discussion of the requirements for satisfactory screening tests, care was taken to distinguish between screening and diagnosis, recognizing that the purpose of the former is to sort out rapidly and effectively those members of a population who probably have the disease in question from those who do not, leaving final determinations to be made by appropriate diagnostic methods.

Among the potentially useful methods for detecting presymptomatic lung cancer, only chest x-ray and cytological examination of the sputum were found to be sufficiently well developed at present to warrant consideration for practical application in screening. Strict control of standards and technical competence is necessary in both cases to ensure reliability. The two tests appear to be complementary in that peripheral tumors are detected more readily by radiography while sputum cytology is more effective in detecting lesions in the larger bronchi.

Interim results of controlled clinical trials that involve screening for lung cancer by radiography and sputum cytology were reviewed. These trials, now in progress, include a total of about 15,000 heavy smokers over the age of 45, judged to be at high risk of developing lung cancer, and a similar number of controls. The results will be analyzed to determine the effect of screening, and subsequent diagnosis and

treatment, on lung cancer mortality, but the data accumulated do not yet show any significant difference in mortality between the screened and the control groups. It is believed that any difference in mortality which might be achieved due to screening should be detectable in another two-three years.

Other studies on the effects of screening by radiography or sputum cytology, or both, on mortality from lung cancer also showed equivocal results.

The following conclusions express the findings of the conference:

1. Current prospective studies of asymptomatic individuals who have been screened for lung cancer by chest x-ray examination and sputum cytology do not at present show any evidence of a reduction in mortality from the disease. These studies must be continued for several more years before the accumulated information will be sufficient to allow a relationship between screening and mortality to be determined. Results of these studies should be kept under continuing review.

2. Until the value of screening for lung cancer by these methods has been demonstrated, mass screening programs should be limited to well designed, controlled clinical trials, with provision for analysis of results, and for proper diagnosis and treatment when required.

3. While some screening programs for lung cancer have been initiated among workers in certain industries, caution is strongly recommended in starting any new ones. Screened workers can not be assured of an overall benefit on the basis of existing data.

4. Continued research on better methods of screening for lung cancer, including improvements in the methods now under trial, should be strongly supported. At present, no other techniques appear to be ready for clinical application.

5. None of the recommendations above on the application of radiography and sputum cytology in screening is intended to apply to their diagnostic use in individuals who present to physicians with signs or symptoms that suggest lung cancer.

6. Whether for screening or diagnosis, the control of quality in performance and interpretation of radiography and sputum cytology is essential. Radiographic quality and interpretation can be assured through supervision by qualified radiologists and in screening situations through double reading of chest x-rays by appropriately trained individuals. Qualifications of cytopathologists and cytotechnicians should be assured, and the standards of performance of cytopathological laboratories should be determined by an appropriate accrediting body.

7. Since screening by current methods is unlikely to solve the problem of lung cancer control, strenuous efforts should be devoted to primary prevention. The greatest reductions in mortality can be achieved by cessation of cigarette smoking, and reduction or elimination of exposure to other respiratory carcinogens (environmental and occupational). Elimination of combined exposure to cigarette smoke and other airborne carcinogens is particularly important because their effects on lung cancer incidence are often synergistic.

The steering committee for the colorectal cancer screening conference included Joseph Painter, Univ. of Texas, chairman; Thomas Almy, Dartmouth; George Hutchison, Harvard; Charles Moertel, Mayo; and Paul Sherlock, Memorial Sloan-Kettering.

Lung cancer screening conference steering committee members were Howard Andersen, Mayo, and John Bailar, NCI, co-chairmen; Victor Archer, NIOSH; Robert Fontana, Mayo; Anthony Miller, NCI-Canada; Geno Saccomanno, St. Mary's Hospital, Grand Junction, Colo.; and William Tuddenham, Pennsylvania Hospital, Philadelphia.

CLEARINGHOUSE FINDS INSECTICIDE, HAIR DYE CARCINOGENS; LATTER HUMAN THREAT

The Clearinghouse on Environmental Carcinogens may be on its way out, with the reorganization of the government's toxicity testing efforts (*The Cancer Letter*, Nov. 17). Its subgroups are still in business, however, and are continuing to offer advice on which chemicals should be tested, how they should be tested, and what the results of completed tests mean.

The Data Evaluation/Risk Assessment Subgroup recently evaluated reports on 20 compounds which went through NCI's Carcinogenesis Testing Program, including the largest selling insecticide in the world and one of the most widely used chemicals in hair dyes (both were found to be carcinogenic in animals, and the hair dye compound was considered by the subgroup as a potential risk to humans).

Subgroup member Michael Shimkin, who had previously expressed concern over interpretation of bioassay results, opened this meeting with a statement that "absolute definitions of carcinogenesis are arrived at on the basis of data that are neither scientifically supportable nor societally responsible." Increases in lymphomas and hepatomas in rats or mice, without accelerated mortality and adequate control groups, are insufficient evidence to label chemicals as carcinogens, Shimkin said. Other points he made included:

- Increased incidences in hormonally regulated tissues should suggest primary effects on the endocrine system, rather than carcinogenesis.
- Rare tumors should indicate a need for more investigation, as should unfamiliar neoplasms that do not metastasize.
- Conclusions of carcinogenicity should be restricted to chemicals that induce "lethal neoplasms in a significant proportion of the animals" and only for such compounds should an estimate be made regarding potential human hazard.
- More stringent criteria should be used for deter-

mining carcinogenicity in both past and future studies.

Clearinghouse member William Lijinsky commented that the purpose of bioassay studies was to establish the safety of tested chemicals. Any chemical which increases the tumor incidence should be considered as less safe than a substance which does not, Lijinsky said.

Clearinghouse Chairman Arnold Brown responded that the function of the subgroup is not to deal with safety but rather to determine whether the evidence supports a conclusion of carcinogenicity.

Subgroup member Joseph Highland commented that the basic issue relates to the extent of evidence necessary to determine carcinogenicity. He said that differences arise because individuals disagree on the extent required for a determination. The level of evidence on which conclusions are now based is adequate, Highland insisted.

The subgroup agreed with the Program report on toxaphene, which R.S. Waritz, representing the manufacturer, Hercules Inc., said was the largest selling insecticide in the world. The report found the compound induced a neoplastic response in the rat thyroid and the mouse liver and that there was an increased number of liver carcinomas in low dose treated male rats.

Clearinghouse member David Clayson, primary reviewer of the report, agreed with the conclusion that toxaphene was carcinogenic in animals but cautioned against estimating the potential hazard for man, particularly since no evidence exists that polychlorinated alkanes or terpenes are human carcinogens.

Clayson noted that the test compound came from a single batch of toxaphene. Since it is a mixture, he wondered if the carcinogenic components would be common to all batches. He recommended that the test batch be analyzed to determine its quantitative similarity to other batches of toxaphene in general use.

Program Director Richard Griesemer said that although the staff viewed the thyroid tumors as "suspicious," the histopathology was confirmed at several review levels. He noted that the liver tumors in mice were clearly treatment related.

Waritz said that Hercules disagreed with the conclusion of carcinogenicity in animals. Hercules consultants who evaluated the histopathology and statistics concluded that the follicular cell thyroid tumor incidence in treated and pooled control male rats was virtually identical, Waritz said. He insisted that the incidence of follicular cell thyroid tumors in females was not statistically significant. Classic thyroid carcinogens induce mainly bilateral tumors, whereas those observed in the control and treated animals were essentially unilateral, Waritz said. He objected to the use of the term "carcinogen" in reference to benign tumors. He said there was a discrepancy in the historical control tissue count between that given in the report and the number found in the Hercules evaluation.

The subgroup approved the report without making any reference to possible human risk, leaving that issue to the Environmental Protection Agency and the courts, when and if EPA decides to take regulatory action.

It was a different story with 2-nitro-p-phenylenediamine, which T.F. Corbett, representing Clairol, said has been a compound commonly used in hair dyes since the early 1900s. The subgroup approved the report which found it carcinogenic in animals and also determined that it should be considered a potential human risk.

Brown, the primary reviewer, said that the bioassay data indicated a positive association between the induction of liver tumors and treatment in female mice. He agreed that the number of control mice used was too small but said that should not affect the interpretation of results. Based on the bioassay and on mutagenicity findings in salmonella, Brown concluded that the compound may pose a risk to humans.

Subgroup member Louise Strong questioned the relevance of the route of exposure. She noted the histopathological description of the liver tumors indicated they were composed of large eosinophilic hepatocytes and wondered if this characteristic was sufficiently unusual to add to the significance of the tumors. She said the questionable relevance of the route of exposure prevented a statement regarding the potential human risk. The mutagenicity data was of questionable significance because of the weak positive response observed, she said.

NCI staff member Jerrold Ward said that the liver tumors in treated female mice were morphologically different from ones observed in control animals. The treatment relatedness of the liver tumors could be based on an increased incidence and morphological difference as compared to controls, Ward said.

Shimkin questioned the significance of the results, given that a positive finding was observed only in female mice. He suggested that a true positive would not have been sex linked. Lijinsky said he has found that several nitrosamines induce tumors in one sex of rats and none in the other.

Clearinghouse member Norton Nelson, referring to the appropriateness of the route of exposure, commented that the accepted practice for testing compounds for carcinogenicity is to expose animals to the largest doses that are compatible with survival. It is legitimate, he said, to use the oral route to increase the exposure level, even though humans may be primarily exposed through the skin. He noted that one reason for using high dose levels is to overcome the statistical insensitivity of the bioassay, resulting from the use of relatively small numbers of animals. Despite the difference in exposure routes, Nelson said, the compound must be considered to pose some possible risk to humans.

Strong moved that the report be accepted as written and that no statement be made assessing the human risk. She argued that the term carcinogen should not be used since the compound induced primarily hepatocellular adenomas. She predicted that the hepatocellular carcinomas would not be statistically significant if they were evaluated independent of the adenomas. She also emphasized that the response was observed in only one sex and species.

Highland argued that it was appropriate to combine adenomas and carcinomas in evaluating results. Lijinsky said that similar compounds have been demonstrated to be absorbed through the skin into body fluids and excreted in the urine.

Griesemer said that a conclusionary statement had been omitted from the report. The statement should have included that the compound was considered to be carcinogenic in the female mouse. Staff member Cipriano Cueto added that the increased incidence was statistically significant at the high dose level and that the conclusion was supported by a trend analysis and a comparison of the liver tumor incidence with historical control data. Griesemer said it was appropriate to combine the benign and malignant liver tumors, since the adenomas are considered to be part of a spectrum leading to carcinomas.

Based on the revised conclusion, Strong withdrew her motion.

Corbett, presenting Clairol's case against the finding of carcinogenicity, argued that:

—The only significant finding was increased incidence of hepatomas in treated female mice.

—Metabolism would not be the same when given orally as when applied as a hair dye used by humans.

—Solubility of the compound differs considerably in aqueous and acidic systems, and absorption would be facilitated by acidity of the GI tract.

—Dose in the high dose group was a 150,000-fold exaggeration of human exposure.

Nevertheless, the subgroup approved Highland's motion that the compound be considered a potential human risk, with two abstentions.

The compound 3,3-dimethoxybenzidine-4,4-diisocyanate is an experimental compound which would be used in coatings, gaskets, and shock absorbers, among other items, if it is considered acceptable. In what may be one of the rare instances when a compound is found carcinogenic before it becomes widely used, the subgroup agreed unanimously that it was an animal carcinogen and that it posed a potential carcinogenic risk to man.

Compounds found to be carcinogenic in animals but for which the subgroup did not recommend that they be considered potential threats to humans were:

- N,N-diethylthiourea, an industrial anticorrosion agent.
- Trimethylthiourea, a chemical intermediate.
- Piperonyl sulfoxide, an insecticide enhancer.

Other chemicals reviewed and found in the Program not to be carcinogenic included:

- Titanium dioxide, a white pigment widely used in cosmetics, drugs and foods. However, there were enough questions to lead the subgroup to recommend the compound for retest.
- Endrin, parathion, dl-menthol, sulfisoxasole, GI vat yellow 4, piperonyl butoxide, carbromal, n-1 (1-naththyl) ethylenediamine hydrochloride, lithocholic acid, 4-(chloroacetyl) acetanilide, a solution of B-nitrostyrene and styrene, 2,4-dimethyoxyaniline hydrochloride, and dibenzo-p-dioxin.

RFA ANNOUNCEMENT

New Approaches in Surgical Oncology

NCI is accepting applications for support of research projects relevant to cancer treatment by the introduction of new approaches in surgical oncology. The Div. of Cancer Treatment desires to support research studies that fall within three general areas of investigation, for which surgical oncology expertise and experience are needed. These fall into the following general areas:

1. Investigations on the introduction of modified or new surgical procedures, possibly in conjunction with other modalities, as substitutes for standard surgical or other standard treatment approaches. For example, these studies may range from the use of laboratory animal models to explore clinically relevant combined modality treatment, to actual clinical trials in cancer patients designed to establish the value of less extensive surgery relative to standard radical approaches. These trials may be internally controlled studies or pilot programs designed to be adequate for comparison with appropriately matched historical controls. Novel surgical procedures or development and implementation of new methodologies and techniques with which to carry out new approaches would be relevant. For example, the introduction of limb-sparing operations in osteosarcomas with development of appropriate prosthesis would be investigations responsive to the aims of this announcement. In addition, studies evaluating the role of cytoreductive surgery in advanced ovarian or pulmonary cancer may also be considered responsive. Although a principal investigator with a primary interest in hyperthermia, immunotherapy, chemotherapy or radiotherapy may be acceptable, grants must reflect extensive surgical expertise for these approaches to be considered adequate for evaluation.

2. Development and testing of therapies dependent on vascular interruption or perfusion. These investigations could include animal laboratory studies or clinical studies in cancer patients either as comparative clinical trials or individual pilot programs evaluating new techniques. Studies to be included could test the value of graded or total interruption of vascular supply by a variety of techniques on local tumor control or resectability, or by studies includ-

ing the isolation of a local area for perfusion with cytotoxic agents. The emphasis should lie in development and evaluation of new techniques and methodologies rather than testing of new chemotherapeutic agents by well-established techniques of vascular infusion. However, well designed clinical trials comparing the addition of such local approaches to other therapeutic measures will be given appropriate consideration.

3. Studies on clinical and biological consequences of surgical procedures. These investigations could involve solely experimental tumor models, or cancer patients, or both. Pertinent topics could include assessment of cell kinetic changes, immunologic studies, metastatic behavior following primary surgery, and metabolic or nutritional changes occurring in the host as a result of tumor presence or surgical therapy.

All of the areas of investigation described above may inlcude studies on biological markers in conjunction with clinical trials, including correlation of such markers with staging of the disease and with consequences of treatment.

Applications should be submitted on form PHS 398, utilizing the conventional presentation for grant applications. In both the covering letter and the application, reference should be made to RFA NIH-NCI-DCT-7.

For further information contact: Gregory Wolf, Special assistant for surgical oncology, Clinical Investigations Branch, DCT-NCI, Room C819, Landow Bldg, Bethesda, Md., 20014, phone 301-496-4844; or Raymond Weiss, Chief, Clinical Investigations Branch, DCT-NCI, Room C803, Landow Bldg., Bethesda, Md. 20014, phone 301-496-6056.

Deadline for receipt of applications is March 1, 1979, for possible funding on or after Dec. 1, 1979. Funding may be requested for a period of up to five years. Renewal of projects beyond the original funding period (under this announcement) is not contemplated, although successful applicants may then apply for traditional research grants.

Funds will be earmarked in support of these projects, although the specific amount cannot be determined at this time.

In order to encourage communication among investigators, an annual meeting of successful applicants will be arranged.

NCI CONTRACT AWARDS

Title: Pathology quality control, modification
Contractor: Vanderbilt Univ. School of Medicine, $138,063.

Title: Development of detailed methods and protocols for carcinogenesis screening using cell culture assays—task II—BALB 3/T3 cells, task III—Fischer rat embryo cells
Contractor: Arthur D. Little Inc., $586,015.

Title: Encapsulation of retinoids for administration in laboratory diets
Contractors: Univ. of Georgia, $203,040; and Southwest Research Institute, $328,586.

Title: Study of pharmacokinetics of anticancer drugs
Contractor: Univ. of Texas System Cancer Center, $335,631.

Title: Planning and analytical support services
Contractor: CDP Associates, $905,121.

Title: Synthesis of kilogram amounts of retinoids for long term animal studies
Contractor: Southern Research Institute, $997,414.

Title: Comprehensive cancer centers communications network, renewal
Contractor: Memorial Hospital, New York, $432,834.

Title: Biostereometric assessment of nutritional status of cancer patients and normal indivuals
Contractor: Texas Institute for Rehabilitation & Research, $305,981.

Title: Gustatory evaluation of cancer patients
Contractor: Univ. of Pennsylvania, $141,770.

Title: Induction of colon tumors in guinea pigs
Contractor: Cornell Univ., $100,951.

Title: Prototype clinical chemotherapy program in cancer control, renewal
Contractor: Cornell Univ. Medical College, $156,222.

Title: Whole body inpedence as a predictor of total body water and extracellular fluid volume
Contractor: Univ. of Pennsylvania, $250,518.

Title: Investigational studies for gastrointestinal cancer, modification
Contractor: Mayo Foundation, $61,000.

Title: Establishment of a rodent production colon, continuation
Contractor: Charles River Breeding Laboratories, $339,523.

Title: Studies of natural inhibitors of chemical carcinogens
Contractor: Univ. of Minnesota, $654,391.

Title: Significance of mutation in carcinogenesis
Contractor: Johns Hopkins Univ., $309,124.

Title: Animal models for treatment of minimal residual systemic tumor
Contractor: Pennsylvania State Univ., $231,492.

Title: Effect of regulations on conduct of cancer treatment research
Contractor: Carnegie-Mellon Institute, $294,000.

Title: Mass screening for breast cancer by electronic infrared pattern recognition, continuation
Contractor: Univ. of Oklahoma, $117,200.

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-CN-95436-02

Title: *Pathology continuing education in early breast, cervical and colorectal cancers*

Deadline: *Feb. 15*

NCI intends to issue an RFP to obtain the services of an organization with demonstrated capability to supplement existing programs in continued pathology education, especially for pathologists unable to regularly attend national workshops, including recent planning and discussions focused on early (minimal) cancers of the breast, cervix, and colorectal area.

NCI has a great need for these concepts and standards in pathology in its various programs and can play a potentially great role in supporting efforts to pull together both the traditional and the relevant recent discoveries of basic, morphologic, and clinical research focused educational materials in cancer. These would supplement (rather than just do more of the same on different scales) such ongoing pathology and the regular national and regional workshops, slide seminars, postgraduate pathology courses, convention presentations and other efforts as are presently offered by several pathology associations and institutions.

NCI requests additional educational emphases on the difficult to diagnose small or "minimal" cancers (i.e., pre-cancerous or premalignant, non-invasive and early invasive cancers) limited for this contract to those of the breast, cervix, and colorectal sites.

NCI will support the development and production, and provision and distribution of updating and standardizing diagnostic pathology educational materials and if necessary smaller necessary items of specialized educational equipment in possibly 300-500 large and small centers of pathology education and practice to use in teaching, seminars or individual study.

1. Medical schools and osteopathic medical schools.
2. Major hospitals with pathology residency programs.
3. State and metropolitan pathology societies.
4. Pathologists in the field for home/office study, particularly those estimated 50-70% of the 12,000 pathologists in the U.S. who do not attend many, if any, of the above mentioned workshops, seminars, professional educational courses.

NCI intends to fund one contractor for this effort. An RFP will be mailed to requestors on Dec. 15.

Contract Specialist: Susan Yablon
Control & Rehabilitation
301-427-7984

SOURCES SOUGHT

RFP NCI-CM-97270

Title: *Support services for extramural clinical trials in testicular cancer*

Deadline: *Dec. 8 (for submission of resumes)*

Only one source is known which can perform the above. That source is Georgetown Univ. Specifically, the work required involves monitoring, coordinating, preparing and maintaining materials and reports and serving as organizational center for the intergroup cooperative study of testicular cancer. The source shall provide administrative support coordination, preparation and communication of materials, and provide assistance in protocol design. The source shall carry out randomization procedures for the clinical trials, working in coordination with the statistical contractor, as well as with the clinical research contractors. The source shall monitor drug requests and maintain records, and obtain copies of patient records as requested for reference for chairmen/principal investigators.

The source shall prepare progress and annual reports and agenda and minutes of meetings for distribution to the investigators and to NCI. It is expected that they will meet bi-weekly with the project officer at NCI.

If any organization feels that it has the demonstrated technical capability, the submission of complete and concise resumes is invited. Such resumes must clearly demonstrate extensive experience in the area of services for support for cancer trial and substantial experience in working with related task forces, cooperative groups and projects involved in similar research. Information submitted must be pertinent and specific in the technical area under consideration. Unnecessarily elaborate brochures are neither required nor desired. Resumes must be submitted in 10 copies.

Contracting Officer: Charles Lerner
Cancer Treatment
301-427-8125

The Cancer Letter —*Editor* JERRY D. BOYD

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