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Blacks At 11% Greater Cancer Risk, 27% Higher Mortality, NCI Tells President's Cancer Panel

Black Americans have an 11 percent greater risk of developing cancer than whites, a 25 percent lower five year survival rate and a 27 percent higher mortality rate, the latest data collected by NCI show. The data were presented to

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In Brief

Senate Confirms Sullivan, Who Fires 100 HHS Political Appointees; Wyngaarden Still On Job

LOUIS SULLIVAN was confirmed as secretary of the Dept. of Health & Human Services by a vote of 99-1, the negative vote cast by Jesse Helms (R-NC). One of Sullivan's first actions was to notify the department's 100 political appointees that they would be out of jobs as of April 1. The White House had directed department secretaries to fire "Schedule C" political appointees to make way for new Bush Administration appointments. No NIH employees are Schedule C. Meanwhile, NIH Director **James Wyngaarden**, a presidential appointee, remains on the job despite having submitted his resignation at the direction of the White House. Wyngaarden feels strongly that it would be a mistake to politicize the NIH directorship by replacing him at the start of a new administration. He has pointed out that no President has ever fired an NIH director early in his first term, although Richard Nixon axed Robert Marston at the start of his second term. . . . **SUZANNE BRENNAN** has been named administrator of Fox Chase Network Inc., a subsidiary of Fox Chase Cancer Center formed to manage community oncology programs established as joint ventures with Philadelphia area hospitals. Brennan has been associate administrator of the Network. . . . **ISRAEL CANCER** Research Fund will award $2 million in grants to investigators conducting cancer research in Israel when the Fund's scientific review panel meets March 13-14 in New York. Founded in 1975 by American, Canadian and Israeli physicians, ICRF is the largest private organization supporting cancer research in Israel. . . . **LONG DELAY** (nearly a year) in publication of the node negative breast cancer study results by the "New England Journal of Medicine" appears to have justified the controversial clinical alert NCI issued last May. "We saved nine months," Div. of Cancer Treatment Director Bruce Chabner commented when the article finally appeared last month. He pointed out that 5,000 women a month are diagnosed with node negative breast cancer.

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Blacks Lead In Cancer Risk, Deaths; DC Cancer Death Rate Highest In US

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the President's Cancer Panel, which met at Howard Univ. in Washington this week as part of what Chairman Armand Hammer has said is his plan to focus for the next year on minority cancer prevention, diagnosis and treatment.

The Panel heard comments from NCI Director Samuel Broder, Howard Cancer Center Director Kenneth Olden, and Reed Tuckson, District of Columbia public health commissioner, on what some officials are calling the "differential burden" of cancer incidence and mortality among minorities.

Broder told the Panel and the audience at Howard's Blackburn Auditorium that reducing the gap is one of his major priorities as NCI director. He outlined several steps NCI is taking to address the problem.

In a comment that he has repeated to several audiences since becoming director, Broder said, "I do not wish the next director of NCI to be faced with the same set of statistics showing a disproportionate rate of deaths from cancer among minorities."

The Panel "is in full agreement with Dr. Broder on this matter," said Hammer in a statement read by Panel member William Longmire. Hammer said he has the flu and is under doctor's orders not to travel.

"We are all aware that there is a disproportionate incidence of cancer in minorities, and that this gap seems to be growing yearly," Hammer's statement said.

Some reasons for the gap seem to be tobacco use, heavy alcohol use, poor nutrition, occupational risk, and patterns of medical care related to early diagnosis and treatment, Broder and other NCI officials said.

Nowhere is the cancer death rate higher than in the District of Columbia. The city has a cancer death rate one third higher than the national average, which translates into nearly 200 more cancer deaths per year than would be expected given the city's population, Barry Gauze, acting chief of medical oncology at the Howard Cancer Center told the Panel.

According to one estimate, there will be 1,700 cancer deaths in D.C. this year, a death rate of approximately 365 deaths per 100,000.

"There's no question that cancer is a serious problem in the District of Columbia, the question is how can we resolve this problem quickly," Broder said.

Nationwide figures collected by NCI's SEER program for 1981 to 1985 show that even when data is adjusted for age, blacks have a 6 percent higher incidence rate than whites for all cancer sites, and a 27 percent higher mortality rate than whites, according to Claudia Baquet, chief of the Special Populations Branch of NCI.

Blacks have an especially high incidence of cancers mainly caused by smoking, including oral, esophageal, lung, and larynx. Blacks have three times the incidence rate and mortality rate of esophageal cancer than whites.

Other data Baquet presented:

Oral cancer--blacks have a 28 percent higher incidence rate and a 77 percent higher mortality rate than whites. Stomach--67 percent higher incidence, 90 percent higher mortality. Pancreatic cancer--46 percent higher incidence, 37 percent higher mortality. Larynx--37 percent higher incidence, 92 percent higher mortality. Lung cancer in black males--43 percent higher incidence, 33 percent higher mortality. Prostate cancer--72 percent higher incidence, 117 percent higher mortality. Multiple myeloma--141 percent higher incidence, 100 percent higher mortality.

In addition, black females under age 40 appear to have a 50 percent higher incidence and 3 percent higher mortality rate of breast cancer. Over 40, white females have higher death and incidence rates. Baquet said these were preliminary data, but that "in view of various breast cancer screening campaigns, this warrants further study."

Black females have twice the risk of getting cervical cancer that white females, and are almost three times as likely to die of it. "This cancer is preventable," Baquet said.

The data also show that blacks have a higher death rate from all cancers at every age group.

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Although the death rate for cervical cancer increases as women age, that increase is even greater for black women, Baquet said.

"This makes a striking statement," she said. "We know that women in the reproductive years of their lives have periodic contact with prenatal and family planning services, including access to routine Pap smears. Whereas, as a women advances in age, she loses that contact. We must come up with program interventions that will allow a woman to have pelvic health all throughout her life despite moving out of the reproductive years."

Five year survival data for black and white cancer patients are also show a gap. Of the 16 cancer sites for which survival data was collected, blacks survive less than whites for 10 of those sites.

Overall, black five year survival is 70 percent of the white survival rate. For uterine cancer, survival is 40 percent lower in black patients. For bladder cancer, survival is 30 percent lower in blacks. Oral cancer, 30 percent lower survival; breast, 20 percent lower; rectal, 30 percent lower; cervical, 10 percent lower.

Baquet listed several factors that increase the risk of cancer.

--Tobacco. The prevalence of cigarette smoking in blacks is higher than that of whites, but blacks tend to be lighter smokers. About 40 million Americans have quit smoking since 1984, including 3 million blacks. However, in 1989, about 55 million Americans over age 18, or 30 percent of the population, still smoked.

There has been some progress in getting black men to stop smoking, Baquet said. In 1965, 60 percent of black men smoked, compared to 40 percent now. However, more black women smoking than white women: 32 percent of black women smoke, compared to 28 percent of white females.

--The combination of smoking and heavy alcohol use.

--Diet and nutrition. The typical black diet, Baquet said, is high in food preparation practices than increase carcinogens, such as frying, and the addition of fat at the end of food preparation process.

--Occupational risk is thought to contribute to about 4 percent of cancer deaths internationally, Baquet said. "We feel there is possibly a greater percentage of occupational risk for blacks," she said. The black population has a higher proportion of blue collar workers, tend to be less skilled and may suffer from discriminatory work assignments in certain industries, she said.

For example, in the steel industry, a higher proportion of blacks are assigned to work the coke ovens, which contributes to lung cancer.

--Delay in seeking medical care. Blacks will delay for six months to a year before seeking treatment, Baquet said. This results in more advanced stages of cancer.

--Lack of health insurance. About 22 percent of blacks do not have health insurance, compared to 13 percent of whites.

--Quality of care. Economically disadvantaged blacks use outpatient facilities and emergency rooms at higher rates than whites. Since emergency rooms are geared for catastrophic conditions, they generally do not provide the consistent care needed in preventing and treating cancer.

--Possible differences in immune function in relation to socioeconomic status. There is infomation to suggest that undernourished or lower income blacks will do poorer than better nourished or upper income blacks in responding to treatment. However, this data is very small and more studies need to be conducted, Baquet said. When data is adjusted for socioeconomic status, the gap between black and white mortality goes down, but not entirely.

--Histologic differences. Blacks develop more agressive tumors for uterine cancer. "We don't know exactly why," Baquet said.

--Co-morbidity, or the appearance of other diseases in the same cancer patient, such as diabeties, which has ramifications for therapy.

Gause presented data on the black cancer death rate for D.C. compared to the U.S. and Chicago, which was picked as a comparable city.

From 1970 to 1979, the death rate per 100,000 in D.C. was 349 for black males, compared to 287 in Chicago and 232 in the U.S. For white males, the rate is 210 in D.C., 230 in Chicago and 204 in the U.S.

For black females, the rate is 172 in D.C., 164 in Chicago and 133 in the U.S. For white females, the rate is 150 in D.C., 149 in Chicago and 132 in the U.S.

Gause said there is not enough data to support an environmental factor for the high D.C. rates.

In his remarks, Broder said the role of NCI in addressing the high rate of cancer among minorities is "the generation of knowledge."

"In my lexicon, the phrase 'generation of knowledge' means the promotion of advances in science and technology to help all members of

society," Broder said. "I am concerned that as new technologies for the prevention, early diagnosis and treatment emerge, the differential burden for cancer mortality will get worse. We must make sure that knowledge is applied on an equitable basis."

Broder said there are "signs of movement in the right direction," including Louis Sullivan's appointment as secretary of HHS. Sullivan was instrumental in getting the National Cancer Advisory Board to support a program to make spaces available at selected cancer centers for minority health professionals, which was called the National Black Leadership Initiative.

"It is important that black leaders be mobilized across the country," Broder said. "NCI can conduct research and disseminate knowledge, but individuals have to make personal changes, and changes have to occur in the community."

Cancer mortality "could be cut in half using what we already know about cancer prevention, early diagnosis and treatment," Broder said. "What we really need to do is carry out these good ideas. In order to make a change, a program has to be created and integrated into the structure of the community."

Broder stressed that an individual must take responsibility for his or her health. "We would hope to ensure that individuals play an active role and become partners in their own health care," he said.

No Single Test

He cautioned against reducing the push for better health care to "a single test."

"While certain tests will be of extreme importance, and may by themselves be crucial in changing certain cancer death rates, I do not beleive it is appropriate, and may send the wrong signals to people, to suggest that cancer or other health related issues are reduced to a single test or technology."

Broder said NCI is currently reviewing several programs with respect to addressing the minority cancer problem, including cancer prevention and control, the grants process, the Cancer Centers Program, and cancer communications.

"We wish to use every institute mechanism available to help address the issue of the cancer death rate in minorities," he said.

One way that minorities could get better treatment is to enroll in NCI clinical trials, Broder said.

"It is essential that memebers of the minority community seek seek out the appropriate clinical trials," he said.

To encourage minority enrollment, NCI began a minority satellite program three years ago to supplement the budgets of institutions capable of enrolling large numbers of minority patients to clinical trals. The supplements pay for personnel, data management and related expenses. Currently there are 18 of the grants operating in Newark, Chicago, New York, Boston, Louisville, Miami, Detroit, DC and several other cities.

In his statement, Hammer said the Panel was "pleased" with the appointment of Sullivan to the Cabinet, since his previous experience on the NCAB "gives him a special understanding of the National Cancer Program, as well as the specific problem of reducing the excessivley high mortality rate of blacks and other minorities of cancer."

Hammer's statement continued: "We are confident the situation can be improved by better coordination and communication between NCI and the local community. Certainly the Howard Cancer Center has a role to play in this process."

However, Hammer said, the Panel "is very concerned that recent budget increases for cancer research and training have not been sufficient even to sustain the existing activity. This means a great deal of very good research is not being funded."

Olden told the panel that the Howard Cancer Center has as its primary mission "to decrease the minority cancer incidence both locally and nationally."

The center's other goals are to become a national leader in training black oncologists, and to develop state of the art treatment.

He said the hospital is treating 10 percent more patients this year than last year. "We ought to be treating three times more patients than we do," he said.

Olden said Howard plans to expand its participation in institutional and cooperative clinical trials, and expand its cancer screening and detection activities. The center plans to buy a mobile mammography unit.

Howard is also a member of the D.C. Cancer Consortium, a group of hospitals. One goal of the consortium was to upgrade the tumor registry in the city, which was "in a shambles a few years ago," Olden said. The city also has a Bureau of Cancer Control as a result of the consortium's efforts, he said.

In response to a question from the audience on funding, Olden said that NCI "has bent over backwards to make sure the Howard Cancer Center stays in existence."

Study Of Diuretic Use As Risk For Renal Cell Cancer Given DCE Approval

NCI is planning a study to determine whether the use of diuretics causes an increased risk of renal cell cancer.

There is strong evidence suggesting that diuretic use, as well as obesity and smoking, are associated with renal cell cancer, including a 1988 study in Minnesota by NCI researchers, but the data is not conclusive enough to pinpoint diuretics as a risk factor.

A concept for a master agreement for support services for the study was approved unanimously by the Div. of Cancer Etiology Board of Scientific Counselors. The project is estimated to cost total of $900,000 over four years.

The number of cancer centers that would take part in the study "remains to be seen," said Joseph McLaughlin, an epidemiologist in the Epidemiology & Biostatistics Program and one of three project officers for the contract concept.

Other Risk Factors

The population based study would take place in selected areas of the U.S. that have relatively high rates of renal cell cancer and large numbers of individuals of Scandinavian and German extraction, who have been found to have a higher risk of renal cell cancer, the concept statement statement says. Other risk factors, including smoking, obesity, genetic susceptibility, diet pill use and the use of drugs containing phenacetin and its active metabolite, acetaminophen, also will be studied.

The concept was part of a master agreement concept previously approved by the Board, but the Board had asked that any request for funds over $500,000 be brought back for consideration.

"This is an important study," said Board member Roy Shore.

The Board also approved other contract concepts, including recompetition of a $3 million contract for studies of tumor induction, biological markers and tumor therapy in primates, a project that has continued since 1961.

The Board gave concept approval to two noncompetitive procurements. One is for procurement of human tissues from donors with an epidemiology profile, an interagency agreement with Walter Reed Army Medical Center estimated to cost $112,351 over four years. The other is for dosimetry support for studies of radiation workers, held by Tech/Ops Landauer Inc., estimated to cost $235,000 for five years.

Concept statements for the competitive contracts follow:

Diuretic use and other factors in the etiology of renal cell cancer. This is a new concept for master agreement order, proposed first year award $225,000, proposed project plan award of $900,000 over four years.

In 1988, approximately 23,000 cases of kidney cancer were diagnosed in the U.S. and about 10,000 died from the disease. Almost 85 percent of these neoplasms are adenocarcinomas of the renal parenchyma, or renal cell cancer. From 1969 to 1985, incidence rates for renal cell cancer in both sexes have increased 30 percent. The etiology of this cancer remains for the most part an enigma, although a population based study by NCI has shown that perhaps a third of these tumors among men and a fourth among women can be attributed to cigarette use.

A number of other etiologic clues have recently emerged. Of special interest is an association of renal cell cancer with diuretic use observed in a small case control study based in Los Angeles. Women who used diuretics (24 cases and 10 controls) for six weeks or more during any one year had almost a five fold increased risk. The excess was found among those who were hypertensive as well as those who were not.

Use was common: 50 percent of the female cases and 20 percent of their controls took diuretics. These results were confirmed in the NCI study of renal cell cancer which was completed in 1988 in Minnesota. As in the Los Angeles study, the risk of renal cell cancer associated with diuretics was mainly in women, with female users having about twice the risk as nonusers; however, the elevated risk was seen among nonhypertensive individuals but not among hypertensives. Eighteen percent of the female cases and 10 percent of the controls used diuretics prior to 1974. Adjustment for weight and cigarette smoking did not affect the risk among nonhypertensives. In neither study was information collected on length of use, type of diuretic, or reasons for use.

The observed relationship seems biologically plausible, since diuretics act directly on the renal tubules where renal cell cancers originate. Recently completed bioassays have found an increased incidence of tubular cell adenomas of the kidney in rats given the diuretic hydrochlorothiazide, and an increased incidence of renal adenomas and carcinomas in rats given the diuretic furosemide. Furosemide also has been found to increase chromosomal aberrations in Chinese hamster cells and human lymphocytes. The public health implications of these findings are significant, as diuretic use has increased since the 1960s and early 1970s, the period covered by the two epidemiologic studies. A recent survey of physician prescription practices showed diuretics to be the second and third most commonly prescribed drugs in the U.S., and hydrochlorothiazide to be the most common generic ingredient prescribed by physicians.

In view of the widespread use of diuretics and suspicions about their possible role in renal cell cancer, a timely assessment of risk is proposed using a large scale case control study.

This study would provide an opportunity to clarify a number of other potential risk factors for renal cell cancer. The use of phenacetin containing drugs will be evaluated, since the NCI study and two other recent studies of renal cell cancer have reported an increased risk with phenacetin use. In earlier studies, heavy phenacetin use was causally associated with transitional cell carcinomas of the renal pelvis, but its relation to renal adenocarcinomas was unknown. Although this drug is no longer marketed in over the counter or prescrip-

tion preparations in the U.S., acetaminophen is the active metabolite of phenacetin, and it is now the most popular analgesic in the U.S. The pharmacologic similarity of phenacetin and acetaminophen and the increasing use of acetaminophen warrants investigation of this relatively new analgesic, which was not widely used until the 1970s. The NCI and Los Angeles studies found a suggestive association with diet pill use, which deserves further study.

A consistently observed risk factor for renal cell cancer is high relative weight. This association was reported initially only in women, but two recent studies have found a significant increase in risk for overweight men. More detailed investigation of weight gain over a lifetime is necessary to evaluate timing effects. In the NCI study, weight gain in later life seemed to be especially important. Dietary factors such as animal protein and meat intake have been related to an increased renal cell cancer risk in case control studies. More complete dietary assessment including caloric and fat intake and methods of cooking is needed to better assess the role of diet and nutrition in the etiology of this neoplasm.

Although cigarette smoking has been linked to kidney cancer in cohort studies and to renal cell cancer in case control studies, some studies have not found an association. A recent IARC monograph on the carcinogenic risk of tobacco smoking does not include renal cell cancer among the sites for which there is sufficient evidence of a causal association with smoking. A large, population based study is necessary to clarify this relationship.

Little information is available on genetic susceptibility to renal cell cancer, despite occasional reports of familial aggregation and association with the dominantly inherited von Hippel-Lindau syndrome. In a familial aggregation of renal cell cancer studied by NCI staff, a 3.8 translocation of chromosomes was found in peripheral blood lymphocytes of affected members. Subsequent studies have revealed abnormalities of chromosome 3 in renal tumors of nonfamilial cases.

In the proposed investigation, patients with a positive family history, bilateral disease, or early age at onset, will be asked to donate blood, as will affected relatives, to permit further characterization of chromosomal changes in relation to this tumor. A portion of the blood will be stored to permit examination using future molecular techniques. Whenever possible, in familial occurrences, paraffin embedded specimens of tumors will be obtained for DNA analysis. Any genetic defects observed will be related to epidemiologic variables of genetic or environmental determinants.

A number of other suspected factors will be evaluated including exposure to asbestos, coke oven emissions and gasoline. The last exposure is noteworthy since unleaded gasoline has induced renal cancer in animals. Individuals of German and Swedish background in the U.S. have been found to be at elevated risk for this neoplasm, but the reasons for ethnic predisposition are unknown.

The main objective of the proposed study is to examine in detail the role of medicinal agents in the etiology of renal cell cancer, with special attention to diuretics. The study also will clarify other proposed risk factors such as obesity, smoking, diet and nutrition, occupational exposures and genetic susceptiblity.

A master agreement order will be competed among organizations holding master agreements to provide support services for studies to address emergent cancer issues. The contractor will assist NCI and collaborating groups in a population based study performed in selected areas of the U.S. In order to increase the likelihood of success, the areas will be at high risk for renal cancer and have a large number of individuals of Scandinavian and German background. The collaborating research units should demonstrate response rates in recent studies of at least 85 percent for both cases and controls. Cases will be prospectively ascertained over a two year period or until 600 cases between the ages of 20 to 79 have been identified. All cases will be microscopically verified. Controls will be chosen from the general population, using random digit dialing procedures for those 20 to 64 years, and the records of the Health Care Financing Administration for those 65 to 79 years old. Controls will be frequency matched to cases by age, sex and race.

Subjects will be interviewed in person, using a questionnaire designed by NCI investigators. The instrument will focus on medications, body weight, diet, tobacco use, medical and occupational history. Questions on diuretic use will be more detailed than previous studies, with information on amount, timing and reason for use.

Blood will be drawn and stored from cases with a positive family history of renal cancer, bilateral disease, or a diagnosis under the age of 45 years. Peripheral leukocytes will be examined for cytogenetic aberrations, particularly involving chromosome 3, and stored for future studies. Paraffin embedded tumor specimens of familial cases also will be obtained for studies of molecular genetic defects.

Analysis of the data will be conducted by NCI staff in collaboration with the participating centers. Standard methods for case control data analysis will be employed. Summary odds ratios, corresponding confidence intervals, and population attributable risks will be calculated, with logistic regression models developed for further analysis of multivariate relationships.

Using an alpha level of 0.05 (two sided), a study with 600 cases and 600 controls will have a 95 percent chance to detect an odds ratio as low as 1.9, assuming a 10 percent prevalence rate for diuretic use. A more recent NCI study involving other cancers in three areas of the U.S. found a prevalence rate of diuretic use of almost 25 percent among the population based controls. This rate would permit detection of an odds ratio between 1.5 and 1.6 with 95 percent power.

Induction, biological markers and therapy of tumors in primates. Recompetition for a proposed first year award of $600,000, $3 million over five years. The contract is currently held by Hazleton Laboratories of America Inc.

Although there are several in vitro tests for mutagenicity, mice and rats are used extensively to evaluate compounds for carcinogenic effects. However, there is no agreement on how accurately rodent data can be extrapolated to humans. There is a need to utilize nonhuman primates and other animal species more extensively to complement rodent studies and to verify the rodent data by comparative studies in other animals.

Until May 1982 this project was supported by the Div. of Cancer Treatment, when it was transferred to DCE. The present colony, consisting of 488 animals, is comprised of three species: Macaca mulatta (rhesus), Macaca fascicularis (cynomolgus) and Cercopithecus aethiops (African green). Forty-eight of these monkeys are adult breeders whose offspring are used for experimental studies. A total of 30 chemicals have been or are being evaluated for their carcinogenic potential in lifetime studies in monkeys.

Results acquired over the past 26 years indicate that primates are not always susceptible to chemical carcinogenesis as rodents, that the induction period is often in the range of seven or more years and that the organ or tumor type may differ considerably between rodents and primates for a particular carcinogen. However, data with some compounds, for example diethylnitrosamine, indicate that the induction period is dose related and that tumors can be induced in an average of 21 months.

The colony has been in existence for 26 years and supports the largest study of chemical carcinogenesis in

nonhuman primates undertaken in this country. In addition to providing data on the carcinogenicity of a variety of chemicals, including antitumor and immunosuppressive agents in clinical use, it has also been possible to acquire information on the spontaneous tumor incidence in nonhuman primates and on their life span in captivity. Normal animals of all ages as well as tumor bearng animals have been used in pharmacologic studies and chemotherapeutic trials.

The objectives of the program are: 1) Obtain comparative data on the response of nonhuman primates to known rodent carcinogens and to suspected carcinogens in humans; 2) Evaluate the long term effects of antineoplastic agents which are being used clinically for long term remission, in adjuvant therapy, and in the treatment of diffuse collagen disorders; 3) Obtain model tumor systems in nonhuman primates to ascertain the potential usefulness of various anticancer agents in man; 4) Attempt to develop models for chemoprevention therapy; 5) Develop biological markers and diagnostic tests for detecting preneoplastic changes, frank neoplasia and for monitoring nonhuman primates or patients prior to, during and after therapy; 6) Make available normal and tumor bearing animals for pharmacologic, toxicologic, biochemical and immunological studies; and 7) Maintain a breeding colony of various species of primates.

The majority of the animals are housed in an facility which contains only animals committed to this study. With the exception of the breeding colony, most animals are housed in individual cages. Antineoplastic and immunosuppressive agents are administered at doses likely to be encountered in a clinical situation; other substances, such as environmental contaminants, are given at levels of 10 to 40 fold higher than the estimated human exposure level. The remainder of the chemicals tested are administered at maximally tolerated doses which, on the basis of weight gain, blood chemistry, hematology findings and clinical observations, appear to be devoid of acute toxicity. Dosing continues until a tumor is diagnosed or until a predetermined exposure period has been completed.

A variety of clinical, biochemical and hematological parameters are monitored weekly or monthly. A laparoscope is used to periodically examine the abdominal cavity, mainly the liver, for evidence of tumor. Surgical biopsies are obtained and submitted for histopathological evaluation. Surgical procedures are performed under Ketamine hydrochloride or sodium pentobarbital anesthesia. Animals that die or are sacraficed are necropsied and the tissues subjected to hisopathologic examination.

Animals are bred, housed and dosed with test chemicals by the contractor. Surgery, biopsies and other procedures are performed by the project officer and the contractor. The project officer provides the contractor with written protocols for all experimental studies. Test materials are prepared by NCI personnel and monkeys are necropsied by NCI personnel.

Several Board members commented on the primate program's strength and wealth of material gathered over the 26 years, but some were concerned about the program's focus.

"My concern is that the objectives may be too much for this budget," said Board member Alice Whittemore. "Any one of these items, it seems, could take up all the time and resources."

DCE Director Richard Adamson noted that the program was reviewed by an outside evaluator, and that he has become more involved in it recently. Unnur Thorgeirsson was appointed project officer of the contract in January.

Board member Anna Barker suggested that the program make its resources better known to other investigators. Only about eight or nine other researchers use the material now, Thogeirsson said.

Shore suggested that the Board appoint a steering committee to provide more oversight for the program. Adamson said he favored the idea, and the concept was approved unanimously with that provision.

Support services in virology, tissue culture and immunology. Recompetition of a contract held by Biotech Research Labs for a proposed first year award of $355,000. The proposed project plan award is $1.53 million over four years.

The Laboratory of Tumor Cell Biology is interested in identifying a contractor to provide routine support services such as karyotypic analysis, immunofluorescence assays, Elisa assays, preparation of monoclonal and polyclonal antibodies against purified retroviral proteins, supply small quantities of purified viral antigens, retroviruses and tissue culture cells, and maintain a nude mouse colony.

The annual objectives of the contract are: 1) To supply up to 50 gms of fresh viable tissue culture cells for cell biology and molecular biology studies; 2) To carry out up to 400 tests by immunofluorescence analysis on fixed and viable cells for retroviral antigens; 3) To perform karyotypic analysis on up to 50 samples per year including further analysis of up to 25 samples per year by chromosome banding technique; 4) To analyze up to 100 serum specimens per week by Elisa for retroviruses followed by Western blotting of positive samples; 5) To develop monoclonal and polyclonal antibodies against viral antigens to be specified by the project officer; 6) To supply small quantities (up to mg each) of purified viral and structural proteins (up to 6 per year), and small amounts (up to 5 liters) of purified human and Simian retroviruses, not to exceed a total of 50 liters per year; and 7) To maintain a small nude mouse colony (up to 20 nude mice per month) to inoculate specimens to be provided by NCI for tumorigenicity studies.

Board member Lawrence Fischer asked Prem Sarin, the project officer for the virology concept, why this contract was separate from other similar contracts.

"This contract can get some new viruses in small quantities," while other contractors are set up for large scale production, Sarin said. Nevertheless, the contract has been "very cost effective," he said.

The concept was approved unanimously.

Resource for human esophageal tissue and cells from donors with epidemiological profiles. Recompetition of a contract held by Univ. of Maryland for a proposed first year award of $90,000. The proposed project plan award is $382,182 over four years.

The objectives of the contract are to provide the Laboratory of Human Carcinogenesis with 1) a resource for the the collection of normal appearing and neoplastic human esophageal tissue and cells at the time of surgery, and at immediate autopsy; and 2) the culture and storage of esophageal epithelial and fibroblastic cell stocks.

Essential components of the resource wil include a) approval of the institutional committee for the protection of human subjects, b) routine obtainment of donor informed consent, c) an epidemiological profile of the donors obtained by trained interviewers, d) proven methods for collecting, culturing and transporting the specimens in a viable condition to NIH, and e) characterization of the functional and pathological status of the tissue by histochemical and immunological methods and by light and electron microscopy.

The contractor will provide the laboratory with matched normal esophageal tissue and cell cultures from each donor. These tissues and cells will be used in the laboratory to study malignant transformation caused by chemical, microbial and physical carcinogens and cocarcinogens. The tumorigenic potential of treated cells will be further tested in athymic nude mice.

The contractor also will provide tumor and nontum-

orous tissue from patients with esophageal carcinoma. These tissues will be used for allelic deletion analyses.

These projects and their corresponding support contracts were reviewed at the most recent LHC site visit. The review committee unanimously approved the contract concept. Highlights of the project include:

--Common abnormality in chromosome 11p has been identified in all 14 esophageal cell lines newly established from tumors provided by this contract.

--Tumorigenic cell lines have been derived from primary esophageal carcinomas that will be used as recipients of certain normal human chrmosomes transferred by microcell methodology.

--Nontumorigenic SV-40 "immortalized" esophageal epithelial cell lines have been established and are being used to determine the neoplastic potential of certain activated proto-oncogenes, hst and Ki-ras.

--When compared to normal epithelial cells, keratin patterns were altered in esophageal carcinomas and were dependent on the tumor type and the degree of tumor differentiation.

--In contrast to reports of an increased number of epidermal growth factor receptors on skin carcinomas, esophageal carcinomas have fewer receptors than do normal human esophageal epithelial cells.

The concept was approved unanimously.

Biomedical computing, design and implementation. Recompetition of contracts currently held by Capital Systems Group Inc. and Information Management Services Inc. for a proposed first year award of $2.5 million, proposed project plan award of $9.99 million over four years.

The research projects of the Epidemiology and Biostatistics Program are becoming increasingly reliant upon computer processing. Since 1970, the program has used computer support services contracts to provide a large percentage of the data management and statistical computing necessary to support hundreds of projects. This concept provides for the continuation of these support services, at level funding, for the next four years for the Environmental Epidemiology Branch, the Biostatistics Branch, the Clinical Epidemiology Branch and the Radiation Epidemiology Branch.

The contracts will support data entry and editing activities, file management, software development and analysis, and presentation of large scale data resources resulting from methodologic and field studies of cancer etiology undertaken by EBP alone or in collaboration with extramural investigators.

Support contracts resulting from this concept will continue to be the mechanism providing the major portion of the computer related support to EBP investigators for a wide variety of studies.

Contractor services will be provided by organized teams of project managers, computer professionals and support personnel. End products include carefully edited and documented machine readable datasets, computer programs ans systems for data management and statistical analysis applications, other technical documentation and computer output such as listings, tables and graphs.

Contracts will continue to be administered and monitored by the chief of the Information Resources Management Section. Assistant project officers will be named to represent each branch receiving support. Each contractor's project manager and the appropriate EBP branch chief will meet at least monthly to allocate contract resources.

Board Member James Felton asked whether the computer contractors make an effort "to make the software compatible" among the four branches supported by the services.

Michael Stump, the project officer for the computing contract, said there is compatibility and that originally there were four separate contracts which were combined in order to provide standardization and sharing of resources. "We pay considerable attention to standardization," he said. The project supports software development, editing, data management and statistical analysis, he said.

"Who does the actual statistical analysis?" Whittemore asked.

"It is done by the investigators, who specify to the contractors how they want the data crunched," Stump said. Since investigators must work closely with the contractors, there is a requirment that contractors must be able to get to NCI in a half hour.

Whittemore said the budget for the concept "seems high, considering new data management programs on the market."

Adamson said the budget has been held level, and the program is "under the gun to reduce the costs."

The concept was approved, with Whittemore abstaining.

RFPs Available

Requests for proposals described here pertain to contracts planned for award by the National Cancer Institute unless otherwise noted. NCI listings will show the phone number of the Contracting Officer or Contract Specialist who will respond to questions. Address requests for NCI RFPs, citing the RFP number, to the individual named, the Executive Plaza room number shown, National Cancer Institute, NIH, Bethesda, MD 20892. Proposals may be hand delivered to the Executive Plaza, 6130 Executive Blvd., Rockville, MD. RFP announcements from other agencies will include the complete mailing address at the end of each.

RFP NCI-CM-97580-30

Title: Operation and maintenance of the DTP biological data processing system

Deadline: April 30

NCI's Div. of Cancer Treatment Developmental Therapeutics Program is seeking an organization to provide support for its data processing system. This is a small business set aside and a recompetition of a contract held by VSE Corp.

This system provides laboratory microcomputer support and large scale database management for the anticancer, anti-AIDS drug discovery activities, which include the annual in vitro screening of many thousands of synthetic compounds and natural product extracts. The contractor shall take responsibility for the current biological data processing system and all of its subsystems. The responsibility shall include design and/or redesign of system programs as well as initial coding, revising, testing, debugging, documentation, operation, and/or maintenance of all system software.

The contractor shall also provide support for installation and operation of the systems and development of new hardware and software systems as required for further development of the DTP drug discovery and development programs. The current system involves a series of Intel 80386 based laboratory microcomputers running SCO XENIX connected via Ethernet.

The in vitro drug screening database resides in a relational database management system on a VAX 8820 computer running VMS. Some components of the system also utilize IBM 370 facilities at NIH's Div. of Computer Research & Technology.

It is anticipated that one level of effort contract shall be awarded, for a five year period, with incremental funding each year. Offerors will be invited to submit proposals at two levels of effort: Level 1, 18,800, or Level 2, 9,400 direct labor hours per year.

Contract Specialist:Elsa Carlton
RCB Executive Plaza Rm 603
301/496-8620