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NCI To Fund 840 Competing Grants In FY 1991; No Downward Negotiations, But Careful Review

NCI expects to fund 840 new and competing research project grants in FY 1991, 112 more than the previous year, for a 27 percent funding rate of those submitted. The total number of competititive and noncompeti-tive awards will be 3,076, or 60 more than in FY 1990, a 6.7 percent increase. In response to Congressional concerns, there will be no "downward negotiations," or across the board cuts in funded grants, but grants will be subject to very careful funding review, NCI

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In Brief

Taxol Development Is NCI 'Emergency Priority'; Dodd To Focus ACS Effort On Breast Screening

TAXOL DEVELOPMENT is an "emergency priority," NCI Director Samuel Broder told the National Cancer Advisory Board this week. Taxol is the "most important new drug in the last 10 to 15 years" to show possible activity in the treatment of refractory ovarian cancer. An intragovernmental working group has been formed to lower barriers to finding sources of the the drug, which is currently made from the bark of the yew tree. The working group is made up of representatives from the Depts. of Agriculture, Interior and Health & Human Services. . . .

NEW AMERICAN Cancer Society President Gerald Dodd said in his term he will focus on improving the quality of screening mammograms and promoting more aggressive cancer detection tests and therapies therapies for the elderly. "One major problem is the limited number of radiologists experienced in the operation of screening programs. I plan to intensify quality assurance efforts because we have a long way to go in making optimal mammography available to all women," he said in a statement upon the announcement of his term. . . . **FIVE FACULTY** appointments were made recently at M.D. Anderson Cancer Center: **Andrew von Eschenbach,** chairman of the urology department, was awarded the Irving and Nadine Mansfield and Robert David Levitt Cancer Research Chair; **Donald Pinkel,** director of the Pediatric Leukemia Research Program, was appointed to the Kelcie Margaret Kana Research Chair; **Grady Saunders,** professor of biochemistry and molecular biology, was appointed to the Anise Sorrell Professorship; **Kenneth Hogstrom,** chairman of the radiation physics department, was appointed to the P.H. and Fay Etta Robinson Professorship in Cancer Research; **Phillip Frost,** deputy chairman of the cell biology department, was appointed to the Hubert and Olive Stringer Professorship in Cancer Research.

NCI To Fund 840 Competing Grants In FY '91, No Downward Negotiations

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Director Samuel Broder told the National Cancer Advisory Board this week.

The more than 15 percent increase in new and competing grants reflects the high priority NIH has placed on grants this fiscal year, in response to Congress, which has recommended that NIH fund a total of 6,000 competitive grants in FY 1991.

NCI's FY91 operating level is $1.7148 billion, an $80.6 million, or 4.9 percent increase over FY90. The 1991 appropriation began at $1.767 billion, but was hit by a 2.41 across the board cut, or $42.6 million, plus a $9 million cut for federal salaries and expenses.

The $1.7 billion figure does not include the newly created authority of the NIH director to transfer 1 percent from any institute to any other program area. However, Broder said the institute is preparing its budget "as if the 1 percent tap has been taken."

"We've been instructed that a 1 percent tap will occur," he said, especially since NCI received the largest dollar increase over 1990 of any of the institutes. "The most likely scenario" is that the NIH director will use the 1 percent tap on each institute and put the resulting funds into a pool to be redistributed among the institutes for research project grants. In NCI's case, the tap could result in removal of $17 million from the operating level.

"I feel that this will cause special challenges for us," Broder told the NCAB at its meeting this week.

In NCI for FY91, "there is no doctrine of fairness" between the intramural and extramural programs, Broder said. The intramural program will be funded at $329 million, which includes AIDS funding and all salaries and AIDS funding. The majority of NCI's AIDS money comes out of the intramural program.

Cancer centers funding will increase from $105 million to $110 million. The prevention and control line will increase from $75 million to $85 million, a 13.6 percent increase.

Construction funding will increase from $5 million to $6.8 million.

The average cost of noncompeting grants will be $263,000, a $15,000 increase over FY90; competing grants will remain at an average of $235,000.

NCI will hold the line on MERIT awards and Outstanding Investigator Grants, the long term grant programs.

"We have heard Congress and your concerns about the length of awards," Broder said. "Without limiting the value of long term awards, we will have to put limits on them....We are being exceedingly cautious about OIGs." He said a goal is to bring a "stabilization" between short and long term awards in order to meet the four-year average limit on average length of awards as mandated by Congress this year.

Broder also noted that taken in total, the House and Senate, in their separate budget reports, made $62 million worth of earmarks in the NCI budget. However, most of the earmarks did not remain in the conference committee's budget report.

NCAB Chairman David Korn questioned whether NCI was under any obligation to comply with earmarks that did not make it into the conference report. Korn noted that for many reasons, language is introduced in the Senate and House budget reports but does not survive.

"We take the report language in either report very seriously," Broder said. While he noted that NCI does not have the money to fund all of the earmarks mentioned, it must "at least be prepared to address the concerns in either report."

Broder said his point was that, "Those who want to conduct business by earmarks rather than through the standard process will run into this fiscal reality."

"I think that the whole NIH, and NCI as a part, is struggling with trying to meet mandated objectives with a total resource pool that is, while generous, less than adequate," Korn said. The choices that must be made "raise tremendous policy issues....Nothing you do will be painless."

Korn noted that, for example, the House budget report said NIH should be able to fund 6,000 competing grants in FY91, but the figure did not make it into the conference report. "I think you may be overlooking some of your executive flexibility," he said.

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National Cancer Institute
1991 Operating Level
(dollars in thousands)

	1990 Obligations	1991 Operating Level	Increase Over 1990 Obligations Amount	Percent
Research Project Grants:				
Noncompeting	$561,127	$581,434	$20,307	3.6%
Administrative Supp.	7,061	7,000	-61	-0.9%
Competing	171,291	200,538	29,247	17.1%
Subtotal, RPG	739,479	788,972	49,493	6.7%
Cancer Centers	105,268	110,082	4,814	4.6%
Other Research:				
Research Careers	8,520	8,781	261	3.1%
Cancer Education	2,955	3,115	160	5.4%
Clinical Cooperative Groups	60,208	62,357	2,149	3.6%
Minority Biomedical Research	2,676	2,831	155	5.8%
Other	10,045	10,500	455	4.5%
Subtotal, Other	84,404	87,584	3,180	3.8%
Total, Research Grants	929,151	986,638	57,487	6.2%
National Rsch. Serv. Awards	35,793	37,252	1,459	4.1%
R&D Contracts	191,934	188,243	-3,691	-1.9%
Intramural Research	316,464	329,128	12,664	4.0%
Rsch. Mgmt. and Support	80,420	81,034	614	0.8%
Cancer Prevention and Control	75,432	85,689	10,257	13.6%
Construction	5,006	6,800	1,794	35.8%
Total, NCI	$1,634,200	$1,714,784*	$80,584	4.9%
Transfer for Construction	10,129			
Total, NCI	$1,644,329			

*Does *not* include one percent transfer by the NIH Director.

"I feel comfortable with 840 grants," Broder said. In addition, he said, "We will not do downward negotiations. We will do very careful, grant by grant scientific negotiations."

NCAB member Enrico Mihich said he was "worried" about whether there is adequate funding for the intramural program.

"We will do what we can" as the fiscal year goes along, Broder said, "but the priorities for this year have already been set. Support for research project grants is a very high priority."

Congress also mandated that the total costs of grants should be considered at all phases of the review process, and that study sections should decide if a project merits funding based on its "inherent value."

"We feel we are in compliance" with these provisions, Broder said. "Study sections are asked to look at the reasonableness of total direct costs."

Board member Erwin Bettinghaus said some in the scientific community have assumed that study sections would now begin to examine indirect grant costs. Broder said study sections would not do this.

Broder noted that the budget report did not mention indirect costs by name, only total costs. "We can assure Congress that we do look at total costs," he said.

NIH has come up with a draft proposal to address the Congressional budget report, which called on NIH to draft a four-year financial management plan.

NCAB OK's Funding First 3 Years Of Diet Trial Design, Phase-In

The National Cancer Advisory Board this week recommended that NCI spend up to $7.5 million for a two to three-year study to determine the feasibility of conducting the full, 15-year, $106 million Women's Health Trial.

The board voted in favor of a motion recommending that NCI prepare an RFP for a study coordinating center to develop the protocol for the Women's Health Trial and an RFP for the clinical units that would conduct feasibility studies on the proposed dietary intervention trial.

After two to three years, the study would be reviewed and results would be evaluated by the NCAB before the full trial would begin.

The $7.5 million would come out of the prevention and control budget, with an estimated $2.5 million to be spent in FY 1991.

The Women's Health Trial, approved in concept by the Div. of Cancer Prevention & Control Board of Scientific Counselors in October (**The Cancer Letter,** Oct. 26), would enroll 24,000 healthy women aged 50-69 years, who get 38 percent of their calories from fat, at 12 clinical centers around the U.S. The intervention group will be taught to follow a low fat diet, in which 20 percent of calories are from fat. The primary endpoints are the incidence of breast and colorectal cancer, and overall mortality. The secondary endpoint is the incidence of heart disease. Changes in blood lipids and hormones also will be monitored.

It was not necessary for the NCAB to vote on the trial, but the board had asked for the opportunity to review the proposal. All board members present voted in favor of the recommendation, with one abstention, Ralph Yodaiken, director of the Office of Occupational Medicine at the Dept. of Labor, who sits on the board for the labor secretary.

The National Heart, Lung & Blood Institute is expected to participate in the trial and that institute's advisory council is scheduled to consider adding some funding to the trial at its next meeting, in February.

An NCI/NHLBI policy board would be created to provide advice and set policy for the Women's Health Trial.

DCPC Director Peter Greenwald said that NCI decided that a broad cross-section of women should be recruited to the trial, including low socioeconomic status and minority women. This will make the intervention more challenging, since there is no data available on conducting dietary intervention in these populations, he said.

The RFP for the coordinating center would provide for:

--protocol development with NCI and NHLBI.

--intervention feasibility for low socioeconomic groups and minorities.

--biomarker study options

--document cost efficacy

Board members were concerned that the trial not proceed without review after the initial stages. "I picture that after two years we would look at it very carefully," Greenwald said.

Some board members seemed to favor putting off a decision on the trial for a year or two to allow NCI time to address some of the questions that remain about conducting the trial, especially in low income and minority women.

"It's not wise to start a trial until you know how to do a trial," board member Samuel Wells said. "I think we are starting something that would be difficult to stop. It's like the Stealth bomber." He suggested that NCI come back to the NCAB in February with more information.

But DCPC BSC Chairman Edward Bresnick told the NCAB that his board thought that, "If we are to conduct a nutritional intervention study, this was the best possible one we could do and it would not do to put it off two or three years."

The motion to approve the initial two to three years of the trial was made by board member Helene Brown, Jonnson Comprehensive Cancer Center. Echoing what seemed to be the thoughts of other board members, Brown said, "I'm not willing to go the whole $106 million at this point" due to the major scientific questions that remain about the feasibility and efficacy of such a large, intervention trial involving diet.

Brown also noted that by the February meeting, there could be eight new members of the NCAB and this issue would be "a lot to put on the table" at a first meeting. There are currently eight "lame duck" board members whose successors have not yet been named by the White House.

The uncertainty of how the intervention actually will work in minority and low income women means that, "you're going to have to put things out into the marketplace" before a trial can begin, Brown said. "I'm willing to take a chance," she said. Her motion was seconded by Enrico Mihich.

Cancer Control, Smoking Programs Reorganized In DCPC Overhaul

NCI's Cancer Control Science Program, within the Div. of Cancer Prevention & Control, recently has undergone a complete overhaul that NCI officials say will more effectively organize the program's research and applications activities. The reorganization also establishes a full-time coordinator for smoking and tobacco control.

The reorganization, which was begun this summer, has now been finalized. Associate Director Claudia

Baquet is head of the program. The reorganization has:

▸Dismantled the Smoking, Tobacco & Cancer Branch, which was located in Div. Director Peter Greenwald's office. Personnel and programs of the branch were moved into the Cancer Control Science Program.

▸Coordination of the Smoking & Tobacco Control Program will be handled out of the office of the director of the Cancer Control Science Program. A full time coordinator will oversee smoking and tobacco control.

▸Reorganized the three previously existing branches within the Cancer Control Science Program and established a fourth branch, called the National Outreach Initiatives Branch.

"We spent the last year looking seriously at ourselves and possible deficiencies in the programs," Baquet told the DCPC Board of Scientific Counselors at its fall meeting recently.

NCI officials said the changes in the smoking program do not lessen its importance. The late Joseph Cullen, before leaving NCI last year, coordinated the smoking program in his position as DCPC deputy director, but the smoking program was not his only job. Now there is a full time position solely for smoking and tobacco control.

Donald Shopland, formerly in the old Smoking, Tobacco & Cancer Branch, has been named coordinator of the Smoking & Tobacco Control Program. His job is to act as a liaison between NCI, NIH and HHS in matters concerning tobacco research, policy and applications. The program is to serve as a "focal point" for NCI-wide smoking and tobacco control initiatives, help formulate smoking and tobacco control policy for NCI and HHS, and coordinate dissemination efforts for intervention strategies.

Terry Pechacek, who was acting chief of the Smoking, Tobacco & Cancer Branch, is now an expert in the newly established Prevention and Control Extramural Research Branch, carrying out COMMIT, one of DCPC's major antismoking efforts.

ASSIST, the other major antismoking effort, is now located in the Public Health Applications Research Branch, formerly called the Cancer Control Applications Branch. Katherine Marconi is the branch chief.

"Our organization grew by happenstance over the years, so this kind of gives it a structure," Marconi said of the restructuring.

Baquet distributed a statement to the DCPC Board of Scientific Counselors at its recent meeting describing the purpose of the cancer control program:

"The goal of the Div. of Cancer Prevention & Control is to achieve significant reductions in cancer incidence, mortality and morbidity, with a concomitant increase in cancer survival. The Cancer Control Science Program seeks to further this goal by advancing the science and application of cancer prevention and control. The program's efforts are directed toward administering intramural research initiatives to evaluate the efficiency and efficacy of cancer control interventions; monitoring basic, clinical, behavioral and health education research to identify new intervention strategies; and supporting extramural research programs to address issues such as cancer control problems among particular populations, worksite cancer control activities, and modification of smoking and tobacco use. Each of the CCSP's four research branches attempts to improve services and interventions by focusing on different aspects of cancer prevention and control."

The four branches within the Cancer Control Science Program and their responsibilities:

▸**Prevention & Control Extramural Research Branch.** Baquet is acting chief of this branch until a permanent chief is selected.

The sections within PCERB are:

--Primary Prevention Section, acting chief Tom Glynn.

--Investigator Initiated Research Section, acting chief Claudia Baquet.

According to the statement Baquet prepared, the rationale for the branch is as follows: "The development of a large, multidisciplinary research base in cancer prevention and control intervention is central to improving methods, technology and services as well as ultimately to reducing cancer related morbidity and mortality.

"The newly established PCERB supports primary prevention intervention research as well as investigator initiated grants. It administers an extramural applied research program that investigates intervention methods to modify primary prevention risk factors such as the use of tobacco and alcohol, diet and nutrition and occupational and sun exposure. For example, the Community Intervention Trial for Heavy Smokers (COMMIT) is a randomized community based trial that is testing a protocol of smoking cessation strategies aimed at heavy smokers. The study involves more than 2 million people in the U.S. and Canada and will provide a model to communities across the country.

"PCERB also fosters and supports phase 2 through phase 5 prevention and control investigator initiated

grants. These awards include large multi-study projects such as the Cancer Prevention Research Units and the Cancer Control Science Program as well as single intervention studies. Additionally, PCERB uses small grants and related mechanisms to develop a cadre of highly qualified professionals who can perform rigorous cancer prevention and control intervention research."

Within the CPRUs there are currently 11 ongoing program projects representing approximately 100 prevention and control studies. Research in the CPRUs currently is focused on adherence to cancer control regimens, colon cancer prevention, special populations, dietary interventions, breast cancer screening and community interventions.

In the small grants program, 91 grants have been supported since the program began in 1987, Baquet said. Of these, 26 are still active. More than 40 percent of the principal investigators or the projects involved have "graduated" to RO1 or program project applications. Research has focused primarily on phases 1 to 3, with major emphasis on breast, colorectal and smoking related cancer prevention/early detection.

▸**Public Health Applications Research Branch,** formerly the Cancer Control Applications Branch. Katherine Marconi is the branch chief.

The sections within the branch are:

--Applied Tobacco Research Section, Marconi is acting chief.

--Applications of Prevention & Early Detection Section, acting chief Marc Manley.

--Public Health Agency Section, acting chief Lawrence Bergner.

--Health Education Section, chief Suzanne Haynes.

The rationale for the branch: "The public health system, including federal, state and local agencies, is critical to the successful delivery of tested cancer prevention and control interventions to large numbers of people. These agencies constitute a valuable national infrastructure for reaching not only populations that otherwise would be underserved but also the entire population of a state or locality.

The branch "builds public health capacity for cancer control interventions and supports public health demonstration projects. A major activity of this branch is the American Stop Smoking Intervention Study (ASSIST). This large-scale demonstration program, now in its early stage, will disseminate the results of NCI's smoking and tobacco programs. NCI, the American Cancer Society and other voluntary organizations will work jointly through public health agencies and regional coalitions to conduct interventions and activities at ASSIST sites in 20 geographical areas throughout the U.S."

The branch "also administers applications of primary and secondary interventions in health care settings. For example, the branch is developing training courses that will help physicians and dentists around the country counsel their patients on smoking cessation. The Data Based Intervention Research for Public Health Agencies initiative provides grants that help public health agencies build their capacity to undertake programs in cancer prevention and control. The branch also is responsible for health education initiatives, which currently include worksite interventions that address nutrition, cancer screening and tobacco control as well as breast cancer screening initiatives that are aimed at improving the utilization of mammography and other types of breast examination."

▸**Special Populations Studies Branch.** This branch was established in 1986. Baquet was chief of the branch before becoming head of the Cancer Control Science Program. George Alexander, an MD, began work this week as the branch chief. He was with Jefferson Medical College in Philadelphia.

The branch has one section, the Data Analysis & Coordination Section, headed by John Horm.

The rationale for the branch: "The development of a cancer prevention and control research base with a primary focus on minority and underserved populations will enhance the delivery of interventions that focus on the unique needs of these groups."

The branch "supports programs targeting populations at high risk for cancer incidence and mortality rates. These programs include extramural intervention research projects as well as initiatives that provide rapid response to an identified need or a request for action. For example, the SPSB has funded seven research studies to develop and test innovative cancer control interventions among minority and underserved populations. The branch is also supporting studies addressing the identification and remedy of key factors that contribute to avoidable cancer mortality among blacks and other minority populations. Intra-agency activities with the Indian Health Service and Health Resources Services Administration include initiatives concerning the cancer surveillance of Alaskan Natives and the delivery of cancer control services to community and migrant health centers."

The branch "also focuses on identifying, collecting, analyzing and disseminating data on the cancer prevention and control needs to special populations. To augment data in the Surveillance, Epidemiology & End Results Program on racial and ethnic populations,

the branch is pursuing the inclusion of data obtained from additional registries that are located in geographical areas where SEER representation is low. In addition, the branch is collaborating with federal, state and local agencies to produce the population estimates needed to evaluate cancer risks among special populations."

▸**National Outreach Initiatives Branch.** Baquet is acting chief of this branch until a permanent chief is found.

The rationale for this new branch: "The Cancer Control Science Program is called upon by the DCPC director and the NCI director to plan and implement a variety of research, training and networking projects. These projects may vary in length as well as in intensity and some may involve the entire institute."

The branch "coordinates and maintains networks that seek to increase the involvement of black and Hispanic scientists in cancer prevention and control. For example, the National Black Leadership Initiative on Cancer successfully has mobilized black community and national leaders to spread cancer control messages that emphasize the importance of early detection and prevention. In addition, the branch is developing a National Hispanic Initiative on Cancer, which will establish a similar collaborative effort among Hispanic leaders."

The branch also supports the Science Enrichment Program, which began this summer to encourage minority students to choose careers in science.

DCPC's Early Detection & Community Oncology Program, which was formerly called the Centers & Community Oncology Program before the centers were moved to the Div. of Cancer Biology, Diagnosis & Centers, is also under review for some structural changes, Greenwald said.

Barnett Kramer is the new head of this program. He is a physician and was a senior investigator in the NCI/Navy Medical Oncology Branch.

Currently, the program contains the Early Detection Branch, headed by Charles Smart, and the Community Oncology & Rehabilitation Branch, headed by Leslie Ford. Proposed as new branches are the Preventive Oncology Branch and the Biomarker & Prevention Research Branch.

Other new staff named recently in DCPC are: Barry Portnoy, cancer planning and program officer; Susan Nayfield, medical officer in the Community Oncology & Rehabilitation Branch; Grace Yeh, biologist in the new nutrition laboratory; Marianne Haenlein, public health advisor; John Gohagan, expert in the Early Detection Branch; and Carolin Malott, statistician.

Workshop Suggests Confirmation Of Vitamin C Studies Is Needed

NCI is considering whether to release a program announcement for research on ascorbic acid and may review the "best cases" of investigators who have worked with the vitamin.

A symposium on vitamin C sponsored this fall by NCI and the National Institute of Diabetes & Digestive & Kidney Diseases concluded that studies conducted to date on the biological functions of vitamin C should be "systematically confirmed in other laboratories."

The report of the symposium was presented to the Div. of Cancer Prevention & Control Board of Scientific Counselors at its fall meeting by Donald Henson and Gladys Block, both researchers in DCPC.

The symposium was the first ever held at NIH to examine vitamin C and cancer, according to the report. More than 30 researchers presented data on the antioxidant, enzymatic, immune and cancer related functions of ascorbic acid. According to the symposium report, prepared by Henson, Block and Mark Levine, of NIDDKD's Laboratory of Cell Biology & Genetics, participants were most interested in studies on the in vivo effects on tumor growth. Following are excerpts from the report:

"Linus Pauling reviewed his two animal studies. There was a reduction of skin tumors in UV exposed hairless mice whose diet was supplemented with ascorbate. By 20 weeks, five times as many mice had developed large lesions in the control as compared with the high dose ascorbate group. In RIII mice, the appearance of spontaneous mammary tumors was significantly delayed in animals whose diet was also supplemented with ascorbate. The median age at appearance of first tumor was 83 weeks in controls and 125 weeks in the high dose ascorbate group. At the highest dose, these animals received approximately 10 grams of vitamin C per kg of body weight.

"Joachim Liehr, Univ. of Texas Medical Branch, Galveston, showed that ascorbic acid inhibits estrogen induced renal tumors by 50% in hamsters, by reducing the concentration of estrogen quinone metabolites and their DNA adducts.

"Eymard Poydock, Mercyhurst College, described the inhibitory effect of ascorbate and vitamin B12 on implanted Ehrlich carcinoma and L1210 leukemia in mice. All control mice had died by day 19, while more than 50% of treated mice were still free of tumor after 60 days. In the presence of vitamin B12, the cobalt nucleus is released and attaches to ascorbic acid, possibly forming cobalt ascorbate. The cobalt-vitamin C complex prevents mitoses in transplantable

murine tumors without damage to normal cells.

"Robert Smart, North Carolina State, reported the effect of ascorbic acid and its synthetic lipophilic derivative ascorbyl palmitate on phorbol ester induced skin tumor promotion in CD-1 mice. Large topical doses of ascorbic acid inhibited tumor promotion and ornithine decarboxylase activity, but not epidermal DNA synthesis. Small doses of ascorbyl palmitate inhibited DNA synthesis, ornithine decarboxylase activity and tumor promotion. The number of tumors per mouse was reduced by 90% and the number of mice with tumors by 86%. Dietary ascorbic acid inhibited the induction of ornithine decarboxylase but did not prevent tumor promotion nor epidermal DNA synthesis.

"The inhibiting effect of ascorbic acid on the growth of human mammary tumor xenografts in mice was described by Constance Tsao, Linus Pauling Institute. Ascorbic acid along with cupric sulfate inhibited the growth of tumor fragments implanted beneath the renal capsule of immunocompetent mice. Ascorbate added to the diet had no effect, but incorporated into the drinking water, was effective. A stereoisomer of ascorbic acid, D-isoascorbic acid, which has only 5% the antiscorbutic potency of L-ascorbic acid, had similar antitumor activity. It appears, therefore, that in this system the antitumor activity of ascorbic acid is not due to its metabolism as a vitamin, but to its chemical properties.

"Adjuvant and toxicity-reducing therapeutic applications: Paul Okunieff, Harvard Medical School, described the radioprotective effects of ascorbic acid on skin and bone marrow. Okunieff studied the effect of radiation on mice with established fibrosarcomas. In nonradiated animals, ascorbic acid did not modify or prevent tumor growth. When given immediately preceding radiation there was a significant reduction in the radiation toxicity to both skin and bone marrow, but the tumor was not protected. Okunieff concluded that there was a therapeutic gain of 1.25. Ascorbic acid also reduced the radiosensitizing potency of misonidazole in normal tissue.

"Gary Meadows, Washington State Univ., described the effects of ascorbic acid on transplanted B16 melanoma in mice. Ascorbic added to the drinking water of female B6D2F1 mice inhibited subcutaneous B16 melanoma growth, enhanced levodopa methyl-ester chemotherapy, and singly or in combination increased survival in tumor bearing mice. The tumors were smaller and less invasive, while metastatic lesions tended to be encapsulated.

"In studies that may have therapeutic implications, interesting observations on hypovitaminosis C in patients treated with IL-2 and LAK cells were reported by Stuart Marcus, Lederle Laboratories. During the first phase of treatment (IL-2 alone), plasma levels of ascorbic acid dropped by more than 80%. Plasma levels were undetectable in 12 of 15 patients after the third treatment phase (IL-2+LAK cells). Excessive renal excretion was not the reason for the loss. The finding seemed specific for vitamin C, since blood levels of pantothenate and vitamin E remained normal. In some patients, the cytotoxic activity of lymphocytes cultured in the presence of IL-2 was stimulated by addition of ascorbic acid to the medium. Marcus suggested that a controlled study is needed.

"Kan Shimpo, Japan, described a significant reduction in adriamycin induced toxicity and prolongation in survival in animals receiving ascorbic acid and its derivatives. The reduction was attributed to their antitoxidant actions. Experimentally, ascorbic acid prevented the elevation of lipid peroxide levels found in the heart following administration of adriamycin. Shimpo proposed that ascorbate should be prospectively tried clinically in patients treated with adriamycin. Ascorbate did not reduce the antitumor effect of adriamycin. If these results are applicable to man, then patients treated with adriamycin should be asked about vitamin C intake."

Block summarized current epidemilogic data on the role of ascorbic acid in cancer prevention. "Of 46 epidemiologic studies reported, 33 described significant protective effects on cancer mortality or incidence. Protection by vitamin C, or other components in fruit, is strong for cancers of the esophagus, larynx, oral cavity and pancreas. There is also evidence for a protective effect for cancers of the stomach, rectum, lung, breast and uterine cervix. Factors other than vitamin C may confer additional protection."

In conclusion, the report said, "the conference conveyed clearly that vitamin C has multiple complex effects on a variety of biologic activities, perhaps wider than any other nutrient. Some of these effects are related to the interaction of vitamin C with enzymes, while others are independent of enzymatic function. Many of these biologic effects seem related to its chemical properties and not to its role as a vitamin. What seems needed is a unifying principle that can explain the seemingly unrelated effects of vitamin C. The studies presented in this conference should be systematically confirmed in other laboratories. Any role for ascorbate in the prevention and treatment of cancer will only be established through scientific studies and knowledge of its biologic actions."