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SHARP INCREASE IN CANCER MORTALITY COULD BRING DRASTIC PROGRAM CHANGES; ALL 1975 DATA NEEDED

When the National Center for Health Statistics reported a few weeks ago that cancer mortality had increased 5% over last year during the first seven months of 1975, NCI staff members were as shocked as anyone. The annual increase recorded since the government started collecting reliable data in 1930 had averaged 1%.

A sharp increase of 5%, terrifying if true, is hard to believe—that is, no one wants to believe it. If it does turn out to be correct, NCI and the National Cancer Program are in for some drastic changes.

Benno Schmidt, chairman of the President's Cancer Panel, pointed out to the Panel last week that Congress already was developing a mood

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In Brief

PROGRESS REPORTED IN NCI-FDA FIGHT OVER NEW DRUG TESTS; EPIDEMIOLOGY BRANCH REORGANIZED

SOME PROGRESS has been made in negotiations between NCI and the Food & Drug Administration over FDA's bureaucratic nitpicking that's holding up clinical tests of important new anticancer drugs. NCI is asking FDA to drop the ridiculous demands that it re-establish itself as competent to test drugs with each investigational new drug application; NCI has promised to bring up to date its reporting on clinical tests, in some cases more than a year overdue. . . . **THE SCIENTIFIC COMMUNITY** is "not a permeable one" as far as understanding the National Cancer Program, Benno Schmidt now believes. The chairman of the President's Cancer Panel, who also is a member of the President's Biomedical Research Panel, previously thought he had been getting his message across to non-cancer scientists. But he said recently that there still "is not a widespread perception of progress being made in the cancer program." Scientists not involved in the program "still perceive that we put too much emphasis on contracts, not enough on grants; that not enough support goes to basic research, too much to targeted research, when in fact NCI and the National Cancer Advisory Board have undertaken steps precisely in the opposite direction; that there is not enough peer review involved in development of RFPs and review of contract proposals." Schmidt said the Biomedical Panel has expressed "great concern" about NCI undertaking control programs, "mixing research and service." Some feel that service programs will have more political and public appeal, eventually will get a larger share of the budget than research. . . . **ENVIRONMENTAL EPIDEMIOLOGY** will get increased emphasis in an NCI reorganization under way. The Epidemiology Branch in the Div. of Cancer Cause & Prevention is being split up. Robert Miller, head of the branch, will be chief of a Clinical Epidemiology Branch; Joseph Fraumeni, associate chief of the former branch, will head up the new Environmental Epidemiology Branch.

CONGRESS MAY DEMAND PRIORITY CHANGE IF REPORTED 5% INCREASE HOLDS UP

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to insist that NCI revise its priorities.

Schmidt said what he perceives as "a very marked congressional interest . . . may take an oversimplified form—if 85% of all cancer is caused by outside agents, why do we spend only 6% of the cancer program budget trying to find out what those agents are?"

Oversimplified or not, "the underlying concern is thoroughly justified," Schmidt said. "Are we really doing enough to maximize the effort to see that the minimum number of carcinogenic agents enter the social fabric? People don't realize the complexity of the problem. The question is, how do we do it? We've got to present a very clear picture of what our role is, how it dovetails with that of other federal agencies."

Schmidt asked NCI to develop a summary of exactly what NCI is doing in environmental carcinogenesis, costs, how it fits with what other federal agencies are doing, how well those efforts are being coordinated, what more can be done.

James Peters, director of the Div. of Cancer Cause & Prevention, said there are a number of explanations for the apparent 5% increase, some of which could establish the validity of that figure, some which might show it as an aberration that will not hold up.

"The reporting mechanism is one of the artifacts involved," Peters said. Significant fluctuations in partial year statistics and monthly figures reported by the Center for Health Statistics have occurred in the past. The Center's report for August reveals to some extent monthly variations. The 5% increase was based on data obtained through July 31, which indicated the cancer mortality rate was 176.3 per 100,000, compared with 169.5 per 100,000 in 1974. However, the August rate was 172 per 100,000, which by itself would be an increase of between 1 and 2%. That dropped the rate for the first eight months to 175.8, still an increase of 4.6% over last year.

Peters said that his statisticians are reluctant to accept any figures until data for the entire year are in.

Rep. L.H. Fountain (D.-N.C.), chairman of the House Intergovernmental Relations and Human Resources Subcommittee, had asked NCI for some explanation and discussion of the reported increase. Peters responded, mentioning the reasons why more time is needed to evaluate it, and added, "It is inconceivable" that a five-fold increase in cancer mortality could occur in a seven month period, "especially in a disease which has, for the most part, latent periods of 15, 20, or more years." NCI's experience with cancer death rates "strongly suggests that changes are gradual due to the latent periods, and due to the large number of variables which influence cancer mortality," Peters wrote.

But Peters did not rule out the possibility that the 5% increase has in fact occurred. "This could be the beginning of our long term predictions we made a few years ago, that we would get a doubling of cancer rates. The 4 to 5% increase is right on schedule," Peters told the Panel.

Schmidt had his own theory. "I have a strong feeling, not backed by hard facts, that people—including doctors—are more inclined these days to call cancer cancer than in the past, and to list cancer as the cause of death, no matter what the actual terminal cause is. I think that it was not unusual in the past to list pneumonia, or whatever, as the cause of death when that was only the final disease brought on by cancer. I'm not saying that's what happened, but it could have some bearing on the figures. We're getting more data now, and more explicit data."

Peters said most states now require in their death certificates the listing of the contributing disease as well as the primary cause of death, a practice not always followed in the past.

Meanwhile, the American Cancer Society was claiming in its new publication, *76 Cancer Facts & Figures,* that cancer deaths would be leveling off or even going down, if there were no lung cancer.

"Although it is largely preventable by the elimination of cigarette smoking, lung cancer is the number one cause of cancer deaths among American men—65,200 in 1976—and for American women, the lung cancer death rate has jumped 173% in the 20-year period from 1951-53 to 1971-73. Because of lung cancer, cancer-caused deaths among American men will go over 200,000 in 1976, a new record," the ACS report said.

"At the same time, however, overall five year survival rates have increased for some cancers, and leveled off for most cancers over the past 25 years. In 1976, that means about 225,000 Americans or about one-third of all Americans who get cancer (675,000 in 1976) will be alive at least five years after treatment."

Other figures noted by ACS in the booklet include:

—More than one million Americans will be under medical care for cancer in 1976. The average hospital stay will be 16 days at an average cost of $1,500.

—There is a 71% chance of survival when bladder cancer is detected and treated early, but the chance drops to 21% when the disease has metastasized. Similarly, there is an 82% chance of survival when uterine cancer is detected in a localized stage, but the odds diminish to 44% when the disease has already spread.

—While cancer among children is rare, it does account for more deaths in the 3-14 year-old group than any other disease. Since 1950, cancer deaths among black males have increased by 50%. Although prostate cancer has increased in incidence by more than 20% in the last 25 years, the survival rate for this form of cancer is steadily improving.

In fiscal 1975, ACS received over $107 million from public sources. While 28.7% of its 1974-75 budget, $28.2 million, went to research, 17.2% or $17.1

million went to community services. Another 11.9% of the budget or $11.9 million went to fund raising and 9.9% or $9.9 million went to management.

DCT COUNSELORS PONDER COORDINATION, IDENTIFICATION OF OPPORTUNITIES

Coordination of clinical research involving the various funding mechanisms, identification of research opportunities and NCI-investigator relationships were among the topics covered in a wide-ranging discussion at the last meeting of the Board of Scientific Counselors for NCI's Div. of Cancer Treatment.

Excerpts from that discussion appear below. Participants quoted here included DCT Director Vincent DeVita; Guy Newell, NCI deputy director; Board members Harris Busch, Baylor; Henry Kaplan, Stanford; Charles Heidelberger, Univ. of Wisconsin; Louis Wasserman, Mt. Sinai; Carlos Perez, Washington Univ. (St. Louis); Board consultant James Holland, Mt. Sinai; Giulio D'Angio, Sloan-Kettering, chairman of the Cancer Clinical Investigation Review Committee; and Raul Mercado, chief of DCT's Clinical Investigations Branch.

These excerpts are not verbatim in every instance, but more often represent summaries of the discussion.

DeVita: (Responding to the question, "How is all the work that is going on in basic research areas being monitored to turn up leads for follow up with clinical research?") We will rely on this Board to assist with that job. You have the broad expertise that requires. But we can't monitor the world. Identifying the opportunities has always been the problem in science.

Busch: How does an investigator develop a dialogue with your staff to pursue an idea, or to follow up a lead?

DeVita: Correspond with me. Letters are passed around to the appropriate staff. We may bring the idea to this Board, to get your opinion. One thing is troubling me--it's damn near impossible to harness the world and develop follow up on good new ideas. If it (a proposed new idea) relates to our program and is not the mission of another division, we will bring it to this Board, or to an ad hoc subcommittee of the Board. (On which funding mechanism would be used) --It could go to the Div. of Research Resources & Centers if appropriate for a regular research grant. If it's something that relates to treatment, an exciting new idea that needs further exploration, it could be a CREG (Cancer Research Emphasis Grant). If it's an exciting new idea that needs development, it could be a contract.

Holland: Do you have someone looking at grant progress reports for ideas to follow up?

DeVita: Not in a formal way. My own feeling is that I've yet to meet a good scientist who is in possession of a good idea and sits on it. It gets out, at meetings, or in a variety of ways. Close monitoring by us of all investigator initiated research could be considered meddling. Unless you feel there is a considerable number of people who are sitting on ideas, I personally don't favor a more formal way to monitor grants.

Newell: (Responding to the question of what should an investigator do if his unsolicited contract proposal is determined not proper for a sole source contract) Counsel him to try to fit it into an existing RFP, or rewrite it as a grant application.

Kaplan: I agree that in most instances red hot ideas are not concealed long. However, many times persons don't know the implications of what they have. Hyperthermia is an example. It would be constructive to bring in cell biologists, to enrich the basic science approach to a problem. Molecular biologists are making important advances, with synthetic DNA and RNA, protein synthesis and control methods. Most doing this work haven't the foggiest notion that this might have application to cancer treatment. Bring groups together once in a while to exchange ideas and information.

DeVita: It boils down to identifying the areas for follow up. That's not easy. I need help to do that, and if I don't get it, then you get DeVita's view of the world. That's an excellent view, of course, but . . . (laughter).

The discussion moved on to the Clinical Cooperative Groups.

Heidelberger: How does a group chairman drop an individual member who's not carrying his weight?

D'Angio: Groups are setting up internal surveillance with reports submitted to the group chairmen or to CCIRC. Recommendations for disapproval will be based on those reports.

Heidelberger: Is there no way to get rid of an incompetent member without waiting for the grant renewal period?

D'Angio: No.

Wasserman: It's very difficult to cut off a grantee.

DeVita: That's correct. If he has his grant, has his money, you can't cut him off immediately.

Mercado: If it happens late in the grant period, it's not a matter of carrying someone for two years, and it generally isn't determined until late in the period that someone is not competent. Then you drop him at renewal time.

D'Angio: Groups usually put new members on probation, so they don't have to carry them the entire term if they don't work out.

Perez: Some groups have extraordinary mechanisms for terminating undesirable members.

Kaplan: What can you do about groups that don't have effective methods for dealing with incompetent members?

Wasserman: Change chairmen. Or drop the groups.

Holland: With some people who are in a group for five years, their interest drifts, and they take their grant funds to something else.

D'Angio: The CCIRC in its review of grant renewal

applications attempts to determine if groups are assiduous in weeding out unproductive members, and that is taken into consideration in the evaluation.

Kaplan: In view of the fact that there is no functional communication system, how do the groups deal with redundancy?

D'Angio: That's an enormous problem. The answer is, they don't. It is a major shortcoming, not being able to get the information we need to deal with that. Both the Williamsburg and Potomac Conferences made recommendations in that area. NCI staff is working on it.

Kaplan: (After Mercado had referred to the new system which will use a computer to help NCI monitor cooperative group protocols) What percentage of the protocols are redundant and what are desirably redundant?

Mercado: The system is not up and operating yet. I'll let you know next year.

CLOSE OUT THE BOOKS ON 1975; NEXT ISSUE OF THE CANCER LETTER, JAN. 2

This issue of *The Cancer Letter* is the last issue of 1975 and the final one, No. 50, in Volume 1. The next issue, Vol. 2 No. 1, will be published Jan. 2, 1976.

FINAL MONEY BILL CLEAR ON PERMITTING NCI TO FUND NEW CONSTRUCTION GRANTS

The HEW appropriations bill which finally cleared Congress this week included the Senate language which earmarked $25 million of NCI money for construction and renovation. Acceptance of that earmarking by the House-Senate conferees implied acceptance of the strong language in the Senate Appropriations Committee report, which specifically stated that funds must be made available for new construction.

The Office of Management & Budget rarely lets a loophole in cancer-related legislation go unused, and the fact that the term "new" construction does not appear in the appropriations bill itself may give OMB the opening it needs to continue fighting NCI on that issue. However, an NCI executive said, "We've been assured by Congress that the intent is absolutely clear, that there's no doubt this action allows NCI to make awards for new construction."

OMB's official position remains that it will not approve money for construction of any new health facility but only for renovation and alteration. It has backed down on several occasions in the face of firm pressure from NCI and members of Congress and the fact that it could face legal action by grantees denied construction funds.

The new appropriations bill offers OMB a face-saving way to reinterpret its position. Money bills have the force and effect of law, and so far the Ford Administration has shied away from being burned by court actions overturning illegal fund withholding, as was the Nixon Administration.

Both House and Senate passed the conference report by overwhelming margins—321-19 in the House and by voice vote without any objection in the Senate. Both would appear to be veto-proof votes, unless the President goes all-out to defeat the bill.

Rep. Robert Michel (R.-Ill.), who frequently carries messages from Ford to Congress, said the bill was "veto bait" because it is $915.8 million over the President's budget for HEW (and the Dept. of Labor, which is always included in regular HEW appropriations bills). More than half that excess—$496 million—is for NIH, Michel pointed out. He singled out the NCI budget in his attack:

"Conferees accepted 40% of the Senate increases over the House for the various institutes (at NIH)," Michel said. "This results in a budget of $743 million for NCI, an increase of $74 million over last year, and a 320% increase since fiscal year 1971. There is little if any evidence that such large incremental increases over a very large base produce much progress toward important findings but instead often result in funding low-priority projects. In fact, there is an increasing body of scientific opinion which is critical of such rapid increases in cancer funding. This was reflected to a great extent in debate on the Senate floor . . .

"Many of the same arguments can be made with respect to the Heart & Lung Institute."

Michel charged that NIH could stabilize its budget and "still increase actual research efforts if we start weeding out some of the excess involved in the grantsmanship games being played at NIH." The 16,000 NIH grants and contracts "are awarded through a system of peer group review, a method in which there is certainly plenty of opportunity for backscratching, padding of contracts, favoritism, and conflict of interest. This ought to be probed in depth," Michel said.

He also criticized what he said was the growth in payment of overhead (indirect) grant costs from 15 to 26% and charged that in some cases, as much as 60% of grant payments were used for overhead. The difference between 15 and 26% is $165 million, he said.

"Grants also are being used to pay salaries of researchers in more and more instances, and there are indications that some academic institutions are charging off faculty salaries to the grants, using grant money to finance normal university operations. . . The size of these private research salaries also should be reviewed. How much of the research grant money is going into research, and how much is being used to pay artificially high salaries?" Michel asked.

Only defense of the cancer budget in the House debate was offered by Rep. Joseph Minish (D.-N.J.), who cited cancer incidence and death statistics and said, "The federal anticancer effort is one area that must not be permitted to fall victim to shortsighted

budgetary restrictions. The effort we began with the National Cancer Act of 1971 must be permitted to expand until we have finally conquered this most dreaded of all diseases."

Most of the House debate involved the controversial antibusing amendments added by the Senate, the issue that had been holding up action by conferees for weeks. The amendments, although softened to some extent, remained in the bill. The President reportedly favored those amendments, which could be a factor in whether or not he vetoes the bill.

Other items in the conference report affecting NCI:

- The statement that "conferees agree on the pervasive nature of the problem of environmental carcinogens and direct NCI to utilize up to $3 million to initiate, through and with the National Institute for Occupational Safety & Health, an occupational carcinogenesis program."
- Establishing the number of positions permitted NCI at 1,968, an increase of 62 over the 1975 level and 132 more than asked by the President. The original Senate bill had 94 extra positions for NCI. There were actually 1,903 positions filled at the end of November, and NCI executives were pleased by the final figure. This number is actually spelled out in the bill, along with a total for NIH of 11,154, an increase of 346 over 1975, which thus permits OMB no leeway in restricting the number of positions as it has in the past.

The bill went to the White House Monday, barely beating the deadline required to prevent a pocket veto. If the President does not sign a bill within 10 days, it becomes law without his signature—unless Congress is not in session. In that event, it is pocket vetoed, and Congress has no opportunity to override. Congress plans to adjourn Dec. 19, so a pocket veto now is not possible.

NIH ALREADY TAKING A LOOK AT PEER REVIEW SYSTEM; HEARINGS SCHEDULED

Rep. Michel's attack on the peer review system and call for a close look at it failed to mention that such a review is under way. In fact, the NIH Grants Peer Review Study Team has scheduled three public hearings around the country to find out what the scientific community—and anyone else who might be interested—thinks about it.

The hearings will be held Feb. 12 in Chicago, 219 S. Dearborn St. Room 204A; Feb. 19 in San Francisco, 555 Battery St. Room 503; and Feb. 26 in Bethesda, NIH Bldg 1 Wilson Hall. All meetings will start at 9 a.m. and are open.

The study team, headed by Ruth Kirschstein, director of the National Institute of General Medical Sciences, is soliciting comments on:

- Adequacy of the total review system: effectiveness of the system in serving and responding to societal needs and expectations for biomedical research on disease-related problems; effectiveness of the system in assisting in maintenance of a strong, high quality national biomedical science base; and the extent to which the system assists in meeting the best standards of public accountability for expenditure of public funds.
- Adequacy of the initial scientific review.
- Adequacy of the council review.
- Adequacy of the priority rating system.
- Impact of the Privacy Act of 1974.
- Impact of the Freedom of Information Act, as amended in 1974.
- Impact of the Federal Advisory Committee Act.
- Recommendations as to how the present grants peer review system can be improved.

NIH said attendance and number of presentations will be limited to the space and time available. Those wishing to attend or present statements should contact Mathilde Solowey, executive secretary of the study team, at NIH, Bldg 31 Room 4A35, Bethesda, Md. 20014, or phone 301-496-1231. State which hearing site you plan to attend and whether or not you plan to make a statement. Deadline for signifying such intentions, for any of the meetings, is Jan. 16.

Those planning to make a presentation must file a written statement or detailed summary of their presentation with the executive secretary by Jan. 30. Only speakers discussing subjects relevant to the study will be scheduled, NIH said. Initially, each speaker will be limited to 10 minutes, although more time may be available depending on the number of scheduled speakers. Those who cannot attend the hearings but would like to submit a written statement may do so.

All members of the study team are NIH staff—Robert Akers, policy and procedures officer for extramural research and training; George Brooks, associate director for extramural programs; Carl Fretts, director of the Div. of Contracts & Grants; Norman Gary, Div. of Research Grants; William Goldwater, assistant associate director for collaborative research; Jerome Green, Heart & Lung Institute; Ann Kaufman, research grants officer for extramural research and training; William Raub, National Eye Institute; Richard Risenberg, NIH legal advisor; George Russell, director of the Div. of Management & Budget; Stephen Schiaffino, Div. of Research Grants; and Katherine Wilson, DRG. David Kefauver, with the Alcohol, Drug Abuse & Mental Health Administration, is an ex-officio member.

CONTRACT AWARDS

Title: Procurement of embryonic cell lines with variable growth rates
Contractor: Litton Bionetics, $499,903.

Title: Study for detection of CEA in humans
Contractor: Mallory Institute, $57,512.

Title: Continuation of iso-antigenic typing of mouse strains and tumors
Contractor: New York State Dept. of Health, $151,564.

Title: Development of practical process for producing adriamycin
Contractor: Parke Davis, $29,517.

Title: Continuation of chemotherapy studies in patients with breast cancer
Contractor: Mayo Foundation, $128,212.

Title: Development of methods of bowel preparation preparatory to barium enema or colonoscopy
Contractor: American College of Radiology, $122,806.

Title: Conduct studies of wart viruses in tissue culture
Contractor: Sloan Kettering, $99,492.

Title: Viral-chemical carcinogenesis studies
Contractor: Microbiological Associates, $66,667.

Title: Studies on isolation and characterization of Type C viruses and diagnostic testing and service functions
Contractor: Microbiological Associates, $65,082.

Title: Studies on conditional lethal mutants of RNA tumor viruses
Contractor: Univ. of Southern California, $190,667.

Title: Studies of molecular events leading to transformation by RNA oncogenic viruses
Contractor: Litton Bionetics, $852,337.

Title: Investigations of suspected oncogenic viruses in nonhuman primates
Contractor: Litton Bionetics, $79,975.

Title: Therapy of patients with brain tumors
Contractors: Duke Univ., $537,215; Bowman Gray School of Medicine, $213,092; Univ. of California (San Francisco), $480,481; Clinica Neurochirurgica Deli Universita di Pavia, Italy, $116,041; Indiana Univ., $288,447; Univ. of Kentucky, $349,191; New York Univ., $483,102; Ohio State Univ., $259,444; and Montefiore Hospital, Pittsburgh, $366,045.

SOLE SOURCE NEGOTIATIONS

Proposals are listed here for information purposes only. RFPs are not available.

Title: Immunologic assessment of high risk cancer families
Contractor: Litton Bionetics.

Title: Demographic cancer research program in Hawaii
Contractor: Univ. of Hawaii.

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. Some listings will show the phone number of the Contract Specialist, who will respond to questions about the RFP. Contract Sections for the Cause & Prevention and Biology & Diagnosis Divisions are located at: NCI, Landow Bldg. NIH, Bethesda, Md. 20014; for the Treatment and Control Divisions at NCI, Blair Bldg., 8300 Colesville Rd., Silver Spring, Md. 20910. All requests for copies of RFPs should cite the RFP number. The deadline date shown for each listing is the final day for receipt of the completed proposal unless otherwise indicated.

RFP NCI-CB-64022-31

Title: *Purification of human tumor associated antigens and preparation of specific antibodies to these antigens*
Deadline: *Feb. 10*

To purify human tumor associated antigens and make these available for evaluation by in vitro and in vivo assays of cell mediated immunity. To prepare specific heterologous antisera to these antisera to these antigens, for identification of the antigens during isolation, and for potential use in radioimmunoassays for tumor associated antigens. Since this project will necessitate a regular, close working relationship between the contractor and NCI investigators, the contract facility must be within a 50-mile radius of NIH.

Contract Specialist: Robert Townsend
Biology & Diagnosis
301-496-5567

RFP NO1-CP-65748-62

Title: *Development of decontamination procedures for chemical carcinogens*
Deadline: *Feb. 10*

The purpose of this project is to develop well-documented procedures for treatment of carcinogen-containing wastes. The ultimate objective of this project is to provide scientists in carcinogenesis research with waste-treatment techniques.

Contract Specialist: D.J. Longen
Cause & Prevention
301-496-6496

The Cancer Letter—*Editor* JERRY D. BOYD

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