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DEVITA SUGGESTS CHOP SHOULD BE EXPANDED, GIVEN LONG TERM STATUS, BUT ONLY WITH A "QUID PRO QUO"

The prospect of an expanded and long term Community Hospital Oncology Program was suggested by NCI Director Vincent DeVita when he addressed the Assn. of Community Cancer Centers annual meeting last week.

The current CHOP effort involves the award of 18 month planning contracts to 23 community hospitals, with contracts for two years of implementation to follow for each organization which successfully

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In Brief

KERMAN NEW PRESIDENT OF ACCC, DAVID JOHNSON NAMED PRESIDENT ELECT; WYNDER GETS NY AWARD

HERBERT KERMAN, chief of the Dept. of Radiology at Halifax Hospital Medical Center in Daytona Beach, assumed the presidency of the Assn. of Community Cancer Centers at the organization's annual meeting in Washington. **ROBERT FRELICH**, Wilmington, Del., is the retiring president. **DAVID JOHNSON**, chief executive officer of Deaconess Hospital in Evansville, Ind., was voted president elect. **WILLIAM DUGAN**, Methodist Hospital, Indianapolis, was elected secretary. New members of the board of trustees are **PAUL ANDERSON**, director of Penrose Cancer Hospital, Colorado; and **ROBERT GREENLAW**, Marshfield Clinic, Wisconsin. Reelected to the board were **JOHN YARBRO**, Columbia, Mo., and **ROBERT WROBLEWSKI**, Akron. . . . **ERNST WYNDER**, president of the American Health Foundation, received the first New York State Health Education and Illness Prevention Award. It was presented in Albany by Gov. Hugh Carey. Among other accomplishments, Wynder conducted, with Evarts Graham, the first large scale epidemiological study linking lung cancer to cigarette smoking. . . . **VINCENT DEVITA**, discussing use of contracts with the National Cancer Advisory Board: "The problem (behind some criticism of NCI contract operations by federal inspectors) is that the federal government's contract mechanism was developed to build battleships, and they try to hold us to it." Frederick Seitz noted that some institutions use only contracts to support basic research. "Is there any stigma attached to being a contractor rather than a grantee?" Rose Kushner asked. "Only among superstitious people," Seitz said. "There is some stigma even for me to be standing up here discussing contracts," DeVita said. . . .**MICHAEL LERNER** has received M.D. Anderson's 10th annual Wilson S. Stone Award for his studies of small nuclear RNA protein complexes accomplished he completed work toward MD and PhD degrees at Yale. The award is given for outstanding achievement in the biomedical sciences by a student.

CHOP INSTITUTIONS SHOULD PROVIDE PATIENTS FOR RESEARCH, DEVITA SAYS

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completes the planning process. ACCC, at its leadership meeting last year, had called for expansion of the program to other hospitals if the present model proves successful.

DeVita's suggestion would go beyond even what ACCC had in mind. He said at an ACCC executive committee meeting prior to the annual meeting that NCI might be interested in supporting as many as 75 CHOPs and that it should be fore more than the three and a half years in the present program and five years with the previous Clinical Oncology Program.

In his address to the full membership, DeVita said that one of his criticisms of the current CHOP effort is that "there is no provision for continuing it. If all that is desired is a one shot effort to build an institution's program, if you want only to upgrade the level of treatment, fine. But if as we all expect we will need to continue to develop new therapy for 15 to 20 years, at least, then we will need to continue (the CHOP or similar effort beyond the present plan)."

Any expansion or long term commitment by NCI will require a "quid pro quo," DeVita said—participation by those institutions in the program in clinical research. "Providing patients for research and research for the benefit of patients," as he put it. The quid pro quo should not be just referral of patients to centers, DeVita said, but "entering patients in community hospitals in clinical trials."

DeVita said one of the major failures of the Cancer Control Program was "failure to link up with centers." He noted that the CHOP RFP excluded centers and also excluded prevention efforts. "The major problem I have with the contracts is the failure to require a quid pro quo. If CHOP is expanded we will need the requirement of a contribution to national resources."

DeVita said that "there are few absolutes, but one of them is that the current levels of care are inadequate. Any sustem that tends to perpetuate current levels is inadequate. . . . Perhaps it is unkind to say that the Cancer Control Program has been unsuccessful, but if there is any lesson in the Cancer Program it's in Cancer Control, which we haven't linked up to research. The reason was that it was set up in an isolated division, and did not relate to organizational activities dealing with control."

John MacDonald, director of the Cancer Therapy Evaluation Program for NCI's Div. of Cancer Treatment, told ACCC members that "if we are to do clinical trials with previously untreated patients, we need to work very closely with community oncologists." He cited as an example of "one of the most cost effective" efforts along that line the North Central Cancer Treatment Group, which works with the Mayo Comprehensive Cancer Center. That group "may serve as a model for the development of new regional groups," MacDonald said.

The pilot project will fund two or three new regional groups, primarily with support for operational offices, MacDonald said. The geographic limits of a group will be deliberately left "entirely vague" in the request for applications (RFA) being written which will be issued in three months or less. The region should be defined "basically by how many physicians and patients and other resources are available," MacDonald said.

Operations offices for the new groups "should make it easy for physicians to put patients on trial. Data managers will help eliminate paper work for physicians," MacDonald said. Goals of the new program are: To provide a cost effective resource; encourage multimodal clinical trials and the participation of patients managed by community based oncologists; and facilitate the availability of clinical trials as a first treatment option for patients in communities.

Four speakers discussed aspects of "The Impact of New Technology on Community Cancer Care in the 1980s."

E. James Potchen, chairman of the Dept. of Radiology at Michigan State Univ., speaking on diagnostic radiology, said that "the margin to be gained to achieve total certainty in a diagnosis is very, very costly and in the end, certainty is impossible."

Potchen said that the use of CAT scans in diagnosis of a number of malignancies "is useful . . . clearly the preferred technology. I say preferred because that's my bias. There are no good data to establish that this is clearly preferable. In medicine, so much is tied up in our biases and prejudices that we don't provide room for new technology diffusion."

Other new diagnostic techniques include ultrasound, "which I feel is very exciting, particularly used with computers;" angiography, "very promising;" and other developments enhanced by use of computers.

Stephen Carter, director of the Northern California Cancer Program, discussed the impact of chemotherapy, stem cell assay and bone marrow transplantation on community cancer care.

Attempts to improve the chemotherapy therapeutic index will require increased concentration of agents, sensitivity predicting, combined modalities and analog development, Carter said. One exciting prospect is development of protective drugs, which guard normal tissue against the effects of anticancer agents. Some of those developed as radioprotectors also protect normal cells against chemotherapy toxicity, he said.

Allogenic bone marrow transplantations are

proving effective but the resources required may preclude their use in the community, Carter said. Autologous transplants are still in early stages of investigation and not ready for wide use.

The tumor stem cell assay "could be of great value," Carter said. But it is "clearly, still investigational."

Hybridoma, involving techniques to detect micrometastasis and to destroy micrometastasis with radiolabeled antibodies and drugs linked to the antibodies, theoretically "could destroy all tumor cells. It is the magic bullet dream," Carter said. And of course still very much in the realm of research and far from the clinic.

Arvin Glicksman, chairman of the Div. of Radiation Oncology at Rhode Island Hospital, spoke on new techniques in radiotherapy.

Efforts to increase the sensitivity of tumors to radiation include development of high LET radiation, radiosensitizers, and hyperthermia, Glicksman said.

Neutron radiation is the high LET therapy closest to availability for clinical use, and is being supported by an NCI program to add three new generators to those in existence. However, "I do not believe neutron therapy will be available for community use in the decade of the 80s," Glicksman said.

An alternative is the "software solution"—development of compounds which increase the sensitivity of tumor cells to radiation. If it works, it would be used with standard radiation equipment and be within the range of community hospitals, he said.

Hyperthermia also increases cell sensitivity to a number of cytotoxic agents, Glicksman said. The essential problem with hyperthermia is thermal dosimetry, in getting sufficient temperature increases concentrated on the tumor. Ultrasound, electromagnetic radiation, and implants with radioantennae are being developed to overcome that problem. Total body hyperthermia is still being investigated.

"It's a hardware problem but not as costly as high LET," Glicksman said. "It may well be useful in community settings."

Frank Rauscher, vice president for research of the American Cancer Society, described the current status with interferon.

"Interferon has shown a very decent response rate in treating some human cancers," Rauscher said. "I might add, it shows that maybe we should not give up the theory of a viral cause of cancer." Rauscher was a virologist in his lab science days before he became director of etiology at NCI and then director of the institute.

Patients are still being entered into the trials supported by ACS. Those trials are an attempt to accomplish three things, Rauscher said. "One, to answer the question, Is there activity? The answer is yes. If we include a 50 percent tumor regression as partial response, then the total—complete and partial response—is 45 percent positive response for all tumors. It is nowhere near that good for melanoma patients.

"The second is to try to learn about the pharmacokinetics of interferon. We're working on that—how much to give, when to give it, how does it work, does it work better with other drugs.

"Third, we tried to seduce our friends in the federal government and industry to get in, buy more interferon, do more clinical trials. That has been accomplished. There are 18 commercial labs now which say they can make interferon, and five or six are doing it. Some are finding other ways to make it better, such as the recombinant DNA interferon now becoming available."

Rauscher said protocols are being revised "because of what we learned about the pharmacokinetics."

If interferon activity against tumors shown in the first trials persists, it still will be "at least another two to five years before we can say, hey doctor, try this," Rauscher said. At the very least it should prove useful in medicine as an antiviral drug "and be with us for a long, long time for use against such things as measles, vaginal herpes, possibly even rabies."

GARB'S FIGHT NOW A PERSONAL ONE AS HE RENEWS BATTLE FOR CANCER PROGRAM

. . . Animal studies are now completed on 17 new anticancer drugs that might help cancer patients. There aren't enough funds to test them all clinically, and even without additional budget cuts, NCI will only be able to test seven of the 17 in clinical trials this year. Can they judge which seven of the 17 are the best? Unfortunately not, since animal tests do not predict accurately which anticancer drugs work best in human beings. It may be that among the 10 that cannot be tested this year are two or three that would be lifesavers. . . . You see, Mr. President, I am now being treated for stomach cancer. It may be that one of those new 17 anticancer drugs could save my life, if they get to clinical trials in time. There are over 3 million Americans with cancer today, and almost all feel as I do. We want to live. I hope you understand.

—**Solomon Garb**, in a letter to President Reagan

No one has accused Solomon Garb of deliberately getting adenocarcinoma of the stomach in order to more forcibly present his case to the Reagan Administration against cutting NCI's budget, but that thought may have occurred to some who know him. It certainly is not out of character for someone whose life has been dedicated to fighting cancer in the clinic and in the halls of Congress to turn the irony of his own affliction into a weapon against his hated enemy.

Garb is a clinical pharmacologist who has spent most of his career searching for better ways to treat

cancer patients. His thorough knowledge of then existing anticancer agents, how they worked, and that so many times they did not work, convinced him that surely there must be many other substances which could be used to treat cancer successfully if they could only be identified and brought to the clinic. This led him to join forces with others who agreed the time had come for a massive new effort in the fight against malignant disease. With the powerful support of Mary Lasker, Garb and the late Sidney Farber founded the Citizens' Committee for the Conquest of Cancer. He still cochairs the Committee, with Emerson Foote and Kay Mansolill.

Lasker, the Citizens' Committee and their allies sold former Texas Senator Yarborough on the worth of their crusade. Garb, Lasker, Farber, and Benno Schmidt were among those Yarborough named to a special Senate Panel of Consultants, whose work and recommendations led to the National Cancer Act of 1971.

Garb has been fighting ever since to preserve the Act and to get it fully implemented. His crusade came to demand nearly all his time—when he wasn't fighting to save his patients, he was working to rally support for the cause, writing, phoning, or lobbying in person members of Congress, their staffs, NCI, NIH, FDA, and everywhere he felt the cause could be pushed, including the White House.

Now, the fight has become a personal one. It is as if cancer, recognizing Garb as an implacable foe, struck back.

Early last fall, Garb started experiencing occasional esophageal pain which he attributed to hasty meals in restaurants required by extensive travel during that period. "I felt fine, and although I did lose a little weight, that was okay because I needed to lose some." But a feeling of exhaustion developed in late October, and when he developed abdominal muscle spasms, he consulted his physician and agreed to a full workup.

It was last Nov. 13 when Garb heard the words heard by more than 700,000 Americans each year. He had cancer. No longer was he just fighting for other cancer patients; he had joined them, and the fight now was for his own life as well.

His tumor "was unbelievably enormous," 10 cm in diameter. "I gave myself six months," he said, knowing that half of all stomach cancer is inoperable. He also knew that most stomach cancer has already metastasized by the time it is diagnosed, and that five year survival rates are somewhere between 10 and 20 percent.

Surgery was performed at M.D. Anderson. "I can't tell you how pleased I was when I woke up and was told that an en bloc resection had been performed, and that there was no evidence of gross metastasis." The surgeon had removed almost all his stomach, all the spleen, and part of the tail of the pancreas. A 6 cm clear margin was taken. The surgeon later told Garb he had thoroughly explored the entire area, especially the liver which is the primary site of stomach cancer metastasis. Of 30 to 40 nodes removed, only two "sentinel" nodes were positive.

Garb decided immediately to go on an adjuvant chemotherapy research protocol. He and his M.D. Anderson physician selected FAM—5-FU, adriamycin and mitomycin C. The drugs are given in two month cycles—all three on the first day, 5-FU on day 8, 5-FU and adriamycin on day 29, 5-FU on day 36, and then two weeks of rest before the next cycle. Garb is now finishing the second cycle and will have at least one more, perhaps as many as six.

There is one more agent in this protocol, and it is here that the irony is supreme. FAM is a very tough combination to tolerate, and Garb is convinced he could not handle it without the aid of THC.

Among the various battles Garb has waged in his professional and political war against cancer was one to develop tetrahydrocannabinol as a useful antiemetic and to secure approval for its use from the federal government. Others have been involved in that fight also, and Garb does not claim sole credit for it. But his report on results of his THC protocol helped convince FDA to approve NCI's request to add THC to its "Group C" distribution list. It is available free through registered hospital pharmacies for cancer patients to control nausea and vomiting.

Garb had a protocol using very high doses of THC to control very severe cases of nausea and vomiting, so severe in some instances that patients refused further chemotherapy and resigned themselves to death. FAM can result in uncontrollable vomiting for up to seven days for persons unusually sensitive to emetic effects of the drugs, as Garb is. It is not as bad as it would be with cis-platinum or DTIC, and Garb determined that he could control the effects with the NCI THC protocol of a maximum 10 mg every four hours.

The high doses Garb used in his protocol were combined with phenothiazine, another antiemetic which also blocked the undesirable cerebral effects of high dose THC.

"I've learned a great deal more about THC as a patient," Garb said. "For one thing, I can better define now what its effect can be. I can't understand why anyone would take THC just to produce a so-called high. It's not pleasant, although it beats vomiting. I think there is zero risk that anyone not already a marijuana user would want to continue using THC or switch to marijuana cigarettes after getting THC as a patient. My patients invariably would turn down an extra day of THC when it was offered, and now I can see why."

Garb deviates from the NCI protocol, taking 5 mg every two hours instead of 10 mg every four hours. He tries to take the absolute minimum dose, accept-

ing three to five vomiting episodes a day rather than taking the higher dose.

Even the lower dose produces drowsiness and inability to concentrate, and "a disorientation in the thought processes that is very disturbing," Garb said. "It's a kaleidoscope of thoughts which become depressing, anxious thoughts as I start to doze." That effect lessened with subsequent courses, and Garb learned to combat the depression "by reprogramming myself. I'll select some bland event from the past and try to remember every detail of it when I lie down. A train trip, or a visit to a museum. Some visual image of the past that is mildly pleasant or generally bland. I'll then fall to sleep in a comfortable frame of mind."

His personal experience with THC "more than ever makes me opposed to the decriminalization of marijuana. I think it would be a disaster to make it easily available, particularly if that encouraged people to smoke it and drive. I can't imagine being able to drive safely after smoking marijuana. And I suspect that the level of THC in my blood after a treatment is less than that in a confirmed marijuana smoker."

Garb began his chemotherapy at M.D. Anderson. His physician there then made arrangements with a medical oncologist in Denver, where Garb lives, to administer the drugs. The Denver oncologist readily accepted the responsibility for following the protocol and meeting the reporting requirements. "He's been doing everything exactly as he is supposed to do," Garb said. "I don't see why there should be a problem with patient accrual into research protocols, if the centers can work that well with community oncologists."

Garb said his experience has made him "appreciate a skilled nurse more than ever. I've always appreciated nurses, but especially now. I was very fortunate with the ones I had at Anderson.

The Assn. of Community Cancer Centers last week presented Garb with its annual award to an individual devoted to achieving the best care for cancer patients.

ACCC President Robert Frelich called Garb "a fighter, an outspoken advocate for the support of clinical research to find new therapies for the benefit of cancer patients."

Garb said he was now "wearing a different hat from some I've worn in the past—today as a patient, recovering from extensive cancer surgery and on a research adjuvant protocol. We—cancer patients and those destined to get it—see cancer as a personal problem. We don't see why the Cancer Program is held to an inadequate budget of $1 billion while others less important, with lesser priority, get more. I've yet to see anyone, with or without cancer, who says the space program with its $5 billion budget is five times as important as the cancer problem."

Garb said that the Citizens Committee has been a major factor in mobilizing support for the Cancer Program in the past. "However, it no longer has the clout to overcome opposition from such as some at NIH, the Washington Post, and covertly, the tobacco industry.

"Today, I feel optimistic. It's been said that when God closes one door, He opens another. That other door is the ACCC. We cancer patients appeal to you to carry on the fight for support of the Cancer Program. You will have the overwhelming support of Americans from coast to coast."

CANCER LETTER PUBLISHES NCI DIRECTORY

Extensive organizational and personnel changes within NCI and the recent shifts of several offices to new locations have caused difficulties for many who must identify or contact staff members.

As a service to its subscribers, ***The Cancer Letter*** has published a directory of key NCI personnel which is included with this issue.

The directory contains the names, building and room numbers and phone numbers of only a relatively few of NCI's 1,800 employees. Those listed are primarily the executives, program directors, branch, laboratory and section chiefs. Directions are included for contacting those not listed.

The directory also includes some listings of agencies and individuals outside NCI pertinent to the Cancer Program.

NCAB MEMBER INSISTS HOFFMANN-LA ROCHE SHOULD PAY FOR VALIUM TESTS IF NEEDED

Irving Selikoff, director of the Environmental Sciences Laboratory at Mount Sinai and a member of the National Cancer Advisory Board, brought up the matter of the possible carcinogenicity of valium, one of the most widely used prescription drugs.

Noting that an animal study indicates that valium may be a carcinogen and that no one seems to be paying much attention to it, Selikoff commented, "If we don't believe animal data, we ought to stop doing animal studies."

"This is different," said David Rall, director of the National Toxicology Program and the National Institute of Environmental Helath Sciences. "No one thinks valium is an initiator but that it may be a promoter." Two animal studies with valium have been completed. "One shows an increased incidence in animals, one doesn't," Rall said.

"If using it increased the rate of cancer, we need to know it," Selikoff said, suggesting it should be further tested by NTP.

"I'm confused," said Board member Sheldon Samuels. "Valium is a commercial product. Why is it an NCI or NTP problem? Why not an FDA problem?"

NCI Director Vincent DeVita said FDA asked

NCI's opinion, and that if further testing is deemed necessary, NCI and NTP have the facilities to do the testing.

"Why not require industry to pay for the tests?" Samuels asked. Rall responded that valium is exempt from the Toxic Substances Control Act provision which requires industry to pay for testing. "If it is a public health problem, we need to know it," Rall said.

"The public health obligation is that of FDA," Samuels said. "They should be the ones requiring tests."

"I suspect that if FDA felt the data were alarming, they probably would have asked for more tests," DeVita said.

"It might be appropriate to bring in NCI anyway," Board member Harold Amos said. "There is the scientific issue to be considered, the issue of promoters."

"From the point of view of good science, I would support any test Dave or NCI feel is necessary," Samuels said. "But from the point of view of it simply being a promoter, I would think that would fall into some bureaucratic cubbyhole at FDA. I think there must be some way to do the work and send the bill to Hoffmann-La Roche."

Hoffmann-La Roche holds the patent on valium, which is said to be the most profitable prescription drug of all time.

Richard Adamson, acting director of the Div. of Cancer Cause & Prevention, said that FDA has provided most of the money so far for valium testing and that if an epidemiological study is undertaken, probably would pick up that cost, too.

"If we don't have a good animal test and have to rely on epidemiology, then it just becomes a body count," Samuels said.

NEW PUBLICATIONS

"Cooking for the Cancer Patient," 110 page cookbook with more than 250 recipes selected because they help meet nutritional needs and/or because they are easy to eat or digest, by Kato Perlman and Jerry Kukachka. Wisconsin Clinical Cancer Center, Public Affairs Office/Cancer Control, 1900 University Ave., Madison 53705. $5.

"NCI Patient Materials," a catalog of free materials available from NCI for cancer patients, their families, and the professionals who work with them. Write to NCI, Office of Cancer Communications, Bldg 31 Rm 10A18, Bethesda Md. 20205.

"Guidelines for Smoking Control," edited by Nigel Gray and Michael Daube. Guidelines to help cancer societies and other health related agencies design, develop and carry out smoking control programs. UICC, Managing Editor, rue Conseil-General, 3, CH 1205 Geneva, Switzerland. 11 Swiss Francs plus postage and packaging.

"Cancer and Nutrition: Etiology and Treatment," edited by Guy Newell and Neil Ellison. A comprehensive review of the relationships between nutrition and cancer. Raven Press, 1140 Avenue of the Americas, New York 10036, $45.

"Immunopharmacologic Effects of Radiation Therapy," edited by J.B. Dubois, B. Serrou, and C. Rosenfeld. Focuses on the effects of ionizing radiation on the immune response. Raven Press, address above, $45.

"Coping with Cancer: A Resource for the Health Professional," edited by Barbara Blumberg, Mara Flaherty, and Jane Lewis and published by NCI's Office of Cancer Communications. A reference work on the psychological and social aspects of cancer. Free from OCC, address above.

"Taking Time: Support for People with Cancer and the People Who Care about Them," by Joan Hartman, also published by OCC. Essentially a lay version of "Coping with Cancer." Free, from OCC.

Contract Awards

FOUR MORE CHOPS AWARDED BY NCI

NCI, nearing completion of its negotiations for 23 Community Hospital Oncology Program planning contracts, announced four more awards last week, bringing to 18 awarded to date. The four are South Fulton Hospital, East Point, Ga., $49,816; St. Francis Hospital, Wichita, $105,460; California Hospital Medical Center, Los Angeles, $150,375; and Riverside Methodist Hospital, Columbus, Ohio, $122,022.

Other contract awards announced included:

Title: Long-term followup of the Breast Cancer Screening Project participants
Contractor: Univ. of Pittsburgh, $547,380.

Title: Murine cell line and tumor bank, modification
Contractor: Salk Institute, $124,869.

Title: Pharmacological studies of antitumor agents
Contractor: Southern Research Institute, $187,950.

Title: Long-term followup of the Breast Cancer Screening Project participants
Contractors: Rhode Island Hospital, $323,797; Good Samaritan Hospital and Medical Center, Portland, Ore., $487,251.

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