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PRELIMINARY BUDGET ASKS $876 MILLION FOR NCI AS CARTER, FREDRICKSON IGNORE ZBB JUSTIFICATIONS

The President's budget request for NCI for the 1979 fiscal year will be $876 million if the preliminary White House figures are not changed, *The Cancer Letter* has learned. This would be only $9 million more than the institute will get in the current fiscal year and, significantly,

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In Brief

APPROPRIATIONS APPROVED; GRANTS, CONTRACTS MAY FLOW UNIMPEDED; NCI POSITIONS AN ISSUE

CONGRESS FINALLY settled the abortion issue and approved FY 1978 funds for HEW, including NCI's $867 million. House and Senate agreed to compromise abortion funding language in a continuing resolution which provides funds through Sept. 30, 1978, in lieu of a regular appropriations bill. The resolution contains all the elements of the regular bill, as approved by House-Senate conferees months ago. NCI may award contracts and grants without interruption, and fears by NCI and other HEW and Dept. of Labor employees that they might not get their paychecks before Christmas were eased. . . . **CONFEREES DID NOT** completely settle what will be done with the additional positions both houses decreed for NCI. The conference report did establish the total number at 2,042—20 more than requested originally in the President's budget last January, and 87 more than the Office of Management & Budget now wants NCI to have. The House, at Congressman David Obey's insistence, had earmarked 20 additional employees for the carcinogenesis and environmental epidemiology areas; the Senate broadened that to include contract and grant management support and treatment. NCI will have to thrash that out with Obey, Sen. Warren Magnuson and OMB. . . . **"LIVING WITH LUNG CANCER,"** a reference book for lung cancer patients and their families, is available from the Mayo Clinic. Medical writer Barbara Cox and Mayo MDs David Carr and Robert Lee turned out the book under contract with NCI's Div. of Cancer Control & Rehabilitation. Write to Mayo Comprehensive Cancer Center, Rochester, Minn. 55901. . . . **"AQUATIC POLLUTANTS** and Biological Effects with Emphasis on Neoplasia" is a 600-page overview of a major problem, edited by Herman Kraybill, scientific coordinator for environmental cancer in NCI's Div. of Cancer Cause & Prevention. He was assisted by C.J. Dawe, J.C. Harshbarger and R.G. Tardiff. New York Academy of Sciences, 2 E. 63rd St., NYC 10021, $52. . . . **CORRECTION:** Nov. 25 issue of *The Cancer Letter* had incorrect starting time on the first day of the Breast Cancer Task Force meeting Jan. 10-12. The meeting will be open Jan. 10 from 8 p.m. (not 8 a.m.) until adjournment; Jan. 11, 8:30 a.m.-adjournment, both days in NIH Bldg 1 Wilson Hall. Jan. 12 sessions are closed.

NCI APPEALS $876 MILLION PRELIMINARY BUDGET, PROBABLY WILL GET NOWHERE

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is the exact amount requested for NCI by NIH Director Donald Fredrickson.

The White House has not firmed up its 1979 figures at this point, with agencies having the opportunity to appeal the preliminary amounts listed for them. But *The Cancer Letter's* source there indicated NCI's appeal for reconsideration of its request for $1.036 billion probably will not accomplish much.

The Carter Administration, in its first chance to develop a budget of its own, thus has picked up where the Nixon and Ford budget manipulators left off—talking big about supporting cancer research without asking for the money to back it up. Carter, at least, apparently will not submit a budget request less than the current year's appropriation, which Nixon and Ford each did at least once.

Once again it will be up to Congress to adequately fund the Cancer Program. But NCI, its advisors and other Cancer Program advocates had hoped the Administration would come up with at least $900 million, if not the $925 million that would be required to keep up with a 6% inflation rate.

So much for "zero based budgeting," the heralded system by which the new Administration would make "sound and intelligent" budget decisions. Here's how the $876 million was arrived at:

—HEW and/or the Office of Management & Budget told Fredrickson what his total for NIH would be.

—Fredrickson virtually held NCI even, and spread the little additional money he was given around the other institutes.

—OMB, with HEW Secretary Joseph Califano's approval, took Fredrickson's figures without any consideration of the ZBB justifications NCI had provided.

The White House traditionally attempts to keep secret budget figures for individual agencies and programs, from the time the preliminary figures are established until the final budget goes to Congress in late January. But the White House has never been a leak-proof institution, and the Georgia crowd has not been an exception.

The Cancer Letter (Oct. 14) presented excerpts from NCI's ZBB justifications which described projects that would not be funded in 1979 if the budget was held to $900 million. They were examples of some very important research in biology, carcinogenesis, cancer control, detection and diagnosis, and cancer centers support that would be delayed indefinitely.

Add to that three more projects in cause and prevention, construction, and biology that would be left unfunded in FY 1979 if NCI is held to $876 million and if the ZBB priority list remains as submitted. They are:

Cause & Prevention Research—$21.9 million

Isolate genes and their products from DNA containing viruses and determine their role in the malignant transformation of human cells. Investigations on the initiation of spontaneous and induced tumors in immunologically compromised hosts. The involvement of the immune system in elimination of carcinogens and conversely the effect of carcinogens on immune function. Development of case control, familial and pedigree studies of selected population subgroups. Studies on preneoplastic lesions and of associated diseases. Further development of in vitro tests using a variety of systems.

Short term objectives—Investigate elements in the cell or host that control replication of tumor viruses. Determine whether certain groups of horizontally transmitted DNA-containing viruses are implicated in human cancer. Complete feasibility studies on blocking of viral tumorigenesis. Study the problem of why many cancer patients have advanced disease at first presentation. Develop specialized registries with information on persons with genetic defects, on persons exposed to various contaminants and other hazards, Provide research for better predictability of the short term in vitro testing methods, with some possible substitution for longer range in vivo testing.

Impact on major objectives—This increment of funding would permit an increased effort directed at assessing the significance of a variety of immune reactions, demonstrable by in vitro tests, to the in vivo prognosis for cancer. Development of specialized registries would be slowed considerably (without this level of funding); new risk patterns are discovered on the basis of such registries. As funding and staffing levels permit, emphasis will be placed on in vitro bioassay testing methods to supplement and replace more costly and time consuming in vivo testing.

More clinical data are being reported indicating distinct differences in pre and post menopausal breast cancer. This has not been investigated by epidemiology methods. Without the funds for this increment, studies would not be initiated. Also, with this funding level, studies on the relationships of carcinogenesis and immunity would be delayed; and areas including the role of immune responses in tumor progression, immunoepidemiology, and nutritional effects on immune status would not be developed.

Construction—$767,000

This funding level would allow renovation of research facilities, including those for recombinant DNA, for the tumor biology research program. This program supports a comprehensive spectrum of research including fundamental and comparative studies in histology, pathology, cell biology, molecular biology, biochemistry, genetics, and developmental biology.

Short term objectives—To renovate approximately

10,800 square feet of space for tumor biology research.

Impact on major objectives—Support and provide safe facilities for the research program; upgrade outdated facilities.

Cancer Biology—$544,000

Investigator-initiated research grants would support biomathematical investigations of basic cellular and organic functions as they occur normally and are altered by malignant transformation. Grants also would be supported in an effort to understand the nutritional requirements of tumor cells, the effects of different nutritional status of tumor cell dependence for hormones and polypeptide growth factors, and other areas of nutrition cancer research. Research in this decision package would be carried on through the programs of epidemiology and nutrition.

Short term objectives—Permit continuation of seven previously funded projects concerned with modeling of cell kinetics and cloning. Develop and publish research reports and cancer classifications related to tumor behavior. Complete at least one comprehensive study to test the effectiveness of different carbohydrate energy sources in promoting the growth potential of a single type of malignant animal cell maintained in vitro.

Impact on major objectives—Attempts to further define nutritional requirements of tumor cells and their adjacent normal cell counterparts that specifically contribute to malignant cell loss of growth control, penetration of surrounding tissue, and decrease in susceptibility to the immune system would be carried on with funds in this package. In the area of epidemiology, insight would be sought into the biologic processes of cancer biometric research.

Without this level of funding, no new research applying mathematical concepts to basic problems of cancer biology could be supported. In epidemiological research, there would be a 14% reduction from the previous effort. Non funding of this level would make impossible a comprehensive attack on problems concerning either the nutritional requirements of cultured human malignant cells or the effects of nutrition on metastasis of animal tumors in normal animals and human tumors in immunosuppressed animal models.

Did anyone at OMB, HEW or NIH spend any significant amount of time analyzing NCI's zero based budgeting presentation, the compiling and writing of which required a great deal of time and effort? Did anyone reach the conclusion that those projects not covered by the $876 million level did not merit support?

Obviously not, which is why ZBB is a sham and a political showcase, at least in this instance.

If $876 million did turn out to be the final appropriation, a few projects listed above that level might be supported, depending on final allocations by Director Arthur Upton. But a number of those listed in the ZBB presentation below that level probably would be dropped, and others reduced drastically. The miniscule $9 million increase would not begin to cover inflation—automatic pay raises for NCI staff; increases in NIH charges passed on to NCI; increased costs of supplies for both intramural and extramural activities; cost of living increases for grantees. All that would have to be covered by reducing program levels up and down the line.

The result would be disastrous—almost no new initiatives; competing grants funded at about 20% of those approved; further cutbacks at centers, with some centers either going out of business or at least going out of the cancer business; hundreds of key people leaving cancer research for other fields.

The importance of NCI's independent budget authority as granted by the National Cancer Act is more obvious than ever. This enabled NCI to bypass Fredrickson and Califano and present its case for the $1.036 billion directly to the President, along with the detailed justification. While this has not had any effect so far on the President, it has resulted in development of a case that can be considered by Congress. Later, when the appropriations hearings begin, Upton will have to present the Administration's rationale for the $876 million, weak as it is. But his original presentation to OMB will be available for the record, and Congress will know in detail the needs of the Cancer Program.

THE CARE AND FEEDING OF SITE VISITORS: DON'T LET THE DEAN TALK FOR AN HOUR

Cancer center executives spent most of their time at their meeting in Memphis last month arguing with NCI staff over the proposed new guidelines for core grants, but they did have some time to get a little advice—mostly from each other—on how to prepare for review of their grants.

David Joftes, chief of the Review & Referral Branch in NCI's Div. of Cancer Research Resources & Centers, opened a panel session on cancer center support grant review by asking, "What can NCI do to improve review? What can center directors do to help us improve review? I hope you believe we are committed to full, fair, scientifically rigorous review."

The panel discussion, paraphrased in some instances, follows:

Lowell Orbison, dean of the Univ. of Rochester School of Medicine and former chairman of the committee that reviews core grants—One of the problems is that there never has been a stable time in the Centers Program. There must be a balance between guidelines and peer review. If there is too much emphasis on guidelines, review is meaningless; too little on guidelines, there is a problem of keeping the focus on the Cancer Program. Ad hoc site visit teams have varying degrees of knowledge of the Centers Program. Site visit teams should focus on fact finding, and

leave the judgment of the quality of science to the review committee.

Ernest Borek, Univ. of Colorado Medical Center and current chairman of the Cancer Special Program Advisory Committee—It's a major responsibility (serving on a review committee). We are frequently called upon to decide possibly on the career of a colleague, or the fate of an idea.

We have to consider the impact of Congress on science. We set up categorical institutions which are funded in detail by Congress. We are obliged to give the best review possible so that, when NCI staff is called by Senator X, or worse by his administrative assistant, staff can say this was the best judgment of scientists on why the center wasn't funded.

The first factor to consider is the quality of the center, and the staff. Two, are they making a unique contribution? Strength lies in diversity. Some forces are upon us that tend to homogenize centers. The worst is the concept of comprehensive centers. That came from Congress, not NCI staff or the scientific community. They had a hearing, someone asked, "What is a comprehensive center?" They named three, then asked, "How many do we need?" and the answer was, "Oh, about 20." Benno Schmidt, a very wise man, said never mind about comprehensiveness, look to quality.

How can we improve reviews? With ad hoc members, sometimes you get one who feels he represents the Office of Management & Budget; one who feels he runs a PhD program; one who wants to show how much he knows; worse, you may get one who wants to create a center in his own image. But this can be remedied.

The amount in grant requests is mounting. It's like haggling in an Arab bazaar. You should ask your young staff (in dealing with site visitors) to be scientists, not salesmen. And they should not be patronizing. Find out who your site visitors are, and their accomplishments. Structure the visits better. The usual pattern is to put the dean on for an hour, or the vice president. We could get a much better sense of the quality of an institution by listening for one hour to four graduate students.

John Durant, director of the Univ. of Alabama Comprehensive Cancer Center—We've heard again and again that these applications are difficult to review. That doesn't mean they are not worth doing. What are some ways to make review better? DCRRC has 43% of NCI's budget to administer, but it doesn't have anything like 43% of NCI's staff. The division should have the staff to do the job. Staff does a superb job but they need more help.

Some guidelines could be clarified. I agree with Hilary Koprowski, that the ink is hardly dry on the old guidelines and here we are considering new ones. This is a core support grant to support research. Some applications have some interesting elements, but they are not research.

One device that could help us all would be better use of the center's letter of intent. What happens to it? As a reviewer, I have never seen them. It would be useful to make them available to site visitors.

Some advice for center directors—budget justifications frequently are incomplete, inadequate. Spend more time writing them. What will renovated space be used for, what's going to be in it, who will work in it, who is going to be supported. Sometimes it is difficult to find CVs of people getting the money.

Site visits could be better structured. Spend some time on it. Put your best foot forward, the most important things first.

Mahlon Hoagland, Worcester Foundation—It would help improve reviews if the members of ad hoc committees would get together in advance and decide exactly what they want. Don't let someone (representing the center being reviewed) go on and on, if it's irrelevant to the presentation. Stop them.

Young staff members are forced to be salesmen. No one on my staff wants to be a salesman, but a scientist is often asked to justify his excellent work in terms of cancer.

Borek—I agree, to some extent. But you and I know that an awful lot of junk is published in the name of basic science. NCI staff can't go to Congress and say there is a lot of very good science going on, give them lots of money and in 40 years they will solve cancer.

Orbison—The dean's 30 minutes, the mayor's, the legislator's 30 minutes, may not be important to site visitors, but it may be very important politically to the center. I would be reluctant as a site visitor to cut a man off and say we're not interested. It is the judgment of the center staff to determine what it wants to present.

Donald Putney, Fox Chase Cancer Center—All too often the business and financial people (on site visit teams) are asked to leave to consider business matters, but they miss the most important part of the presentation. Then they are asked to vote on the entire proposal. I frequently feel I shouldn't vote.

NCI TO SURVEY GRANTEES, CONTRACTORS TO FIND BIOHAZARD COMPLIANCE NEEDS

NCI grantees and contractors will be surveyed to determine the status of their experimental facilities in relation to biohazards and chemohazards, to determine what will be required to bring them into compliance with existing and pending federal regulations.

The NCI survey will be in addition to a more comprehensive one being conducted by a National Academy of Sciences-NIH Committee on Laboratory Animal Facilities & Resources.

Harold Amos, member of the National Cancer Advisory Board, is chairman of the Board's Biohazards Subcommittee. He presented the subcom-

mittee's report at the Board's last meeting, which follows:

Investigators have become increasingly concerned about measures to improve precautionary safety and to protect all levels of research personnel and the public at large from potentially hazardous biologic and chemical reagents. Among the biologic agents of chief concern are bacteria, molds, yeast, viruses, non-bacterial parasites and most recently, recombinant DNA.

Some important facts have emerged that appear to be of consequence:

A. The use of delicate inbred lines of small animals is far more widespread today than formerly.

B. Of particular value to much carcinogenesis work is the use of immunologically compromised animals, so called nude mice, as a host for potentially malignant cells. These mice epitomize a degree of susceptibility to infection that requires well monitored isolation facilities and techniques.

C. Facilities must be evaluated and upgraded with several current objectives in mind: (1) protection of the animals from contamination by organisms from their own and other species, as well as from the animal handlers, (2) protection of the animal handlers from infection by the biological agents being used in the experiments, (3) reduction of the circulation of animals for experiemental intervention and sacrifice through corridors and adjacent research laboratories.

Among the needs identified for upgrading a majority of facilities through renovation and/or construction funds are:

A. Isolated receiving rooms for animals and independently isolated receiving rooms for food and supplies.

B. Enlarged and compartmentalized quarantine facilities for processing newly arrived animals.

C. Proper air flow and pressure differentials in different areas of the facility.

D. Strategically placed sterilizing capacity for equipment to be reused and materials to be discarded.

E. Built-in incineration capacity.

F. Inoculating and autopsy facilities that are flexible and sterilizable to maximize retention of animals in the facilities.

G. Adequate facilities for showering and changing uniforms for all personnel.

At the request of NIH, the National Academy of Sciences formed recently a committee to survey the status of animal care facilities in both non-profit and industrial establishments to "determine current and future needs for laboratory animal facilities and resources supporting biomedical research in the United States." The effort will take the form of a questionnaire, the returns from which will be analyzed by a data analysis program, the specific objectives of which will be established by the committee itself. The committee membership includes C. Max Lang, chairman; John Adams, Emerson Besch, Richard Fox, William Knapp, James Pick, Stefano Vivona and Robert Jorgenson.

The survey contract period commenced June 15, 1977 and ends June 14, 1979. We can expect the final report probably in the late spring of 1979.

Thus far two meetings of the NIH-NAS Committee on Laboratory Animal Facilities & Resources have been held, the first on Sept. 26 and the second on Nov. 4. Max Lang, the chairman, is also a member of our subcommittee. He is anxious that we work closely toegether to assure that the survey being conducted addresses itself to questions of importance to us.

The Board subcommittee membership includes Donald Fox, NCI; Max Lang, chairman, Dept. of Comparative Medicine, Hershey, Pa.; Emmett Barkley, Office of Research Safety, NCI; John Robbins, NIH; A.E. New, NCI; and Harold Amos, chairman.

The principal problem of concern to the board subcommittee is how to move ahead to gain some information about our projection while awaiting the results of the more comprehensive survey of the Academy committee.

A decision will have to be made on what minimal standards of animal facilities (to include biohazards, chemohazards, etc.) the Advisory Board will accept.

HEW published in 1970 a report entitled: "Laboratory Animal Facilities and Resources Supporting Biomedical Research" which has served as a guide to standards for facilities and administration of them.

That manual is now being reviewed by a committee of which Barkley is a member. The revised report may be available as early as March 1978.

The suggested questionnaire for NCI contractors and grantees presented by Amos included these questions:

- Have your animal facilities been accredited by the AALAC? Have you any serious deficiencies despite accreditation?
- Do present facilities provide adequate biohazard and chemohazard units for current usage? For anticipated use over the next five years? What is needed?
- Are renovations or a new facility needed for accreditation? Estimated cost.
- Are renovations or a new facility needed for biohazard or chemohazard current requirements? Estimated cost.
- Are renovations or a new facility needed for biohazard or chemohazard for projected use by 1982? Estimated cost.

Cancer Panel Chairman Benno Schmidt suggested that some responders may want to refer those questions to their lawyers. "Those that don't may wish they had. That is a sticky record to be making in a public document," Schmidt said.

Board member Henry Pitot commented that

"interest and requirements for biological hazards have changed drastically. NCI has put out its guidelines for viruses; NIH for recombinant DNA; OSHA (Occupational Safety & Health Administration) for carcinogenic compounds. OSHA's actions were aimed at industry but they included labs. The lab regulations have since been vacated, but 20 states have adopted the OSHA regulations for labs."

FINAL ISSUE OF THE CANCER LETTER FOR THE YEAR – NEXT, JAN. 6, 1978

When you don't find your copy of *The Cancer Letter* in the mail in the next two weeks, don't blame it on the Postal Service. This issue is the final one for 1977 and the last, No. 50, in Volume 3.

The next issue will be published Jan. 6, 1978. The office of *The Cancer Letter* will be closed from Dec. 24 until Jan. 3.

Best wishes for the Holiday Season and the New Year.

SELECTED ABSTRACTS FROM PAPERS GIVEN AT THERAPEUTIC RADIOLOGISTS MEETING

The following abstracts were selected from papers presented at the annual meeting of the American Society of Therapeutic Radiologists last month in Denver. Most of the papers from which these abstracts were derived are available. Write to Charles Honaker, ASTR, 20 N. Wacker Dr., Chicago, Ill. 60606.

Results of Curative Radiation Therapy in Surgically Staged Hodgkin's Diseases: Univ. of Minnesota Experience from 1970 to 1975 – *Chung Kyu Kim Lee, Seymour Levitt, Clara Bloomfield, Univ. of Minnesota.*

One hundred cases of Hodgkin's disease were treated for curative purposes at the Dept. of Therapeutic Radiology, Univ. of Minnesota Hospitals from 1970 to 1975.

These cases were all clinically and surgically staged and had curative radiation therapy to extended or total nodal fields. There were 13 cases in 1970, 12 cases in 1971, 15 cases in 1972, 20 cases in 1973, 18 cases in 1974 and 22 cases in 1975.

Five cases treated with mantle only in early 1970 will be disregarded in this discussion. Of the remaining 95 cases, 14 were stage I, 55 were stage II and 27 were stage III using the Ann Arbor classification. Histopathology indicated 63% nodular sclerosis, 24% mixed cellularity and 8% lymphocytic predominant Hodgkin's Disease. There was one case of lymphocytic depletion, one case of undetermined type and two cases of atypical type. Prognosis of cases in each stage and pathology will be discussed. There were 11 cases of IA, three cases of IB, 41 cases of IIA, 11 cases of IIB, 22 cases of IIIA and five cases of IIIB. Stage IA revealed 100% disease free survival, stage IIA 80% excluding one lymphocytic depletion and one atypical type and stage IIIA showed 60% of disease free survival. The prognosis of the B (symptomatic) group is much worse than that of the A (nonsymptomatic), with extended or total nodal radiation.

Seven out of nine cases of IIB and four out of five cases of IIIB recurred within 28 months following treatment.

Since 1975, all the stage IIB and IB cases have been treated with chemotherapy after radiotherapy. The nature of each recurrence will be discussed and assigned either to lack of local control or extension of disease outside the treatment volume.

The group with large mediastinal mass will be discussed separately. There are 71% of failure among those cases who had large mediastinal masses.

Carcinoma of the Vagina – *Robert Marcus Jr. and Rodney Million, Univ. of Florida*

Twenty-two patients with stage I through IV primary vaginal squamous cell carcinomas treated for cure with radiation therapy are reviewed, with particular emphasis on the relationship of dose to complications and local control. All but one patient received 4000 to 6000 rads whole pelvis irradiation plus at least one radium application. Local control was 91%, with an absolute disease-free survival of 82% overall. The degree of anaplasia was found to influence prognosis, with all local and distant failures resulting from high-grade lesions. The complication rate was modest, with no fistulae or serious bowel complications. An analysis of total dose (external plus radium) with respect to local failure and complications showed that no major complications occurred at a combined dose below 9000 rads. An analysis of the individual contributions of external irradiation and radium implants showed that all but one very minor complication occurred at a radium dose of 4000 rads or higher, while all the local failures occurred with radium doses less than 2000 rads.

Systemic Radiation for the Treatment of Micrometastases in Non-Oat Cell Lung Cancer – *Philip Rubin, Omar Salazar, Charles Scarantino, Univ. of Rochester Cancer Center*

A phase II-III pilot study utilizing radiation as a systemic agent by means of hemibody (HB) fields for the treatment of micro metastases after conventional split-course chest irradiation was attempted in 16 patients with non-oat cell carcinoma of the lung. Conventional split-course chest irradiation consisted of 250 rad x 10 to the primary target volume (PTV) and regional lymph nodes – 2 weeks rest – 250 rad x 10 to the PTV with posterior cord shields. The HB technique consisted of 800 rad delivered in a single fraction with a dose-rate of 30-40 rad/minute at over 200 cms S.S.D. A large field encompassing the upper half of the body (UHB-above iliac crest) with a protective block corresponding to the field delivered in the first part of the conventional split-

course chest irradiation was delivered first. After peripheral blood counts had returned to normal in 6-8 weeks, a large field encompassing the lower half of the body (LHB-below iliac crest) was delivered next. There was an early pattern of dissemination in non-oat cell lung cancer localized to the chest; six patients had evidence of distant metastases before the UHB field was applied.

Tumoricidal effects of the 800 rad single dose will be presented with individual examples. Detailed accounts of acute and subacute toxic manifestations as well as direct effects on vital signs, blood counts, bone marrow and lung toxicity will be given. In general, UHM radiation was a well tolerated procedure which only requires careful monitoring of patients with cardiac disease in whom transient hypovolemia could lead to isolated incidents of myocardial ischemia.

Treatment of Hodgkin's Disease in a Cancer Oriented Community Hospital – ***Bruce Saxe, Perry Mandel, Nassau Hospital, Mineola, NY***

Seventy-five patients with Hodgkin's Disease, stage I through III have been treated definitively with radiation therapy durint the period from July 1966 through July 1976 (28 stage I, 28 stage II, 19 stage III). No patients initially accepted for treatment were excluded from the study. The mean follow-up period is greater than five years following the last treatment (range one to 10 years). Staging procedures and treatment techniques have been continually refined during this period, but the single most significant factor which reflected an improved disease-free survival has been the detection of occult subdiaphragmatic disease, primarily splenic involvement.

Of 75 patients treated, none were lost to follow up, and in all stages 84% (63/75) remain free of disease with radiotherapy alone. Twelve patients were considered radiotherapy failures because of extension of disease or true metastases, six have died with active disease and one patient died of leukemia at five years. Four patients are free of disease after multiple drug chemotherapy. Most failures (9/12) occurred prior to the institution of staging laparotomy (1970). There were no true or marginal recurrences. The overall survival at this point is 90% (68/75) and no failures have been recognized to date in patients who have at least finished the first year post-therapy free of disease. Other than the one death from leukemia there has been no impairment in quality of survival in any patient which can be attributed to radiotherapy.

Critical Analysis of Supervoltage Photon Modalities in the Irradiation of Pituitary Neoplasia and Craniopharyngiomas – ***Alptekin Ucmakli, Bahman Emami, and Herbert Mower, Tufts-New England Medical Center Hospitals***

A total of 55 patients with pituitary neoplasms and craniopharyngiomas were treated with supervoltage radiation modalities during the period 1969-1977. A variety of external irradiation techniques was applied with the use of individualized computer treatment planning. Radiation qualities which were utilized consisted primarily of low-energy supervoltage photons (^{60}Co γ) and high energy photons (45 Mev Betatron x-rays). The purpose of this report is to present the physical characteristics of different irradiation techniques which were used in this study and to determine the optimal techniques based on computerized dosimetry.

Of 55 cases, there were 51 pituitary neoplasms and four craniopharyngiomas. The majority of pituitary neoplasms in this series were those of non-functioning adenomas, mostly chromophobe adenomas on histological grounds.

The total radiation doses, which were defined as the doses within the tumor volume in this study, were in the range of 4400 rad to 5400 rad for pituitary adenomas and 5400 to 7000 rad for craniopharyngiomas. Treatments were administered with a weekly dose rate of 1000 rad, five days per week fractionation as a rule. The treatment field sizes, tailored individually, were specified at skin surfaces (nominal fields) for stationary field techniques and were specified at isocenter as depth fields for rotational techniques.

Analysis of the computerized data indicated that the parallel opposed field technique proved to be the most unfavorable, especially with low-energy photons, for the irradiation of pituitary and parapituitary neoplasms. The maximum dose (d_{max}) regions with this technique were in the temporal lobes. The use of parallel opposed fields with 45 Mev Betatron photons resulted in a relatively significant improvement by bringing the d_{max} region into the target volume. There was still, however, some disadvantage with this treatment approach even with Betatron photons due to undesirably high exit doses. The most favorable irradiation technique in terms of clinical dosimetry was that of arc rotation with any supervoltage photon quality. The wedged 180° double arc rotational technique with ^{60}Co γ) beam and the similar technique with non-wedged 45 Mev photons were equally superior when compared to other field arrangements. In the three-field technique high-energy photons, even without wedges, provided more favorable dose distributions, both within the tumor volume and in the brain, in comparison to that of low-energy photons with wedged lateral fields.

In conclusion, high-energy photons in this study demonstrated superiority for any field arrangement over low-energy photons. The irradiation technique utilizing arc rotation proved to be the most favorable in terms of clinical dosimetry for any photon quality in the treatment of pituitary neoplasia and craniopharyngiomas.

Radiation Therapy for Carcinoma of the Prostate – The Experience with Small Intestine Injury – ***Nathan Green, Roy Wilbur Melbye, Gerald Iba and Larry Kussin, Valley Presbyterian Hospital, Van Nuys, Calif.***

Treatment regimens used in the management of primary prostate carcinoma usually employ large portals to encompass the pelvic and periaortic nodes and reduced portals to deliver a booster dose to the primary tumor. Significant and at times fatal injury to the small intestine have occurred. Between 1971 and 1974 52 patients received definitive irradiation. Two patients developed small intestine injury and one patient died. Small intestine injury was observed in a patient who probably inadvertently had the small intestine included in the booster portal and in the patient who underwent pelvic surgery following irradiation. Between 1975 and 1977, 74 patients had small intestine x-ray studies to determine the anatomic relationships of the small intestine to the pelvic portal and to the prostate carcinoma.

In patients with large cancers ultrasound studies were done to delineate the superior extent of the tumor. The inferior border of the small intestine was observed to be at the superior extent of the carcinoma in 19 patients and overlapped the prostate carcinoma in 10 patients. Therapeutic efforts to reduce the tumor size prior to booster portal irradiation included hormone therapy and whole pelvic irradiation. A "shrinking field" could then be used. Considerations for tumor control, cure and complications influenced the booster field size. Recognition of the relative position of the terminal ileum to the pelvic portal was important for patients who underwent surgery following irradiation. Precautions could then be taken to avoid surgical trauma. Since initiation of this study no patient has developed small intestine injury. Tumor control rates remain constant.

Treatment of Hodgkin's Disease in Pediatric Patients Stage IIB - IVB – ***Beverly Lange, Philip Littman, Louise Schnauffer, Audrey Evans, Children's Hospital of Philadelphia, Hospital of Univ. of Pennsylvania***

From 1970 to 1976, 21 patients with pathologic IIB to IVB Hodgkin's Disease were treated at Children's Hospital of Philadelphia. Five patients were to receive radiation alone: three developed progressive disease during radiation, and two relapsed after 18 months. All achieved remission on COPP. Three patients are long-term survivors, one has suffered a second relapse, and one has died.

Sixteen patients received COPP and extended-field radiation (2, IIB; 2, IIE; 4, IIIA; 4 IIIB; 4, IV). In 14 chemotherapy was given first. Ten stage II or III patients received subtotal nodal radiation or low dose radiation. Relapse-free survival rate in stages II and III is 100% with a median follow up of 24 months (range 17-87). Two stage IV patients developed progression during chemotherapy; a third relapsed at 28 months, and one is alive with no evidence of disease at 27 months.

No patient treated with combination therapy encountered life-threatening toxicity. One patient had moderate radiation pneumonitis, three had hemorrhagic cystitis, and eight had herpes zoster. Gonotrophins were normal in seven males tested. Three of seven females have ovarian failure.

RFPs AVAILABLE

Requests for proposal described here pertain to contracts planned for award by the National Cancer Institute, unless otherwise noted. Write to the Contracting Officer or Contract Specialist for copies of the RFP, citing the RFP number. Some listings will show the phone number of the Contract Specialist, who will respond to questions. Listings identify the respective sections of the Research Contracts Branch which are issuing the RFPs. Their addresses, all followed by NIH, Bethesda, Md. 20014, are:
Biology & Diagnosis Section – Landow Building
Viral Oncology & Field Studies Section – Landow Building
Control & Rehabilitation Section – Blair Building
Carcinogenesis Section – Blair Building
Treatment Section – Blair Building
Office of the Director Section – Blair Building
Deadline date shown for each listing is the final day for receipt of the completed proposal unless otherwise indicated.

RFP NCI-CP-VO-81004

Title: *Molecular biology of oncorna viral proteins*
Deadline: *Jan. 31*

NCI is seeking qualified investigators to conduct studies on the molecular biology of oncorna viral proteins. Specific experience in the following areas is required: (1) Purification of oncornavirus virion proteins; (2) preparation of monospecific heterologous antisera to purified oncornavirus proteins; (3) development of procedures for isolation of specific cellular receptor for virus; (4) development of radioimmunoassay systems; (5) development of systems for analysis and preparation of purified viral and cellular proteins.

Contracting Officer: J. Thomas Lewin
Viral Oncology
301-496-1781

CONTRACT AWARDS

Title: Study of common antigens
Contractor: Institute for Medical Research, $100,000.

The Cancer Letter –*Editor* JERRY D. BOYD

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