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INTERFERON RESULTS COOL EXPECTATIONS, BUT OTHER REPORTS AT ASCO/AACR DEMONSTRATE SOLID PROGRESS

Reports on the American Cancer Society supported interferon clinical trials described at last week's annual meetings of the American Society for Clinical Oncology and the American Assn. for Cancer Research cooled expectations somewhat, although investigators still insisted the substance shows enough promise to warrant continued research.

The unexciting interferon results were all but forgotten, however, in the wake of reports from studies which demonstrated solid progress in

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In Brief

CLARKSON, FREIREICH HEAD AACR, ASCO; ONCOLOGY NURSING SOCIETY MEMBERSHIP TOTAL NOW 2,369

NEW ASCO, AACR officers: Emil (Jay) Freireich assumed the presidency of the American Society of Clinical Oncology at last week's annual meeting; Charles Moertel is the outgoing president. John Ultmann was named president elect. New directors are Brigid Leventhal and Saul Rosenberg. Bayard Clarkson took over as president of the American Assn. for Cancer Research from Paul Carbone. Sidney Weinhouse was elected vice president and will move up to president next year. New directors are Leila Diamond, Gerald Mueller, Lloyd Old and Richmond Prehn. . . . **ONCOLOGY NURSING** Society members elected Mary Maxwell vice president, Novella Ann Cox secretary and Delores Esparza director at large. President Connie Henke Yarbro is in the middle of a two-year term. ONS membership is fast approaching that of the other two organizations; at the fifth annual meeting last week, it was 2,369. ASCO's total was 2,746, and AACR's about 3,300. . . . **NATIONAL CONFERENCE** on gynecologic cancer sponsored by the American Cancer Society will be held in Los Angeles Oct. 9-11. Latest methods of detection, diagnosis and treatment will be explored. Saul Gusberg, ACS president and a gynecologic oncologist, is chairman. There will be no registration fee, but advance registration is requested. Contact ACS—National Conference on Gynecologic Cancer, 777 Third Ave., New York 10017. . . . **PHS AWARDS** went to Thomas Waldmann, chief of the Metabolism Branch in NCI's Div. of Cancer Biology & Diagnosis for "a landmark discovery of suppression of immunoglobulin synthesis by suppressor lymphocytes in patients with hypogammaglobulinemia which has revolutionized understanding of immunodeficiency diseases;" and to Umberto Saffiotti, chief of the Experimental Pathology Branch in the Div. of Cancer Cause & Prevention, for "outstanding service to NCI, the Interagency Regulatory Liaison Groups, and the President's Regulatory Council in the development of a national policy for cancer risk assessment."

BONADONNA: FULL DOSE CMF DID BENEFIT OLDER PATIENTS; ABVD IMPROVES MOPP

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a variety of modalities or which turned up new information that will be the base for further advances.

The interferon results were reported at a joint AACR/ASCO session on clinical pharmacology and clinical trials, and at an AACR session on breast cancer.

Contrary to earlier expectations (and to the general impression left with congressmen who were sold on interferon as a nontoxic agent), the leukocyte interferon therapy used in the three studies reported at the meetings did cause a variety of side effects. Reversible leukopenia was common, along with muscle weakness, anorexia and elevated temperature. One patient with pulmonary metastases developed progressive pulmonary insufficiency after interferon therapy and died of sepsis secondary to alternate cytotoxic treatment.

Elliott Osserman reported on interferon treatment for multiple myeloma at Columbia, M.D. Anderson and Johns Hopkins. Of 14 patients treated at the three institutions, "some significant response" was seen in four, Osserman said. The patient with the most impressive response developed the most serious complications and therapy had to be interrupted.

Osserman said the interferon batches differed in composition; "one was more effective and more toxic. . . . We had a considerable problem with some of the batches (all the ACS supplied leukocyte interferon was produced in Helsinki). Preparations were less than one percent pure. Something in the preparations had some activity. At present, interferon is no cure and is not as good an antimyeloma agent as chemotherapy."

Osserman agreed with a suggestion from the audience that some of the toxicity could be caused by contaminants in the preparation.

Ernest Borden reported on interferon breast cancer studies at Wisconsin, M.D. Anderson and Mt. Sinai. Five of 16 patients have had a partial response. Two others had measurable tumor reduction but not enough to meet partial response critieria.

The results place interferon "in perspective," Borden said. While it does have a certain amount of activity in metastatic breast cancer, "it is no more active than chemotherapeutic agents."

Susan Krown reported on a study at Memorial Sloan Kettering in which 16 lung cancer patients received leukocyte interferon for 30 days, with no measurable effect on the disease. However, the study showed that interferon enhanced the activity of natural killer cells in all patients during the time they were receiving it, and also increased the amount of DR antigens.

As usual, the clinical scientist getting the most attention and drawing the biggest crowds was Gianni Bonadonna with three reports of profound significance.

Bonadonna's colleague, A. Rossi, presented the five year results of the reknowned CMF adjuvant breast cancer study—they continue heavily in favor of the group receiving the drug combination following radical mastectomy over that receiving surgery alone:

	RM (%)	RM+CMF (%)	P
Total RFS*	48.2	63.5	0.0005
N+ 1-3	53.3	70.5	0.0007
N+ >3	35.6	45.3	0.03
Premenopause	44.3	69.4	0.0001
Postmenopause	51.5	56.0	0.22
Survival	66.4	76.5	0.04

*Relapse free survival

The failure of CMF to significantly improve survival for postmenopausal patients was observed earlier in the study. Bonadonna suspected that it might be related to lower doses administered to many of the older women, as well as to some of the younger patients. He undertook an analysis of the dose response effect and reported on it: Dose reductions did indeed affect survival. Patients who received at least 85 percent of the optimal dose did equally as well regardless of the menopausal status, Bonadonna said.

"Not all patients can receive the full dose because of the schedule," Bonadonna commented. "My own opinion is that changes should be made in the schedule so that 100 percent of the optimal dose can be administered. There is no question that when they receive the full dose, they do better."

The third presentation by Bonadonna and his colleagues at the Istituto Nazionale Tumori in Milan was on their study combining MOPP chemotherapy in treatment of advanced (stage 4) Hodgkin's disease with a non-cross resistant combination of adriamycin, bleomycin, vinblastine and DTC (ABVD).

MOPP alone now cures 50 percent of advanced HD patients, and the results are improved very little with the addition of radiotherapy, Bonadonna said. His study alternated MOPP monthly with ABVD for a total of 12 cycles. A total of 61 patients randomized to MOPP only or MOPP plus ABVD completed the 12 cycles.

At three years, total survival for the MOPP only group was 64.9 percent; for MOPP plus ABVD, 84.9 percent.

Myelosuppression was not increased by MOPP plus ABVD, Bonadonna said. Cardiomyopathy or lung fibrosis were not observed. One patient in the MOPP only group who had received prior radiotherapy developed acute leukemia.

Improvements in complete response (87 percent to 63 percent for MOPP alone) and in relapse free sur-

vival (95.9 percent to 65.4 percent) also were seen.

Bonadonna concluded that (1) the incidence of complete response was significantly increased by the alternating chemotherapy; (2) although results were not significant for the limited number of patients at risk, there is a trend in relapse free survival and total survival in favor of MOPP plus ABVD; (3) MOPP plus ABVD appears superior to MOPP in the presence of more aggressive disease while in patients with no symptoms MOPP seems as effective as the alternating regimen.

Charles Moertel reported on an Eastern Cooperative Oncology Group study with profound implications for the treatment of metastatic islet cell carcinoma of the pancreas.

The study compared streptozotocin (STZ) alone with STZ plus 5-FU. Eighty-one patients were randomized to one of the two arms.

Response rates: For STZ alone, 14 of 41 (34%); STZ plus 5-FU, 25 of 40 (63%). Complete response rates were 12% and 33%. Median duration of all responses was 17 plus months and of complete response, 24 plus months.

"In spite of distressing GI side effects, combined STZ and 5-FU therapy would appear to be of significant value to patients with advanced islet cell carcinoma," Moertel said.

ASCO Program Committee Chairman Sydney Salmon, in a briefing for journalists, noted that the complete response in one third of patients and average duration of complete response now at more than two and a half years "suggests a cure in a form of cancer that was formerly incurable."

Combination chemotherapy and radiotherapy in the treatment of locally unresectable gastric cancer, previously thought too toxic, now appears to have long term benefit, according to a report by Philip Schein on a study by the Gastrointestinal Tumor Study Group.

The study compared 5-FU plus methylCCNU with 5-FU plus radiotherapy followed by 5-FU and meCCNU maintenance. The median survival for the chemotherapy only group is 70 weeks, compared to 36 weeks for the radio-chemotherapy group.

"The difference can be attributed to increased early toxicity and tumor deaths with radiotherapy plus chemotherapy during the first 26 weeks of treatment," Schein said.

The long term benefit for the combined modality therapy has now been demonstrated with a plateau level at 20 percent between years two and three. "Despite initial superiority, 5-FU plus meCCNU treated cases show a continued probability for relapse and death. Aside from the form of treatment, resection of the primary tumor was the most important prognostic factor for long term survival."

Schein concluded that the study "provides important data for the design of future chemotherapy-radiation therapy trials for locally unresectable gastric cancer, and emphasizes the need to reduce the early toxicity of radiation-chemotherapy treatment. Attention must be directed to decreasing the toxicity of irradiation of the upper abdomen, such as the use of smaller radiation portals as well as aggressive nutritional support. Newer forms of combination chemotherapy for gastric cancer have now been developed, such as FAM and FAMe, which produced higher response rates and survival when compared with the 5-FU plus meCCNU regimen. Pilot studies combining these factors are now in progress."

Photoradiation therapy of metastatic soft tissue breast carcinoma was reported by T.J. Dougherty of Roswell Park. The treatment uses hematoporphyrin derivative (Hpd) activated by light in the red region of the spectrum.

Hpd is accumulated and retained in malignant tissue and when activated by the light destroys tissue. Since it is retained longer by malignant than normal tissue, it can be used selectively against tumors. It has been found especially useful in areas previously receiving tolerance doses of radiation.

Dougherty said that all treated lesions in 14 evaluable patients in his study responded to Hpd plus local red light. There have been eight recurrences in two to six months, five with no recurrent disease for two to nine months, and one patient treated for control rather than eradication because of the impairment of the area by previous therapy. Repeat photoradiation is being carried out to treat recurrences.

Application to other types of solid tumors is being examined at various institutions, Dougherty said.

Two studies reported by NCI investigators demonstrated (1) that chemotherapy does not necessarily jeopardize unborn children and (2) small cell lung cancer patients survive longer if they stop smoking immediately on diagnosis.

Julie Blatt said that information from questionnaires sent to 448 cancer patients treated at NIH over the past 10 years indicates moderate to high dose chemotherapy given to a woman or her spouse before conception or after the first trimester probably does not harm the infant.

Blatt cautioned, however, that the numbers of patient pregnancies examined so far are small and the data do not assure that offspring of cancer patients who conceive after chemotherapy will be normal.

There were 42 pregnancies reported in the questionnaire responses, with 28 live births resulting. Twelve of the pregnancies ended in abortions, two spontaneous and 10 elective. Two of the women were still pregnant when the report was prepared. Parents cited concern about birth defects as the

reason for each of the elective abortions, but obstetricians reported no malformations in the aborted fetuses.

The children were examined either by NCI investigators or local pediatricians. Only one abnormality was observed, in the child of a man who was receiving chemotherapy at the time his wife became pregnant. The child had a minor abnormality that has been associated with spina bifida, incomplete fusion of the spine. In this case, spina bifida had not yet resulted at the time of examination.

Anita Johnston-Early, a nurse in the NCI-VA Medical Oncology Branch, reported on the prognostic implications of cigarette smoking status of 112 small cell lung cancer patients. Nineteen had stopped smoking two months to 21 years (median 2½ years) prior to diagnosis and one patient had never smoked. Thirty-five stopped smoking at diagnosis, and 57 continued smoking.

Prognostic characteristics such as performance status and disease stage were comparable among the groups or favored the smoking group. Treatment included chemotherapy with or without chest radiotherapy and/or thymosin fraction V.

The overall survival difference among the three groups was significant, Johnston-Early said. Twenty to 25 percent of the nonsmoking patients are projected to survive beyond 30 months, while none of those who continued to smoke are expected to live beyond that point.

The actual cancer free survival at 18 months from the start of treatment was 28 percent for patients who stopped smoking prior to diagnosis, 16 percent for patients who stopped smoking at diagnosis, and only six percent for those who continued to smoke.

Hyperthermia studies continue to show possibilities for that modality. E. Tilchen reported on a phase 1 trial with his colleagues at M.D. Anderson, using ultrasound hyperthermia for superficial tumors.

Thirty-one patients who received that therapy had failed to respond to other conventional radiation and chemotherapy regimens. Their diagnoses included melanoma, sarcoma, breast cancer, and head and neck cancer.

The temperature in the tumor started at 43°C and in a few patients was increased to 50°C, as measured by a needle probe or thermocouple. The side effects to this local therapy were pain, in six patients, and blistering, in four patients. Twenty-eight patients were able to complete their therapy (two stopping early because of pain and one because of blistering). Of the 28 remaining, 16 (51 percent of all treated patients) had at least a 50 percent decrease in the size of the tumor. Six of the tumors disappeared completely. Two of the six patients who responded completely, and are still living, still have no evidence of disease in the treated area at nearly 300 days later. Both of these patients were treated at 50°C. Patients responding at 43°C to 50°C relapsed by six weeks.

"From this study we conclude that ultrasound induced hyperthermia is a safe and effective means of treating metastatic lesions in the skin," Tilchen reported. "With higher treatment temperatures we may be able to produce more durable responses."

The report noted that a number of clinical investigators are now evaluating the use of heat when given with drugs and radiation therapy to determine if their efficacy may be enhanced, as well as finding different ways to heat tumors with microwave radiation or electromagnetic heating. "This would seem to be a logical direction to proceed because of the disappointing short duration of response except in the few patients treated at very high temperatures."

Another clinical trial demonstrating the value of additional chemotherapy non-cross resistant to MOPP is being carried out by NCI investigators, this one in treating advanced diffuse lymphoma.

As with the Milan Hodgkin's study, it is demonstrating remarkable results. Richard Fisher reported that 33 patients had completed treatment with a combination known as ProMACE (cyclophosphamide, adriamycin, VP-16, prednisone and high dose methotrexate with leukovorin rescue) and MOPP (nitrogen mustard, oncovin, procarbazine, and prednisone).

Patients received ProMACE every 28 days until they either achieved complete disappearance of all disease or the rate of shrinkage of the cancer slowed. "In this study, we allowed the patient's reponse to determine how many corses of drug should be given," Fisher said. All patients received at least two cycles of ProMACE.

Patients then were given an equal number of MOPP courses, "consolidation therapy," which was followed by at least two more courses of ProMACE at two month intervals.

Complete responses were achieved in 23 (67 percent) of the 33 patients. Previous clinical studies at NCI using MOPP, or MOPP plus cyclophosphamide, or BACOP (bleomycin, adriamycin, cyclophosphamide, oncovin and prednisone) achieved as much as 46 percent complete response.

Disease free survival with those previous combinations at five years is 38 percent. NCI statisticians predict that 60 percent of the ProMACE-MOPP patients will be alive at two and a half years.

Two studies involving treatment of advanced ovarian cancer showed promising results.

A clinical trial at Princess Margaret Hospital in Toronto compared three treatment arms: L-PAM alone; Hexa-CAF (methotrexate, 5-FU, cyclophosphamide, and hexamethylmelamine); and CAP (cyclophosphamide, adriamycin, and cis-platinum).

Progression free survival at one year shows an advantage for CAP (p=.05). Although there is a trend suggesting improved survival for CAP, this has not reached statistical significance. Complete clinical responses were seen in six of 22 CAP patients, two of 24 hexa-CAF patients and two of 21 L-PAM patients. Symptomatic improvement occurred earlier with CAP than with the other two arms. Toxicity was more severe in patients receiving the combinations but no treatment related deaths have occurred.

"Early results show improved progression free survival for CAP, and suggest that this combination is safe, acceptable and may also be more effective initial treatment for patients with advanced ovarian cancer," the report concluded. "Further study is necessary to determine its ultimate effect on survival."

The other study, with advanced ovarian cancer patients, was reported by Anthony Greco on behalf of his colleagues at Vanderbilt.

"The purpose of this study is to evaluate by second look staging laparotomy the effects of brief intensive chemotherapy often following substantial surgical debulking in patients with stage 3 and 4 ovarian carcinoma," the report said.

Since August, 1977, 59 patients underwent initial laparotomy with the idea of removing as much tumor as possible. Twenty-four patients were debulked by more than 50 percent of the estimated volume of tumor. Fifteen patients were left with limited stage 3 ovarian cancer (lesions less than 3 cm in diameter) and 44 patients had lesions greater than 3 cm.

Patients then received 28 day cycles of hexamethylmelamine, adriamycin, cis-platinum, and either cyclophosphamide or 5-FU. Nausea and vomiting were universal and myelotoxicity was moderate to severe. Nuerotoxicity was moderate and nephrotoxicity mild.

Forty-five patients had a second look staging laparotomy to assess response six months following the start of chemotherapy. Of the 15 patients with less than 3 cm lesions, 13 had a complete response, one had all known residual disease resected and one had only positive peritoneal washings.

Four of 30 patients with more than 3 cm lesions had a complete response and eight had all known residual disease resected. There have been no recurrences in the 17 patients with complete responses (median followup 14 months, range seven-27 months) but four of nine patients who had all known residual disease resected have recurred.

"Most patients with limited stage 3 ovarian cancer (do novo or as a result of surgical resection) have complete responses to this therapy as judged by careful restaging at second look laparotomy and this group of patients has a high potential for cure," the report said.

TEDDY DEVITA, "AN INSPIRATION," DIES AFTER EIGHT YEARS IN LAF ROOM AT NIH

Teddy DeVita has lost the fight he had waged so courageously for eight years.

The son of Vincent and Mary Kay DeVita died May 27 from complications of repeated blood transfusions required to help combat aplastic anemia. He was 17 and had lived in a laminar air flow room at the NIH Clinical Center since he was nine years old.

Philip Pizzo, senior investigator in NCI's Pediatric Oncology Branch who was Teddy's physician, said that the boy "was an inspiration to me. It's remarkable he was able to adapt so well to that environment." He made history as the longest survivor on record of aplastic anemia. The research benefits "have been enormous," Pizzo said.

Contributions in Teddy's memory may be made to the Patient Emergency Fund–Pediatric Oncology, and may be sent to the Social Work Dept., NIH Clinical Center, Bldg 10 Rm 7D51, Bethesda, Md. 20205.

MILLERS, JENSEN, BERENBLUM NAMED 1980 WINNERS OF GM $100,000 AWARDS

Elwood Jensen, Elizabeth and James Miller and Isaac Berenblum will be the recipients of the three $100,000 GM Cancer Research Foundation 1980 Awards.

The Millers will share the Charles S. Mott $100,000 prize "for their outstanding contributions concerning the critical importance of metabolic activation and covalent binding of chemical carcinogens to informational macromolecules," the Foundation announcement said. James Miller is professor of oncology and Elizabeth Miller professor of oncology and associate director of the McArdle Laboratory at the Univ. of Wisconsin.

Jensen, director of the Ben May Laboratory of Cancer Research at the Univ. of Chicago, will receive the Charles F. Kettering prize for discovering of the mode of action of estrogen in target tissues and recognition of the predictive value of estrogen receptor measurements in human breast cancer.

Berenblum, retired professor of experimental biology at Weizmann Institute in Israel, will receive the Alfred P. Sloan Jr. prize for his discovery of the initiation promotion mechanism of carcinogenesis. "The discovery opens new avenues for understanding what cancer is, how it works and suggests new approaches to cancer prevention," the GM announcement said.

The Kettering award is for the "most outstanding recent contribution to the diagnosis and treatment of cancer;" the Mott award for "the most outstanding recent contributions to the prevention of cancer, including environmental influences;" and the Sloan award "for the most outstanding recent basic science contribution to understanding the etiology and pathogenesis of cancer."

HHS CARCINOGEN HANDLING GUIDELINE PROPOSALS PUBLICATION CONTINUES

A draft of guidelines proposed by the Dept. of Health & Human Services for intramural laboratories handling chemical carcinogens was published in part last week by *The Cancer Letter.* The proposal has not been published previously and HHS has no plans to do so. Since the guidelines eventually may be adopted by federal regulatory agencies, they could be applied to nongovernment labs.

Section I, Responsibilities, of the guidelines was included in last week's publication. The proposals continue:

II. Health Surveillance

A. Pre-assignment Health Assessment

A baseline health assessment should be provided to all employees who work with chemical carcinogens or who are assigned duties in work areas where chemical carcinogens are used. The health assessments should be provided under the occupational medical (employee health) program established by each operating agency. The medical officer responsible for the occupational medical program, after consultation with the principal investigator and the safety committee should determine the content of the pre-assignment health assessments.

The purpose of this pre-assignment health assessment is to establish a baseline health record and to provide counseling on health matters related to the work environment. To be complete, the pre-assignment assessment should include: a work history, a medical history, physical examination, customary laboratory studies; and when available, agent specific studies (examinations and/or laboratory tests) to establish baseline values for any variables that are to be followed subsequently. If evidence of any risk factors or predisposing conditions is uncovered, e. g. smoking, chronic use of medications, pre-existing diseases or conditions, employees should be so informed and counseled concerning the advisability of working in areas where chemical carcinogens are used.

B. Periodic Health Assessments

To insure that the medical record is up to date and to provide opportunities for counseling, periodic health assessments should be provided to all employees who work with chemical carcinogens or who are assigned duties in work areas where chemical carcinogens are used. The periodicity and content of these assessments should be determined by the medical officer responsible for the occupational medical program after consultation with the safety committee and the principal investigator responsible for supervising the employees and the research in which the chemical carcinogens are used.

The assessments, to be meaningful, should include an updating of the employee's work and medical histories, including occurrences of any accidental exposures previously unreported. The following information should be included in the employee's medical record: names of carcinogens used in the laboratory; information on the probability, frequency, and extent of exposures; and any environmental measurements relating to carcinogenic substances that may have been made. The periodic health assessment may also include a physical examination, biochemical or other surveillance of body fluids, and an evaluation of pertinent functional systems of the body.

C. Records

Medical records should be maintained by the occupational medical program of the operating agency for the duration of the employee's employment. Upon termination of the employee's employment, including retirement or death, the medical records should be maintained for at least 30 years after the individual's last work with carcinogens, or until more specific advances in the state of the art of medical surveillance would dictate otherwise.

III. Employee Education

All employees working with, or who may be potentially exposed to, chemical carcinogens should receive sufficient information that will enable them to work safely and to understand the relative significance of the potential hazards as they relate to them personally. Principal investigators, with the assistance of the safety officer, should review relevant safety information with their employees on a regular basis to ensure that they are properly informed and that their knowledge is up to date.

Laboratory and other involved workers, for example, those involved in housekeeping or maintenance work, should be periodically apprised by persons qualified by training and experience including their supervisors, principal investigator and safety officer about (1) the possible sources of exposure, (2) adverse health effects (carcinogenic and other) associated with exposure, (3) laboratory practices and engineering controls in use and being planned to limit exposure, (4) environmental and medical monitoring procedures used to check on control procedures and on the health status of employees, and (5) their responsibilities for following proper laboratory practices to help protect their health and provide for the safety of themselves and fellow employees.

The types and functions of monitoring equipment, such as personal samplers, should be explained so that each employee understands his or her part in environmental monitoring. Medical monitoring procedures should be explained, especially any unusual procedures such as sputum cytology or biologic monitoring of metabolites in the urine. The benefits to workers of participating in these environmental and medical monitoring procedures should be discussed with employees.

The safety plan, safety data sheets, and other appropriate written information describing the relevant toxic, physical, and chemical properties of carcinogens used or stored in the laboratory must be kept in a file that is readily available to employees.

IV. Laboratory Practices and Engineering Controls

The laboratory practices and engineering controls recommended in this section detail general safeguards that should be observed when working with chemical carcinogens in the laboratory. These safeguards will provide protection from exposure to chemical carcinogens to the laboratory worker in the majority of situations. There are instances, however, when the physical and chemical properties, the proposed use, the quantity of chemical carcinogens needed for a particular use or the carcinogenic or other toxic hazard of a chemical carcinogen will be such that either additional or fewer controls might be needed to protection the laboratory worker (See Section V). Professional judgment is, therefore, essential in the interpretation of these recommendations.

A. Personnel Practices

1. Protective Clothing. Laboratory clothing that protects street clothing, such as a fully fastened laboratory coat or a disposable jumpsuit, should be worn in any laboratory area in which chemical carcinogens are being used. Clean clothing should be provided weekly and should not be worn outside the laboratory area. Clothing overtly contaminated by chemical carcinogens should be removed immediately and disposed of or decontaminated prior to laundering. When clothing decontamination methods are unknown or not applicable, disposable protective clothing should be worn. Gloves which are appropriate to the task and chemicals in use should be worn when handling a chemical carcinogen. Disposable gloves should be discarded after each use and immediately after overt contact with a chemical carcinogen.

2. Eye Protection. Devices to provide appropriate eye protection should be available and used in the laboratory work

area. The type of device used will depend upon the hazard presented by the operation and/or chemical in use.

3. Eating, Drinking and Smoking. There should be no eating, drinking, smoking, chewing of gum or tobacco, application of cosmetics or storage of utensils, food or food containers in laboratory areas where chemical carcinogens are used or stored.

4. Pipetting. Mechanical pipetting aids should always be used for all pipetting procedures. Oral pipetting should be prohibited.

5. Personal Hygiene. All personnel should wash their hands immediately after the completion of any procedure in which a chemical carcinogen has been used and when they leave the laboratory. Immediately after an exposure to a carcinogen, personnel should wash or, if appropriate, shower the affected area.

B. Optional Practices

1. Work Area Identification. Each entrance to a work area, where chemical carcinogens are being used or stored, should have affixed to it a sign with an appropriate warning such as:
CAUTION – POTENTIAL CANCER HAZARD
AUTHORIZED PERSONNEL ONLY.

2. Access Control. Work areas, where chemical carcinogens are being used or stored, should be entered only by persons authorized by the principal investigator. Potential problems and hazards that may be encountered in the laboratory should be reviewed with maintenance and emergency personnel prior to their being needed. Access doors to work areas should be kept closed while experiments involving chemical carcinogens are in progress.

3. Work Surfaces. All work surfaces (bench tops, hood floors, etc.) on which chemical carcinogens are used should be covered with stainless steel or plastic trays, dry absorbent plastic backed paper or other impervious material. The protective surfaces should be decontaminated or disposed of after the procedure involving a chemical carcinogen has been completed.

4. Use of Primary Containment Equipment. Procedures involving volatile chemical carcinogens and those involving solid or liquid chemical carcinogens that may result in the generation of aerosols should not be conducted on the open bench; they should only be conducted in a chemical fume hood, a class I biological safety cabinet, a glove box, or other suitable containment equipment. Examples of aerosol producing procedures are: the opening of closed vessels; transfer operations; weighing; preparation of feed mixtures; blending; open vessel centrifugation; and the application, injection or intubation of a chemical carcinogen into experimental animals. Tissue culture and other biological procedures involving chemical carcinogens may be conducted in a class II, type B biological safety cabinet. A class II type A biological safety cabinet may also be used in the cabinet's exhaust air is discharged to the outdoors. The selection and use of a class II biological safety cabinet should be a joint decision of the principal investigator and the safety officer. Primary containment equipment used for containment of chemical carcinogens should have affixed to it a label with an appropriate warning such as:
CAUTION – POTENTIAL CANCER HAZARD

5. Use of Analytical Instrumentation. Vapors or aerosols produced by analytical instruments, when used with chemical carcinogens, should be captured through local exhaust ventilation at the site of their production or they should be vented into a chemical fume hood, or a class I biological safety cabinet. When a sample is removed from the analytical instrument it should be placed in a tightly stoppered sample tube or otherwise safeguarded from contaminating the laboratory. Any analytical equipment that becomes overtly contaminated should not be used again until it has been decontaminated.

6. Use of Respirators as Personal Protective Devices. A respirator use program should be provided for all personnel, including emergency and maintenance personnel, who enter areas where airborne contamination is present. This program should meet the requirements of the OSHA safety and health standards for respiratory protection as detailed in 29 CFR 1910.134. The respirators should be selected in accordance with the requirements of the National Institute for Occupational Safety & Health under the provisions of 30 CFR Part 11. The joint OSHA/NIOSH standards completion program respirator decision logic should be used to determine the proper type of respirator to be used. The respirator type should be approved by the safety officer prior to its selection.

7. Storage and Identification of Stock Quantities. Stock quantities of chemical carcinogens should be stored in a specific storage area or cabinet that is secured at all times. It is possible that such a storage area or cabinet might be located within the laboratory work area. The storage area or cabinet should have affixed to it a sign with appropriate warning such as:
CAUTION – POTENTIAL CANCER HAZARD
AUTHORIZED PERSONNEL ONLY

The principal investigator or person responsible for the storage area should maintain a listing of stock quantities of chemical carcinogens stored within the storage area. The inventory should include the quanitites of chemical carcinogens acquired and the dates. of acquisition. Storage vessels containing stock quantitites should have affixed to them labels with an appropriate warning such as: CAUTION – POTENTIAL CANCER HAZARD. Additional storage precautions may be required for these compounds based upon o ther properties (i.e., flammability, radioactivity, etc.).

8. Working Quantities. Working quantities of chemical carcinogens present in the work area should be kept to a minimum. Quantities should not exceed the amounts required for use in one week. This does not include amounts stored in a specific chemical carcinogen storage area or cabinet that is located within the laboratory work area. Storage vessels containing working quantities should have affixed to them labels with an appropriate warning such as: CAUTION – POTENTIAL CANCER HAZARD.

9. Laboratory Transport. Storage vessels containing chemical carcinogens that are to be moved from one site to another (i.e. storage area to work area) should first be placed in an unbreakable outer container. Contaminated materials which are to be transferred from work areas to disposal areas should first be placed in a closed plastic bag or other suitable impermeable a nd sealed primary container. The primary container should be placed in a durable outer container before being transported. The outer container should be labeled with both the name of the chemical carcinogen and an appropriate warning such as: CAUTION – POTENTIAL CANCER HAZARD.

10. Housekeeping. General housekeeping procedures which suppress the formation of aerosols such as the use of a wet mop or a vacuum cleaner equipped with a HEPA filter to remove particulates should be used. Dry sweeping and dry mopping should not be used because of the hazard of aerosol formation. In those instances where a chemical carcinogen or contaminated material is spilled, special clean-up procedures developed for the individual compound should be employeed.

11. Protection of Vacuum Lines. Each vacuum service, including water aspirators, should be protected (e.g., with an absorbet or liquid trap and a HEPA filter) to prevent entry of any chemical carcinogen into the system. When using a volatile carcinogen, a separate vacuum pump should be used. This device should be placed within or vented into an appropriate laboratory-type hood.

12. Packaging and Shipping. Chemical carcinogens should be securely packaged to withstand shocks, pressure changes, and any other conditions which might cause the leakage of

contents incident to ordinary handling during transportation. Information concerning the proper methods for packaging and shipping of hazardous materials is detailed in Dept. of Transportation regulations 49 CFR Parts 170-178.

13. Decontamination. Contaminated materials should either be decontaminated by procedures that decompose the chemical carcinogen to produce a safe product or be removed for subsequent disposal.

14. Disposal. Prior to the start of any laboratory activity involving a chemical carcinogen, plans for the handling and ultimate disposal of contaminated wastes and surplus amounts of the carcinogen should be completed. The principal investigator and the safety officer should jointly determine the best methods available that are in compliance with federal, state and local codes and ordinances.

C. Facility Recommendations

1. Handwashing Facility. A handwashing facility should be available within the work area. This need not be a facility used exclusively for handwashing. The use of liquid soap is recommended. When new facilities are installed, foot- or elblow-operated faucets should be provided.

2. Shower Facility. A shower facility, other than emergency drench showers, should be located in the building in which chemical carcinogens are used. The shower facility should be available and readily accessible at all times.

3. Eye Wash Facility. An emergency eye wash facility should be located in each laboratory. It should be designed to wash both eyes at the same time with a continuous stream of potable water.

4. Exhaust Air from Primary Containment Equipment. The exhaust air from glove boxes should be treated by filtration, reaction, absorption, adsorption, electrostatic precipitation or incineration. The need for and type of treatment of exhaust air from other primary containment equipment, including open face laboratory-type hoods should be determined by the safety officer in consultation with the principal investigator. Treatment systems that remove chemical carcinogens from the exhaust air by collection mechanisms such as filtration, absorption and adsorption should be oeprated in a manner that permits maintenance so as to avoid direct contact with the collection medium. All exaust air from primary containment equipment should be discharged to the outdoors so that the possibility of entry into a building's air supply is minimized.

5. Exhaust Ventilation. A mechanical exhaust ventilation system should be provided for controlling air movement. The movement of air should be from areas of lower contamination potential to areas of higher contamination potential (i.e. from entry corridors to the laboratory). This directional air flow may be achieved by a common building exhaust system provided that the exhaust air is not recirculated to any other area of the building. Recirculation of air within the individual laboratory area, however, may be provided. The exhaust air from laboratory areas should be discharged outdoors so that the possibility of entry into a building's air supply is minimized. Exhaust air from laboratory areas which is not derived from primary containment equipment can be discharged to the outdoors without being treated.

V. Situations Requiring Special Consideration

The purpose of this section is to generally describe situations involving chemical carcinogens where either more or less stringent safeguards might be considered in providing protection to the laboratory worker. No specific definitions for such situations can be provided; an attempt to do so would be misleading. Any modification to the laboratory practices and engineering controls described in Section IV should be carefully considered by the principal investigator, the safety officer, the safety committee.

The risk of exposure to a chemical carcinogen used in the laboratory is related among other things to the quantity and physical properties of material used and the nature and complexicity of the experimental procedure. There is greater risk of exposure if, under the same procedural conditions, 100 mg of material is used than when 1 ug of material is used. Similarly, when the same quantity of material is used, the potential for exposure is greater for operations such as blending, preparation of dry feed mixtures or the manipulation of powders than it is for operations such as the preparation of aliquots of stock solutions.

The balance of the guideline draft will be published next week if space permits.

RFP 223-80-6013

Title: *Optimization of mammography*
Deadline: *Approximately July 15*

Develop a mathematical model capable of predicting physical imaging performance in mammography as a function of the design parameters involved, and to use this model to design optimal mammographic imaging systems.

Food & Drug Administration
HFA-514
5600 Fishers Ln., Rm 12A-05
Rockville Md. 20852

NCI CONTRACT AWARDS

Title: Prediction of hormone dependency in human breast cancer, continuation
Contractor: Univ. of Chicago, $66,400.

Title: Partial support of Institute of Laboratory Animal Resources, four-month extension
Contractor: National Academy of Sciences, $9,333.

Title: Two additional alteration/renovation/maintenance/upgrading projects at Frederick Cancer Research Center
Contractor: Litton Bionetics, $725,963.

Title: Support services to maintain studies on the role of viruses and experimental oncogenesis and human cancer, continuation
Contractor: Hazleton Laboratories, $65,333.

Title: Operation of a facility to provide and maintain nonhuman primates for cancer research, continuation
Contractor: Litton Bionetics, $261,309.

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