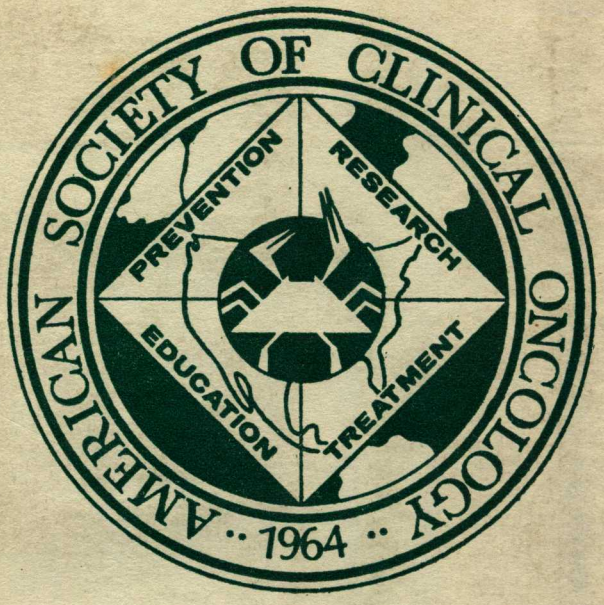
American Society of Clinical Oncology, Inc.



EIGHTH ANNUAL SCIENTIFIC MEETING

SHERATON-BOSTON HOTEL

BOSTON, MASSACHUSETTS

MAY 3, 1972 8:00 A.M. to 9:00 P.M.

American Society of Clinical Oncology, Inc.

1971 - 1972

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American Society of Clinical Oncology, Inc.

ANNUAL MEETING

Wednesday, May 3, 1972

Sheraton-Boston Hotel
Boston, Massachusetts

8:00 a.m. to 5:00 p.m. Registration

MORNING SESSION 8:30 a.m. to 12:15 p.m.

Dr. Kenneth B. Olson, Moderator

8:30 a.m. Symposium: THE CLINICIAN AND CANCER ETIOLOGY

Chairman: Robert W. Miller, M.D.

8:30 - 8:50 Bedside Approaches to Cancer Etiology
Robert W. Miller, M.D.

8:50 - 9:15 Familial Cancer
Joseph F. Fraumeni, M.D.

9:15 - 9:40 Case Studies: New Concepts in Immunology
Joseph A. Bellanti, M.D.

9:40 - 10:15 Clues from Other Continents
J.N.P. Davies, M.D.

10:15 - 11:00 General Discussion

11:15 a.m. THIRD ANNUAL DAVID A. KARNOFSKY MEMORIAL LECTURE

"THE COMPLETE CLINICAL ONCOLOGIST--
A NEW APPROACH TO TRAINING"

Henry Kaplan, M.D.
Professor and Chairman, Department of Radiology
Stanford University School of Medicine
Palo Alto, California

L U N C H

12:15 - 1:30

AFTERNOON SESSION 1:30 p.m. - 6:15 p.m.

Paul P. Carbone, M.D., Moderator

1:30 p.m. (59) TREATMENT OF ADVANCED HEAD AND NECK CANCER BY A COMBINATION OF HYDROXYUREA AND IRRADIATION. A PROSPECTIVE CONTROLLED STUDY IN 154 PATIENTS
S. Stefani, R.W. Eells, J. Abbate, Hines VA Hospital, Hines, Illinois; The Chicago Medical School, Chicago, Illinois

1:45 p.m. (49) EFFECT OF SPLENECTOMY ON CHEMOTHERAPY (MOPP) FOR HODGKIN'S DISEASE (HD).
F. Panettiere, and C.A. Coltman, Jr. Wilford Hall USAF Medical Center, Lackland AFB, Texas

2:00 p.m. (28) IMPROVED COMBINATION CHEMOTHERAPY (MOPP) FOR REMISSION INDUCTION AND MAINTENANCE IN ADVANCED HODGKIN'S DISEASE
E.M. Hersh, E. Frei III, C. Coltman and J. Luce
For The Southwest Cancer Chemotherapy Study Group
Houston, Texas

2:15 p.m. (23) SINGLE HIGH DOSE DAUNORUBICIN THERAPY FOR ACUTE NON-LYMPHOCYTIC LEUKEMIA (ANLL)
W.H. Greene, D. Huffman, S.Schimpff, N. Bachur.
NCI-Baltimore Cancer Research Center, Baltimore, Maryland (Sponsored by Peter H. Wiernik, M.D.)

2:30 p.m. (33) PHASE I STUDIES OF 5-AZACYTIDINE IN CHILDHOOD ACUTE LEUKEMIA
M. Karon, L. Sieger, J. Finklestein and M. Nesbit
Childrens Hospital of Los Angeles and USC School of Medicine, Harbor General Hospital and UCLA Center for Health Sciences, Los Angeles California and Department of Pediatrics, University of Minnesota School of Medicine, Minneapolis, Minnesota

2:45 p.m. (25) ONCALERT - A NEW APPROACH TO TUMOR REGISTRY
T.C. Hall and B. Lemley, University of Rochester Medical Center, Rochester, New York

3:00 p.m. (70) CARCINOEMBRYONIC ANTIGEN IN PATIENTS WITH NEUROBLASTOMA
J.J. Wang, T.M. Chu, L.F. Sinks, G. Reynoso. Department of Pediatrics and Clinical Laboratories, Roswell Park Memorial Institute, Buffalo, New York (Introduced by Salman Gailani)

3:15 p.m. (57) DISAPPEARANCE OF BLOCKING SERUM FACTORS IN PATIENTS RECEIVING CHEMOTHERAPY FOR DISSEMINATED RHABDOMYOSARCOMA.
J.G. Sinkovics, M.P. Sullivan, and J.R. Wilbur.
The University of Texas at Houston M.D. Anderson Hospital and Tumor Institute, Houston, Texas

3:30 p.m. (75) CANCER IMMUNOTHERAPY WITH HLA COMPATIBLE THORACIC DUCT LYMPHOCYTE TRANSPLANTATION

Robert H. Yonemoto and Paul Terasaki. City of Hope Medical Center, Duarte, California and UCLA Medical Center (Sponsored by Joel Solomon)

3:45 p.m. (37) THE EFFECT OF NEOPLASIA AND CHEMOTHERAPY ON HUMAN MACROPHAGE MEMBRANE FUNCTION

A.F. LoBuglio and S.P. Balcerzak. Ohio State University, Columbus, Ohio. (Sponsored by Stuart Roberts)

4:00 p.m. (69) RECENT ADVANCES IN HEPATOCELLULAR CARCINOMA (HCC)

C.L. Vogel. Solid Tumor Center, Uganda Cancer Institute, Kampala, and Medicine Branch, N.C.I., Bethesda, Maryland

4:15 p.m. (21) CHEMOTHERAPY OF SARCOMAS WITH A COMBINATION OF ADRIAMYCIN AND DIMETHYL TRIAZENO IMIDAZOLE CARBOXAMIDE (DIC)

J.A. Gottlieb and J.K. Luce. M.D. Anderson Hospital and Southwest Cancer Chemotherapy Study Group, Houston, Texas (Sponsored by J.S. Hart)

4:30 p.m. (32) PLATELET AND FIBRINOGEN KINETICS WITH (^{75}SE) SELENOMETHIONINE IN PATIENTS WITH MYELOPROLIFERATIVE DISORDERS

S.B. Kahn and I. Brodsky. Hahnemann Medical College, Philadelphia, Pennsylvania

4:45 p.m. (55) CLINICAL STUDIES WITH CIS-DIAMINODICHLORO-PLATINUM

A.H. Rossof, R.E. Slayton, and C.P. Perlia Rush Presbyterian-St. Luke's Medical Center, Chicago, Illinois

5:00 p.m. (9) THERAPY OF MELANOMA WITH DIMETHYL-TRIAZENO-IMIDAZOLE CARBOXAMIDE (DTIC) AND BIS-CHLOROETHYLNITROSOUREA (BCNU): RESPONSE WITH CEREBRAL METASTASES

Mary Costanza and Larry Nathanson, Department of Medicine, Tufts New England Medical Center, Boston, Massachusetts, for the Eastern Cooperative Oncology Group

5:15 p.m. (47) COMBINED IMMUNOTHERAPY, CHEMOTHERAPY AND PLASTIC SURGERY FOR THE TREATMENT OF EXTENSIVE TUMORS INVOLVING THE SKIN.

J.E. Murray, G. Biano, S. Farber, V. Bakamjian, P. Calamel and E. Klein. Peter Bent Brigham Hospital, Children's Cancer Research Foundation and Harvard Medical School, Boston, Massachusetts and Roswell Park Memorial Institute, Buffalo, New York

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B U S I N E S S M E E T I N G
5:30 - 6:15 p.m.

(M e m b e r s O n l y)

Kenneth B. Olson, M.D. - President

D I N N E R

6:15 - 7:30

EVENING SESSION 7:30 p.m. - 9:00 p.m.

WORKSHOPS

		Moderator
I	7:30 - 8:15 p.m.	
	A. How to Handle the Unknown Primary	Dr. Robert Ravdin
	B. Immunotherapy of Neoplastic Disease	Dr. Herbert Oettgen
	C. Combination Treatment of Hodgkin's Disease	Dr. Joseph Bertino
II	8:15 - 9:00 p.m.	
	A. The Value of Node Dissection in Melanoma	Dr. Edward Krementz
	B. Primary Treatment of Breast Cancer	Dr. W. Bradford Patterson
	C. Treatment of Stage III Ovarian Cancer	Dr. Thomas Griffiths

ABSTRACTS

1 CLINICAL EVALUATION OF CCNU (NSC-79037) AND A COMBINATION OF IMIDAZOLE CARBOXAMIDE (NSC-45388) AND VINCRISTINE (NSC-67574) IN THE TREATMENT OF DISSEMINATED MALIGNANT MELANOMA. D. L. Ahmann, M.D., R. G. Hahn, M.D., H. F. Bisel, M.D., Mayo Clinic, Section of Clinical Oncology, Rochester, Minnesota.

A program utilizing Imidazole Carboxamide, 325 mg./m^2/ day times 5 days with Vincristine, 1.4 mg./m^2 on days one and five I.V. was compared with CCNU, 130 mg./m^2 orally on one day in a randomized clinical trial in patients with disseminated malignant melanoma. Patients were classified as to visceral dominant disease (29/31) or cutaneous/nodal disease (2/31) prior to drug randomization. Failure after initial treatment resulted in treatment utilizing the remaining drug program. Regressions were defined as 50% reduction in the product of the perpendicular diameters of the measurable disease.

Five of 22 patients responded to the combination of Vincristine and Imidazole Carboxamide; one of 19 patients responded to CCNU.

Toxicity induced included G.I.: 22/22 with Imidazole Carboxamide and VCR and 12/19 with CCNU; hematologic: (W.B.C. less than 3,000 and/or platelet less than 100,000) 7/22 with Imidazole Carboxamide and VCR, 11/19 CCNU; neurologic: 9/22 VCR and Imidazole Carboxamide, 0/22 with CCNU; alopecia: 6/22 Imidazole Carboxamide and VCR, 0/19 with CCNU. No drug deaths were seen but one patient experienced life threatening (hematologic) toxicity with VCR and Imidazole Carboxamide.

2 THE USE OF BCG AS ADJUNCT THERAPY IN CANCER PATIENTS. PRELIMINARY REPORT. M. Al-Sarraf, M.D., S. Sardesai, B.S., and V.K. Vaitkevicius, M.D., Oncology Department, Wayne State University and the M.A. Darling Memorial Unit of the Michigan Cancer Foundation, Detroit, Michigan.

BCG and other non-specific stimulators of the reticulo-endothelial system have been used with good results as adjunct therapy in patients with acute leukemia or lymphoma. In this double blind study, BCG was used on patients with disseminated malignancies. All patients who had no previous radio- or immunosuppressive therapy, after admission to our Center, were tested with intermediate PPD. Patients with negative skin test were randomized in treatment and control groups, while patients with positive skin reaction were given no BCG and were used as a second control group. BCG was administered intradermally to treated patients. In-vitro lymphocyte reactivity to phytohemagglutinin and PPD was studied on all patients. So far, 113 patients were studied. Of these, 20 had positive reactions to PPD, 32 patients were given BCG and 61 patients had negative skin tests and did not receive BCG. There were fewer deaths in the group receiving BCG, and the duration of survival in treatment group is significantly longer than in the 2 control groups.

3 BONY METASTASIS FROM ADENOCARCINOMA OF THE COLON. L.H. Baker, D.O., S. Figiel, M.D., and V. K. Vaitkevicius, M.D., Oncology Department, Wayne State University and the M. A. Darling Memorial Unit of the Michigan Cancer Foundation, Detroit, Michigan.

Bony metastasis from disseminated colon carcinoma has been described as an uncommon phenomenon. Of 201 patients with metastatic colon carcinoma, 20 had x-ray evidence of bone metastasis (10%). The x-ray findings demonstrate a preponderance of osteolytic lesions (15 pts.) versus osteoblastic lesions (5 pts.). The site most commonly involved was the lumbar spine and pelvis (14 pts.). Other areas of involvement included the skull, remainder of the vertebrae and the shoulder girdle. No significant difference in survival between those patients with bony metastasis versus those without skeletal lesions could be demonstrated. There was also no difference in the pattern of spread to other sites of metastasis demonstrated between the two groups. Six of the 20 patients developed bone metastases while being treated for hepatic metastasis by intra-arterial hepatic artery chemotherapy. At the initiation of the chemotherapy no extra-hepatic sites of metastasis could be identified. All six patients were responding to intra-arterial chemotherapy when bone metastases became apparent. Our data suggest that bony metastasis in colon carcinoma is more common than usually appreciated. The prolonged survival of patients receiving effective chemotherapy permits these otherwise not recognized to become manifest.

4 ADRIAMYCIN AND BLEOMYCIN IN GYNECOLOGIC CANCER. J.J. Barlow, M.D., M.S. Piver, M.D., J.T. Chuang, M.D. and E.P. Cortes, M.D., Roswell Park Memorial Institute, Buffalo, N.Y. (Sponsored by H.J. Wallace, M.D.)

Adriamycin (ADM) and bleomycin (Bleo) alone or in combination have been given to 37 patients with gynecologic cancer. All had the equivalent of Stage III or IV disease and all but 3 represented failures of prior x-irradiation and/or chemotherapy. The non-squamous cell tumors were treated with ADM alone (30 mg/m^2/day x 3 i.v.) or ADM (20 mg/m^2/d x 3) + Bleo (15 mg/m^2/d x 5 i.v.) and the squamous tumors with Bleo alone (20 mg/m^2/d x 5) or Bleo + ADM. Courses were repeated at intervals of 4 weeks dependent upon hematopoietic and mucosal recovery. Side effects were as previously reported for each agent with no apparent potentiation of toxicity when used together at these doses. Of 27 patients presently evaluable, objective responses were obtained in: 1/2 gonadal stromal tumors (complete response in granulosa cell cancer); partial responses (PR)(>50%) in 2/2 ovarian teratomas, 1/1 uterine leiomyosarcoma and 1/3 endometrial mixed mesodermal sarcomas; improvement (>25%) in 1/1 endometrial stromal sarcoma; PR in 1/7 epithelial ovarian cancers and 1/11 cervical carcinomas. Although ordinarily tumor regression was evident in 4 weeks, regressions began as late as the second course and have persisted 3-9 months in 6 of 8 responders. ADM alone and ADM + Bleo in combination have proved particularly active in gynecologic sarcomas and ovarian teratomas, a group of cancers ordinarily refractory to all other therapy.

5 THE ORGANIZATION AND FUNCTION OF A CANCER EDUCATION PROGRAM IN A UNIVERSITY AFFILIATED COMMUNITY HOSPITAL. J.M. Bennett, M.D., E.D. Savlov, M.D., and B. Sischy, M.D., Highland Hospital of Rochester, and the University of Rochester School of Medicine and Dentistry, Rochester, New York.

A decentralized cancer diagnostic, therapeutic, and education unit has been in operation at the Highland Hospital for the past 2 years. Three independent but interdependent departments [medical oncology (MO), radiotherapy (RT), and surgical oncology (SO),] have consulted on over 750 patients in the past year, with approximately 100 undergoing treatment at any one time. A weekly Lymphoma Clinic (MO + RT) and Breast Clinic (SO + RT) are held with medical students, house officers, and fellows in attendance. In addition a weekly tumor board (MO + RT + SO) meets to discuss problem cases presented by the visiting staff. Two Cancer Teaching Days, sponsored by local agencies, are held yearly. With support from the National Cancer Institute a chemotherapy program, under the auspices of the Eastern Cooperative Oncology Group, has made available the latest drugs and innovations, including infusion: perfusion therapy, in cancer care. A grant from the Regional Medical Program has made it possible to develop meaningful relationships with 7 smaller hospitals in a 3 county area via telephone communication and conferences. The above program demonstrates that federal, regional, and university programs can interdigitate at the community hospital level. Indeed, such a center can become the hub of a delivery system of total cancer care for approximately 250,000 people.

6 COMBINATION RADIOTHERAPY AND CHEMOTHERAPY IN THE TREATMENT OF EARLY HODGKIN'S DISEASE. K. Brace, M.D., A.A. Serpick, M.D., P.H. Wiernik, M.D., and J.B. Block, M.D., NCI - Baltimore Cancer Research Center, Baltimore, Maryland.

Twenty-two patients with previously untreated Stage I and II Hodgkin's Disease were randomized to 3 treatment programs. Patients in Group A received radiotherapy to involved plus adjacent node-bearing areas. Patients in Group B were treated with radiotherapy to involved nodal areas only and then received 3 courses of MOPP therapy. The patients in Group C were treated with 3 courses of MOPP therapy followed by radiotherapy to involved nodal areas. Three of 7 patients in Group A have relapsed 3, 21, and 42 months after the completion of therapy. None of the patients in Group B have relapsed during a follow-up period of 24-45 months (average 36 months). The majority of relapses have occurred in Group C with 5 of 7 patients relapsing 5, 6, 15, 20, and 43 months after the completion of therapy. The results of this study suggest that localized radiotherapy followed by systemic combination chemotherapy may be a reasonable alternative to radical radiotherapy for Stage I or II Hodgkin's Disease.

7 INTENSIVE BLEOMYCIN IN THE TREATMENT OF ADVANCED LYMPHOMA. G.P. Canellos, M.D., R.C. Young, M.D., V.T. DeVita, M.D., Solid Tumor Service, Medicine Branch, National Cancer Institute, Bethesda, Maryland.

Initial clinical trials with Bleomycin in a variety of dose schedules have demonstrated some antitumor activity in patients (pts) with lymphoma. Five-day courses of Bleomycin, 25 mg/m^2/day, were administered to 16 pts with far-advanced lymphoma refractory to other forms of chemotherapy. Nine pts received 2 courses separated by 3-4 week intervals. Seven pts had only 1 course. Of the 7 pts with IVB Hodgkin's disease previously treated with multiple courses of MOPP, BCNU, and vinblastine, 2 had an objective regression of lymph nodes and improvement in symptoms for 3-4 week duration. A further 2 pts derived only symptomatic benefit, characterized by prompt reduction of fever and sweats. Three of 7 pts with advanced lymphosarcoma and 1 of 2 pts with reticulum cell sarcoma had objective lymph node regression. The responses were of short duration. The toxicity of high dose Bleomycin included some epilation and skin changes (5 pts), mucositis (4 pts), and nonfatal pulmonary fibrosis in 1 patient. Myelotoxicity was not seen, even in the presence of bone marrow depression from previous therapy. Although some antitumor effect was noted, Bleomycin used in this dose and schedule does not appear to be very useful in pts with advanced, extensively pretreated lymphoma. Bleomycin may be useful in combination chemotherapy in new cases.

8 ADRIAMYCIN IN ADVANCED RETICULUM CELL SARCOMA. Engracio P. Cortes, M.D. and James F. Holland, M.D., Department of Medicine A, Roswell Park Memorial Institute, Buffalo, New York.

Adriamycin (ADM) a hydroxymethyl analog of daunorubicin has been demonstrated to have a broad spectrum of antitumor activity. Ten patients with stage IV reticulum cell sarcoma, all refractory to prior therapy were given ADM 30 to 35 mg/m^2/d x 3 I.V. Courses were repeated every 28 days if toxicity had cleared. There were 3 complete and 4 partial (>50%) remissions. Complete remissions lasted 1+, 5+, and 7.5 months, and partial remissions 2+, 6, 7 and 8 months. Overall median was 6 months. Toxic manifestation included alopecia and stomatitis in all patients, anemia (drop of $\geq$2 gms.% Hgb.) in 6 patients, neutropenia (<1000 mm^3) and thrombocytopenia (<50,000 mm^3) in 5 patients. No cardiac toxicity was observed. Four of the 7 patients who responded to ADM relapsed from prior combination therapy with cyclophosphamide, vincristine and prednisone and/or BCNU. Activity of ADM in these advanced refractory patients supports its use in disseminated reticulum cell sarcoma, and its exploration in patients earlier in their therapeutic course, alone or in combination with other known effective chemotherapeutic agents.

9 THERAPY OF MELANOMA WITH DIMETHYL-TRIAZ-ENO-IMIDAZOLE CARBOXAMIDE (DTIC) AND BIS-CHLOROETHYLNITROSOUREA (BCNU): RESPONSE WITH CEREBRAL METASTASES, Mary Costanza and Larry Nathanson, Department of Medicine, Tufts New England Medical Center, Boston, Mass., for the Eastern Cooperative Oncology Group.

A combination of DTIC 100 mg./M^2/dx5d and BCNU 75 mg./M^2/dxd2, 3 was randomized against DTIC 150 mg./M^2/dx5d alone. The combination yielded 12/63 responders as compared with 7/42 for DTIC alone. Responders survived significantly longer (6.1 months) than did non-responders (3.1 months). 3/10 patients with CNS metastases treated with DTIC-BCNU showed objective improvement compared to 0/6 for DTIC. Only 5/53 patients treated with DTIC-BCNU developed CNS metastases compared to 7/36 treated with DTIC. Toxicity of both treatments was tolerable with slightly greater GI upset and bone marrow suppression with DTIC-BCNU. Patients were also analyzed for relation between survival and the following: regional node dissection, free interval, and pretreatment estimated survival time. Only the latter relation was positive. We conclude that DTIC is the best agent for the therapy of melanoma, but that with anticipated or known CNS metastases, DTIC and BCNU is the chemotherapy of choice.

Supported in part by Grants Ca-07190, National Cancer Inst., N.I.H., and T-550, Amer. Cancer Soc.

10 COMBINATION CHEMOTHERAPY IN THE TREATMENT OF DISSEMINATED BREAST CARCINOMA. J.J. Costanzi, M.D., Wilford Hall USAF Medical Center, Lackland AFB, Texas.

The results in treating resistant disseminated carcinoma of the breast after appropriate surgery and hormonal manipulations vary in different series. Ansfield, et al (Can Res 29: 1062, 1969) noted a 23% response rate with 5-Fluorouracil. Piro, et al (Cancer 27:1342, 1971) recorded a 33% response with Cyclophosphamide. Using the combination of Cyclophosphamide, Vincristine, Methotrexate, 5 F-U and Prednisone Cooper (Proc Amer Ass Cancer Res 10:15, 1969) achieved an 80% regression rate. The doses used were high, making toxicity an important limiting factor. The same combination given to 18 patients in lower doses noted a 61% response rate with diminished toxicity (Ansfield, et al: Can Chemo Rep 55:183, 1971).

We have treated 32 such patients with Cyclophosphamide 100 mg p.o. q. d., Vincristine 0.025 mg/kg IV weekly, Methotrexate 0.5 mg/kg IV weekly and Prednisone q. d. in diminishing doses over an 8 week period. Of the 17 evaluable patients, 3 complete regressions, 7 partial remissions and one mixed response were noted. Seven of these patients received 8 weeks or more of therapy. Toxicity was evaluable in 17, with 5 having no toxicity, 5 mild toxicity, 4 moderate toxicity and 3 severe--predominantly leukopenia and neuropathy.

This combination of chemotherapeutic agents is effective in the treatment of resistant disseminated carcinoma of the breast.

11 CYCLOPHOSPHAMIDE AND THIOTEPA IN OVARIAN CARCINOMA

L. D. Crandall and B. J. Kennedy. University of Minnesota Hospitals, Minneapolis, Minnesota 55455

Patients with advanced ovarian carcinoma were treated with a chemotherapy program of cyclophosphamide 1.5-2.5 mg/kg daily, androgenic hormone, and Thiotepa 10 mg im weekly. The known antitumor effect of both alkylating agents resulted in the use of this combination. Androgen was employed to stimulate hematopoesis and allow vigorous continuing chemotherapy. Surgical removal of massive tumor masses before chemotherapy allowed time for adequate chemotherapy trials.

35 patients have been treated. Of 20 evaluable patients, 13 have had objective regression with a mean regression time of 14 months. Median survival time from initial diagnosis was 20 months for responders and 7 months for nonresponders.

Three responders had a second abdominal operation and 2 were free of gross tumor; one of these had microscopic cancer in the ovary. The third patient had an isolated peritoneal mass resected. Chemotherapy continues in all three.

12 TREATMENT OF ADVANCED GENITOURINARY CARCINOMA WITH BLEOMYCIN PLUS RADIOTHERAPY. P.F. Engstrom, M.D., R.S. Bornstein, M.D., H.G. Seydel, M.D., J.W. Yarbro, M.D. American Oncologic Hospital, Philadelphia, Pennsylvania.

A pilot study was initiated to determine the effect of pre-radiotherapy chemotherapy on advanced squamous cell carcinoma of genitourinary origin. Six evaluable, previously untreated patients with Stage III or IV tumors have completed the Study. Four tumors originated from the uterine cervix, one from the bladder and one from glans penis. Age range: 44 to 73 years.

Bleomycin was administered 15 mg q 12 hrs IM for 8 doses followed by 15 mg IM weekly for 3 to 10 weeks (120 to 285 mg total). No drug toxicity was noted. All patients showed > 50% regression of tumor within 2 weeks of initiating treatment. Post Bleomycin radiotherapy was administered (4000 r/4 weeks to 6000 r/6 weeks) to the tumor area in 5 patients with further tumor regression, but no increased toxicity.

We conclude that Bleomycin is active against genitourinary neoplasms. The response is apparently not dose dependent. Bleomycin followed by super voltage radiotherapy offered the best palliation in this series and raises the question of synergism between treatment modalities. Consideration should be given to an investigation of simultaneous use of Bleomycin and radiotherapy under conditions permitting an evaluation of efficacy.

13 ROLE OF LYMPHATIC OBSTRUCTION IN ASCITES BY MURINE OVARIAN CARCINOMA. G.B. Feldman, M.D., R.C. Knapp, M.D., S.E. Order, M.D. and S. Hellman, M.D., Harvard Medical School, Boston, Massachusetts (Sponsored by Robert C. Knapp, M.D.)

In normal mice 0-70 percent of Cr^{51}-labelled erythrocytes injected intraperitoneally appear in the peripheral bloodstream within 5 hours. In mice previously innoculated with a transplantable, ascites-producing ovarian tumor, this egress of labelled erythrocytes from the abdominal cavity is significantly impaired before ascites develops. Diaphragmatic lymphatic obstruction is demonstrated histologically. Since red cells leave the peritoneal cavity primarily by way of these channels, this observation suggests that lymphatic obstruction by tumor cells is probably of pathogenetic importance in the accumulation of ascitic fluid.

14 THE USE OF PERIODIC REINFORCEMENT THERAPY TO PROLONG REMISSION AND SURVIVAL IN CHILDREN WITH ACUTE LEUKEMIA. D.J. Fernbach, T.J. Vietti, W.W. Sutow, D.M. Lane, D. Lonsdale, M.E. Haggard, and S.L. George, Southwest Cancer Chemotherapy Study Group(Sponsored by T. Vietti)

In order to determine the better induction regimen, children with acute leukemia (all cell types) were randomly assigned to 1 of 2 treatment schedules: A) prednisone (pred) + vincristine(vinc); or B) pred + 6-mercaptopurine(6-MP). The response rate was 80% (72/90) for A and 89% (77/87) for B. After achieving complete remission, all patients were randomized again to 3 maintenance schedules: 1)6-MP alone; 2)6-MP + pred for 28 days every 3 mo; 3)6-MP + (pred for 28 days and vinc weekly x 4) q 3 mo. Regardless of induction therapy, maintenance with 6-MP alone was inferior to multi-drug maintenance. There was no significant difference between pred or pred+vinc with 6-MP maintenance after induction A, but the trend favors pred reinforcement. After induction with B, pred + vinc with 6-MP maintenance was superior to pred reinforcement. At this time the best therapy--remission and survival--is pred + 6-MP induction followed by pred + vinc with 6-MP maintenance. Over 50% of this group were in remission at 86 wk; 50% were alive at 3½ yr. Regardless of later therapy, this evidence suggests that 1)pred + 6-MP induction is superior to pred + vinc in terms of overall survival; 2)reinforcement of maintenance therapy is superior to single drug maintenance. Standard doses were used. The minimal 5-year survival for this entire study would be 23%.

15 OBSERVATIONS ON PERIPHERAL BLOOD H^3 RNA IN GENITOURINARY NEOPLASMS COMPARED WITH BENIGN PROSTATIC HYPERTROPHY AND NORMAL CONTROLS. B. Fingerhut, M.D., R.J. Veenema, M.D., M.P. Butler, B.S., and G. Hyman, M.D., College of Physicians & Surgeons of Columbia University, Francis Delafield Hospital, Institute of Cancer Research, New York, N. Y.

Studies of peripheral blood specimens by autoradiographic techniques using tritium labelled cytidine were done in 250 patients consisting of: 50 normal controls, 150 patients with cancer of the prostate, 40 patients with tumors of the bladder, 5 patients with kidney tumors, 5 patients with carcinoma of the penis and 70 patients who had benign hypertrophy of the prostate.

In patients with cancer the white blood cell intranuclear H^3 RNA was considerably increased as compared to benign prostatic hypertrophy and normal controls. This finding perhaps has diagnostic value and studies continue.

In addition, the difference in the number of grains and their particular location (intra vs. extranuclear) may give prognostic indications since there appeared to be a decrease in H^3 RNA grain concentration and a shift to an extranuclear position of the grains in the white blood cells when the neoplasms responded to treatment. Failure to respond to treatment showed, either no change, or increased number of grains and persistent intranuclear concentration. Repeated determinations of peripheral blood H^3 RNA in a given patient increased the prognostic value of the study.

16 A COMPARATIVE STUDY OF CNS INVOLVEMENT IN CHILDHOOD LYMPHOSARCOMA AND A.L.L. J. Fitzpatrick, M.D., N. Lieberman, L.F. Sinks, M.D. Roswell Park Memorial Institute, Buffalo, New York

A group of 182 children with acute lymphoblastic leukemia (ALL), reticulum cell sarcoma (RCS) and lymphosarcoma (LS) were divided into 4 groups according to their presenting signs: Group 1 - ALL without organomegaly or gross nodal enlargement, Group 2 - ALL with palpable liver or spleen but no gross nodal enlargement, Group 3 - ALL with gross nodal enlargement or LS or RCS converting to ALL, and Group 4 - non-transforming LS or RCS. Patients in Group 1 were found to have the longest median survival, 42.5 months, and a relatively low incidence of CNS leukemia, 31.8%. In Group 2, the reverse relationship was found. There was a decreased survival duration of 23 months and an incidence of CNS leukemia of 58.8% Group 3 had the shortest median survival (8.5 months), but a relatively high percentage (53.8) with CNS disease. Non-converting LS and RCS, Group 4, was associated with a median survival of 12 months and a 20% incidence of CNS involvement. It would appear from this data that a distinct adverse relationship exists between splenic, hepatic and lymph node enlargement at diagnosis and the survival duration and the subsequent development of CNS infiltration in ALL and transforming LS and RCS. This may reflect a difference in immune capabilities of the host. Patients with LS or RCS converting into leukemia (Group III), did poorer than both ALL and non-transforming LS, thus suggesting a need for re-evaluation of current therapeutic measures.

17 **LOCAL VS. EXTENDED FIELD RADIATION THERAPY OF HODGKIN'S DISEASE.**

H. Forgione, M.D., M. Stutzman, M.D., M. Fridman, M.D. and L. Stutzman, M.D., Roswell Park Memorial Institute, Buffalo, New York.

In a prospective randomized study, 67 pts. received either involved field radiotherapy to tumor-bearing lymph node areas, to a tumor dose of 3000r (IF), or this amount of radiation plus 2000r depth dose extended to adjacent areas (EF).

Of the 33 IF pts., 18 are relapse-free, 13 alive after relapse and 2 dead. Of 34 EF pts., 23 are relapse-free, 6 alive after relapse and 5 dead. There were no recurrences within the tumor areas, but disease appeared in the 2000r areas in 2 pts. Five in the IF group (compared to 1 EF pt.) had relapse on the same side of the diaphragm; 3 have remained well after local radiation to the second area.

10 IF pts. have relapsed across the diaphragm compared to 8 EF pts. Life-table survival shows no difference in the two groups.

The addition of extended fields decreased the incidence of adjacent recurrence, but did not prevent spread to Stage III or IV disease and did not improve survival.

18 THE PATHOPHYSIOLOGIC EFFECTS OF HEPATIC ARTERY LIGATION ON PRIMARY AND SECONDARY LIVER CANCERS IN TEN PATIENTS.

J.G. Fortner, M.D., R.J. Mulcare, M.D., A.P. Solis, M.D., R.C. Watson, M.D., R.S. Benua, M.D., A. Yagoda, M.D. and R.B. Golbey, M.D. Memorial Sloan-Kettering Cancer Center, New York, New York.

Cancers in the liver are supplied by the hepatic artery with little contribution from the portal circulation. Ten symptomatic patients were studied to clarify the pathophysiologic effect of hepatic artery ligation on tumor and liver parenchyma. Six had hepatocellular carcinoma; four had colon carcinomas metastatic to liver. Two died postoperatively of complications unrelated to artery ligation. Seven have obtained significant palliation for 7 weeks to 6 months. Biochemical studies showed immediate elevation of bilirubin, and enzymes with returns to below pre-operative levels in all but the unresponsive patient. Alpha-feto-protein, when positive, decreased immediate post-ligation, increasing again with loss of palliative effect.

Hepatic angiography showed immediate and extensive post-ligation collateralization of hepatic arterial supply. Blood flow studies, utilizing serial radioisotopic scanning techniques, showed early decrease in liver flow. In two patients, selective necrosis of tumor was documented. These data suggest a significant, transient period of selective tumor ischemia. To potentiate this anti-tumor effect, three patients are undergoing continuous chemotherapeutic infusion via a catheter in the ligated artery.

19 TECHNIQUE AND RESULTS OF HEPATIC LOBECTOMY USING ORGAN ISOLATION AND HYPOTHERMIC PERFUSION.

J.G. Fortner, M.D., M.H. Shiu, M.D., W.S. Howland, M.D., R. Lavarello, M.D., D. Kim, M.D., D. Kinne, M.D. and E.J. Beattie, M.D. Memorial Sloan-Kettering Cancer Center, New York, New York.

The high operative mortality (30%) of right hepatic lobectomy is usually due to resection of barely encompassable tumors. Invasion of the vena cava nearly always results in the hepatic tumor being non-resectable. These factors and a low cureability rate for hepatoma (15%) have led us to adapt certain steps from liver transplantation to carrying out partial hepatic resection. The liver is first dissected free of attachments except for major vasculature. These vessels are then occluded temporarily and the isolated organ perfused with chilled (4°C) Ringer's lactate solution containing heparin. A partial hepatectomy is then carried out. After preliminary experimental studies, the concept of organ isolation and hypothermic perfusion and partial removal of the liver has been applied in 8 patients. The results will be discussed and the technique demonstrated by 16 mm movie.

20 **AN ANALYSIS OF EWING'S TUMOR IN CHILDREN SEEN AT ROSWELL PARK MEMORIAL INSTITUTE.**

A.I. Freeman, L.F. Sinks. Dept. of Pediatrics, Roswell Park Memorial Institute, Buffalo, N.Y. (Introduced by Rose Ruth Ellison).

Twenty pediatric patients with Ewing's tumor seen at Roswell Park Memorial Institute from 1954 to 1970 have been analyzed. In 2 cases no treatment was given, in 3 others amputation was performed, and in 6 others radiotherapy alone as the primary treatment was given. These 11 patients are all dead of their disease. The remaining 9 patients were treated with radiotherapy and adjuvant chemotherapy as the primary treatment. Of these 9 patients, 3 are regarded as cures with disease-free intervals from 3 to 11 years. A fourth patient is regarded as a possible cure. The radiotherapy generally consisted of 4000 to 5000 rads tumor dose delivered to the entire involved bone given over approximately 4 weeks. Chemotherapy in recent years has been Cytoxan 300 mg/m^2 I.V. weekly for 6 weeks, followed by a 6 week rest. The chemotherapy cycle is repeated for 1 year. It is felt that the chemotherapy is eradicating the subclinical micrometastases and thus effecting a cure. In addition, five cases with reactivation of their primary sites prior to or simultaneous with metastasis were noted, indicating incomplete sterilization of tumor by present radiotherapeutic techniques and suggesting that more aggressive therapy be directed to the primary site along with the systemic chemotherapy.

21 CHEMOTHERAPY OF SARCOMAS WITH A COMBINATION OF ADRIAMYCIN AND DIMETHYL TRIAZENO IMIDAZOLE CARBOXAMIDE (DIC). J.A.Gottlieb, M.D., and J.K.Luce, M.D., M.D.Anderson Hospital and Southwest Cancer Chemotherapy Study Group, Houston, Texas. (Sponsored by J.S. Hart, M.D.)

Used singly, adriamycin and DIC have shown a 25 and 15% response rate respectively in several types of soft tissue and bone sarcomas. Based on animal and human toxicity studies, the following combination protocol was designed: Adriamycin-60mg/M^2 iv on day 1 and DIC-250mg/M^2 iv on days 1-5 with the regimen repeated every 21 days. A 25% dose reduction of both drugs was used in patients with extensive previous therapy. Fifty-seven percent of the 45 currently evaluable patients had previous radiotherapy and/or chemotherapy--largely vincristine, actinomycin D and/or cyclophosphamide. Of the 36 patients having adequate trials (2 or more courses), 14 (39%) have shown >50% reduction in tumor size including the following diagnoses: neurofibrosarcoma-3/5; rhabdomyosarcoma-2/3; mesothelioma-2/4; leiomyosarcoma-2/5; undifferentiated sarcoma-2/5; synovial cell sarcoma-1/1; liposarcoma-1/2; fibrosarcoma-1/3; osteogenic sarcoma-0/4; angiosarcoma-0/2; chondrosarcoma-0/1 and Ewing's sarcoma-0/1. Nausea, vomiting and alopecia were observed in nearly every patient. Leukocyte depression was also prominent with a median nadir of 2900 occurring on median day 15. Thrombocytopenia and stomatitis occurred in 17% of patients. Retreatment at a 3-week interval was possible in all but 8% of courses. This combination of adriamycin and DIC is effective and well-tolerated treatment of metastatic sarcomas.

22 NEPHROSTOMY AND THE CANCER PATIENT. H. Grabstald, M.D., and M. Mc Phee, Memorial Hospital For Cancer And Allied Diseases, New York, New York (Sponsored by Harry Grabstald, M.D.)

A retrospective study of 170 patients with cancer subjected to nephrostomy have been reviewed. The majority had genitourinary disease, cervix and bladder being the most common. Disease state is classified as localized, locally advanced, or metastatic. Except in patients with localized disease, the operation is not consistently useful. Complication rate is significant, and nephrostomy has little effect upon anemia. Forty-three per cent of patients did not leave the hospital alive, and twenty-one patients died within less than two weeks. In the tumor patient nephrostomy is almost always a permanent drainage procedure.

While many ill defined problems and intangible play a role in the decision to perform nephrostomy, there are several relative contraindications.

23 SINGLE HIGH DOSE DAUNORUBICIN THERAPY FOR ACUTE NON-LYMPHOCYTIC LEUKEMIA (ANLL). W.H. Greene, M.D., D. Huffman, M.D., S. Schimpff, M.D., N. Bachur, M.D., Ph.D. NCI-Baltimore Cancer Research Center, Baltimore, Maryland (Sponsored by Peter H. Wiernik, M.D.)

Daunorubicin (DNR) is converted in vivo to an active metabolite, daunorubicinol, by daunorubicin reductase (DNR Red). Because each of these compounds has a prolonged plasma T-1/2, a clinical trial was conducted utilizing a single high dose (180 mg/M^2) of DNR IV every 9-10 days in 23 adult patients (pts) with ANLL, 15 previously untreated and 8 in relapse. Of the latter 8, 2 sustained a complete remission (CR) and 1 a partial remission (PR): of the 15 previously untreated pts, 4 attained CR status (27%). A total of 10 patients died in therapy: 7 from infection, 2 from hemorrhage, and 1 from unknown causes. Of the 9 pts age ≥60, 7 died in therapy, as compared to 3 of 14 <60 years old.

Pretreatment determinations of myeloblast (M) and erythrocyte (E) DNR Red levels were done in 12 pts, of whom 5 (Group A) had M:E DNR Red ratios >40, with a mean value of 46.5. All of these pts went into complete hematological remission. The other 7 pts had DNR Red ratios <30, of whom 4 (Group B, mean value 20) died in therapy, and 3 (Group C, mean value 19.5) had no response. Mean value differences between A and B, and A and C, were statistically highly significant. Thus, determination of the DNR Red ratios in vitro prior to drug therapy may allow selection of a more responsive group of pts for therapy with DNR.

24 COMBINATION CHEMOTHERAPY WITH CYTOSINE ARABINOSIDE (ARA-C) AND CYCLOPHOSPHAMIDE (CTX) OF CHRONIC LYMPHOCYTIC LEUKEMIA (CLL). J.U. Gutterman, J.E. Curtis, and E. J Freireich, The University of Texas M.D.Anderson Hospital & Tumor Institute at Houston, Houston, Texas.

Single drug chemotherapy of CLL produces complete blood and bone marrow remission (CR) in <10% of patients. Because of high Ara-C kinase/deaminase ratio in CLL lymphocytes (D.H. Ho), Ara-C was combined with CTX in 4 day course every 21 days in the following doses: 75 mg/M^2 of each intravenously in 2 divided doses daily.

Of 12 patients studied to date, 8 have been followed longer than 12 weeks and are evaluated. 4 achieved CR. One achieved PR; 2 had hematological improvement, and 1 failed to respond. 3 patients had unmaintained CR's of 6,9, and 12+ months. One had a maintained CR of 12+ months. All 4 CR patients had return to normal symptomatic and physical status. Immunocompetence was serially evaluated. Improvement was noted in lymphocyte blastogenesis to phytohemagglutin, streptolysin O, and streptokinase-streptodornase in 3 of 3 CR and 1 PR patients. Improvement of immunoglobulins to normal levels occurred in 2 of 3 CR patients but failed to improve in 3 of 3 patients not achieving a CR. Most important toxicity was myelosuppression. Nausea, vomiting and alopecia also occurred.

This pilot study indicates that the addition of Ara-C to the chemotherapy of CLL results in both a significant increase in the complete remission rate and improvement of immunological status.

25 ONCALERT-A NEW APPROACH TO TUMOR REGISTRY
T.C. Hall & B. Lemley, Univ. of Rochester Medical Center, Rochester, N.Y. 14642

Tumor registries have lost favor. This is because 1) the data is entered after diagnosis and discharge, 2) data Registries are hard to retrieve. Record-room delays are up to 2-3 months, and most registries use cumbersome hand-sorting procedures. Information thus obtained relates to incidence and survival, which are less important to the clinician. We need a system by which hospital entry with a possible diagnosis of cancer, "alerts" a data retrieval system which can collate differential diagnosis with current therapy references. "Oncalert" registers the patient on the day of admission, collates the potential diagnosis and specific diagnostic procedures, plus a list of research and treatment protocols, consultations available, and OPD clinics concerned with the specific diagnosis, and prints these on a sheet which is placed in the patient's folder within 24 hours.

Oncalert has 4 parts - a clerk visiting wards and registering patients daily on computer-coded forms, a computer program for entry of references and lab and clinic research programs, the "Inquire" system of entry and retrieval, and the University's IBM 360-65 computer.

The operation of the system for breast cancer will be demonstrated, with details of start-up and maintenance costs.

26 CHLORAMBUCIL VS. CHLORAMBUCIL-PREDNISONE THERAPY IN CHRONIC LYMPHOCYTIC LEUKEMIA. T. Han, M.D., E. Ezdinli, M.D., K. Shimaoka, M.D. and D. Desai, M.D., Roswell Park Memorial Institute, Buffalo, New York

Chlorambucil (CLB) and prednisone (PRD) are both effective in the treatment of chronic lymphocytic leukemia (CLL). To evaluate a possible antitumor synergism and to determine if prednisone might counterbalance the myelosuppressive effect of CLB, patients with CLL were randomized to receive CLB (6 mg/d) and either PRD (30 mg/d) or placebo. Clinical and hematologic data in the 2 groups were essentially comparable. In the combination group, complete and partial remissions were observed in 3 and 10 of 15 patients respectively; in those receiving CLB alone, similar remissions were seen in only one and 4 of 11 patients, respectively ($p<0.05$). Median duration of maintained remission was 18.5 months for patients receiving CLB-PRD therapy and 9 months for those treated with CLB alone. Hematologic toxicity was less frequent in the CLB-PRD group (hemoglobin decreased in 0/15 vs. 3/11; platelets decreased in 5/15 vs. 5/11). Ninety-three per cent of patients receiving CLB-PRD therapy and 52 per cent of those receiving CLB therapy were alive at the end of 2 years. Our results indicate that CLB-PRD is superior to CLB in the treatment of CLL.

27 OSTEOBLASTIC METASTASES IN BRONCHOGENIC CARCINOMA. H.H. Hansen, F.M. Muggia, and L. Napoli, NCI-VA Medical Oncology Service, VA Hospital, Washington, D.C.

Bone metastases in carcinoma of the lung are predominantly of the osteolytic type. Osteoblastic metastases have rarely been reported and exclusively in association with adenocarcinoma of the lung.

We have evaluated the osseous system in 110 pts. with unresectable bronchogenic carcinoma by radiographic bone survey, 85 Strontium bone scan, and bone marrow biopsy and aspiration from the posterior iliac crest. Bone metastases occurred in 28 pts. Nine of these had osteoblastic changes on bone films, including 7/22 pts. with small-cell carcinoma and 2/21 pts. with adenocarcinoma. All 9 pts. had pretreatment biopsy-proven tumor invasion of the bone marrow, but only 2 demonstrated osteoblastic metastases at onset. These were visualized in the other 7 pts. after 4-6 months of treatment with combination chemotherapy. The bone scan was initially positive in 5/7 pts., and became positive in 2 others after 3 and 5 months respectively. Ten of 21 pts. with large cell undifferentiated carcinoma and 9/36 pts. with epidermoid carcinoma had exclusively osteolytic lesions.

The patterns of bone involvement among the various cell types emphasize differences in biologic behavior. Noteworthy is the propensity of small cell carcinoma to disseminate to bone, and if survival is sufficiently prolonged to be associated with diffuse osteoblastic changes on bone films.

28 IMPROVED COMBINATION CHEMOTHERAPY (MOPP) FOR REMISSION INDUCTION AND MAINTENANCE IN ADVANCED HODGKIN'S DISEASE. E.M.Hersh, E.Frei III, C.Coltman and J.Luce. For The Southwest Cancer Chemotherapy Study Group, Houston, Texas 77025.

Intensive, intermittent, combination chemotherapy (MOPP) was given to 146 patients with Stage III and IV Hodgkin's disease for remission induction and maintenance. Complete remission (CR) occurred in 75,77,79 and 51% of patients with Stage IIIA, IIIB, IVA and IVB disease respectively. CR occurred after 6-10 courses of MOPP in 76% of patients with no prior therapy and in 38,57 and 45% with major prior chemotherapy, radiotherapy or both respectively. Major prior therapy was the important poor prognostic factor. Patients entering CR were then randomized to no maintenance or to MOPP maintenance (every 2 months X 9). 35 months (mo.) after randomization, 73% of CR patients given maintenance remained in CR, compared to only 30% given no maintenance ($p=0.05$). The 2 randomized groups were well balanced for stage and prior therapy. At 44 mo. after the start of therapy, survival was 92%, 85%, 10% and 8% in patients with CR maintained, CR unmaintained, PR and no response respectively. In all of 15 patients who relapsed after CR, recurrent disease first appeared at the sites of the largest volume of initial disease. The data suggest that remission maintenance for 18 mo. and added local (x-ray) therapy to the sites of largest disease will be essential to improve the effectiveness of MOPP therapy.

29 MITHRAMYCIN (NSC 24559) THERAPY OF TESTICULAR TUMORS. G.J. Hill, N. Sedransk, D. Rochlin, H. Bisel, N.C. Andrews, W. Fletcher, J.M. Schroeder, and W.L. Wilson. From Central Oncology Group: Universities of Colorado, Wisconsin, California (Los Angeles and Davis), Oregon and Mayo Clinic.

A Phase II clinical trial of mithramycin was performed in 99 patients with evaluable metastatic testicular tumors. Patients received 25 mcg/kg/day until therapy was stopped because of toxicity. In the absence of persistent toxicity or progression, subsequent courses were begun four weeks after discontinuance of the previous course.

In the 74 patients with acceptable studies responses occurred in 26% (five complete responses and 14 partial responses). Complete responses were persistent for periods of up to 160 weeks, and all patients with complete responses were alive and well at last report.

Death occurred within three weeks after the onset of therapy in 10 patients, and coagulopathy was present in five of these patients. Toxicity of mithramycin was relatively unpredictable, and patients who exhibited severe toxicity received relatively little benefit from therapy.

Responses were most common in young men with asymptomatic metastatic disease, and complete responses occurred only in patients with embryonal carcinoma.

30 IMMUNOLOGIC (?) SUPPRESSION OF CARCINOMA BY VERRUCA VULGARIS. J. R. Hoon, M.D., Sheboygan Clinic, Sheboygan, Wisconsin.

Similar to the influence of coxpox against smallpox, verruca vulgaris (caused by PAPOVA virus) may stimulate resistance to certain carcinomas. An earlier "head count" has suggested such influence. More recently implants of whole fragments of warts from young donors have produced locally regressive changes in measurable subcutaneous metastases from breast carcinomas not wholly explained as simply foreign body reactions. Illustrated by gross and microscopic slides.

31 FAVORABLE REMISSION INDUCTION RATE WITH BI-WEEKLY DOSES OF L-ASPARAGINASE (ASE) IN CHILDHOOD LEUKEMIA - N. Jaffe, D. Traggis, L. Das, G. Frauenberger, H. Hann, B. Kim and Y. Bishop (Intr. by S. Farber), Children's Cancer Res. Fndn. and Harvard Med. Schl., Boston, Mass. 02115.

Two dosage regimens of ASE were investigated to determine differences in the production of abnormal reactions and remission induction. Patients were randomly assigned to receive 200 i.u. per kg. daily for 14 days (A) or 1000 i.u. per kg. twice weekly for 2 weeks (B). All were in relapse and refractory to several chemotherapeutic agents. Median duration of disease was 11 months in A and 16 months in B. 3 out of 15 patients in A achieved a complete remission (CR) and 7 out of 15 in B. Median duration of unmaintained remission in A was 33 days and 40+ days in B. Upon relapse re-induction was attempted in all patients using the original dosage. CR was achieved in 1 out of 3 in A (duration 31 days) and 1 out of 5 in B (duration 45+ days).

Six patients in each regimen experienced abnormal side effects comprising hypersensitivity reactions (3 in A and 2 in B), nausea, vomiting, cough, cyanosis, abdominal pain and fever. One patient in A developed hyperglycemia without pancreatitis. The B regimen of ASE permitted less frequent clinic visits and a favorable remission induction rate without significant increase in toxicity.
(Supported by NIH Grant C-6516).

32 PLATELET AND FIBRINOGEN KINETICS WITH (^{75}SE) SELENOMETHIONINE IN PATIENTS WITH MYELOPROLIFERATIVE DISORDERS. S. B. Kahn, M. D. and I. Brodsky, M. D., Hahnemann Medical College Philadelphia, Pennsylvania.

Simultaneous platelet and fibrinogen kinetics were determined with a cohort label, (^{75}Se) Selenomethionine in 5 patients with chronic myelocytic leukemia (SML), 4 with subacute myelogenous leukemia (SML) and 5 with myelofibrosis with myeloid metaplasia (MF). In control subjects with nonhematologic disorders platelet survival ranged between 7.0 and 11.0 days(mean 10.6 days), platelet turnover was 22,000-51,000 (mean 38,000 platelets/ul/day), fibrinogen survival was 6.5-9.5 days (mean 7.8 days), and turnover was 0.33-0.49 mg/ml/days (mean 0.42). In the CML group platelet survival was normal-to-increased (8-15.5 days), platelet turnover was within the control range (22,000-51,000 platelets/ul/day), fibrinogen survival was top normal-to-prolonged (11.0-19.0 days) and fibrinogen turnover decreased (0.12-0.32 mg/ml/day). Platelet survival in MF was decreased in 4 (3-7 d) and normal in one. Nonsplenectomized patients with short survival and increased platelet turnover were benefited by splenectomy. Platelet survival tended to remain short in this disease despite splenectomy. In SML platelet survival was normal, turnover low, indicating that production defect was the cause of the thrombopenia. These studies indicate that ^{75}Se study can aid in the differential diangosis, in establishing criteria for splenectomy, and in evaluating hemostasis in myeloproliferative disorders.

33 PHASE I STUDIES OF 5-AZACYTIDINE IN CHILDHOOD ACUTE LEUKEMIA. M.Karon, M.D., L.Sieger, M.D., J.Finklestein, M.D., and M. Nesbit, M.D., Childrens Hospital of Los Angeles and USC School of Medicine, Harbor General Hospital and UCIA Center for Health Sciences, Los Angeles, California, and Department of Pediatrics, University of Minnesota School of Medicine, Minneapolis, Minnesota.

5-azacytidine (5-azaCR) is an analog of cytidine which is incorporated into and inhibits the synthesis of RNA and DNA. The compound is known to interfere with the acceptance of amino acids by transfer RNA.

22 children between the ages of 2 and 16 years were given 5-azaCR I.V. qdx5 every 2 weeks. The initial dose, 2mg/M^2, was based on 0.1LD_{10} in the mouse. Dose increments were logarithmic until the maximum tolerated dose on this schedule was achieved, 150-200mg/M^2.

13 patients had acute lymphocytic leukemia (ALL), 9 patients acute myelogenous leukemia (AML). 10/13 patients with ALL received "adequate treatment". There were no remissions. In contrast, of 6/9 patients with AML, 2 achieved complete remission (CR) and 1 partial remission (PR). Remissions occurred at a total dose of 1.1mg/M^2. These patients have been maintained in CR using 5-azaCR 150mg/M^2 2 days/week for 9 months+ and 3 months+.

The principal toxicity has been nausea and vomiting, usually controlable by thorazine and limited to the days of drug administration. Two patients died of sepsis while receiving the drug.

These data indicate that 5-azaCR is an active compound for the treatment of AML. The activity of alternate drug schedules as well as the usefulness of 5-azaCR in the treatment of ALL is yet to be determined.

34 CORRELATION OF ALKALINE PHOSPHATASE (APtase) LEVELS IN SERUM, MALIGNANT EFFUSION AND URINE IN CANCER PATIENTS. S. Lahiri, M.D., and A. Lawrence, B.A., Depts of Oncology and Biochemistry, Wesson Memorial Hospital, 140 High St., Spfld., Mass.

In an attempt to correlate APtase levels in serum, malignant effusions (pleural and peritoneal) and urine, a total of 8 cancer pts were investigated. Heat fractionation was done on all specimens. Serial determinations were done in pleural fluid following local chemotherapy in 6 instances. Thirty-four serum (IU/L-mean 153, SD 143), 7 pleural (mean 15, SD 7), 2 urines and 1 peritoneal fluid were studied. Serial pleural fluid levels following repeated local Thiotepa showed a drop of heat stable fraction from 42% to 14% in two weeks; corresponding serum levels being 13% (mean levels IU/L were--serum 99, pleural 13, normal range being 17-81). Three weeks following therapy pleural fluid heat stable fraction returned to 50%. Urinary levels (IU/L) were 14 and 17% of serum levels. Heat stable fractions in serum and urine were comparable.

The study indicates that there is a difference in APtase heat fractionation profiles between serum and malignant pleural effusion which alters in response to local chemotherapy. Furthor isoenzyme studies are being carried out.

35 SIX YEARS OF CLINICAL EXPERIENCE USING CONCOMITANT HYDROXYUREA AND X-RAY IN THE MANAGEMENT OF LOCALLY ADVANCED HEAD AND NECK CANCER (70 PATIENTS). H. J. Lerner, M.D., Pennsylvania Hospital, Philadelphia, Pa. (Sponsored by H. J. Lerner, MD)

70 patients with proven advanced epidermoid carcinomas of the head and neck were treated with the concomitant use of hydroxyurea and irradiation.

Hydroxyurea is administered as a single oral dose of 80 mg/kg. of body weight every 3rd day. Seven days after hydroxyurea is initiated, x-irradiation (1 million electron volts or cobalt source) is given three times a week for 6 to 10 weeks in full therapeutic doses. In almost all 70 patients there was prompt regression of the primary tumors; maximal regression was evident after 6 to 8 weeks of therapy. 43 of the 70 patients have been clinically free of the disease for periods of 3 to 60 months. Of the 70 patients, 56 showed a 100 percent regression in tumor size: 7 patients had an 80 percent or more regression, and 7 patients had a 50 percent or more regression.

70 outpatients with proven advanced epidermoid carcinomas of the head and neck have undergone complete treatment with concomitant hydroxyurea and irradiation therapy. 56 patients showed complete regression of the primary tumor. All patients have become candidates for operation following completion of combination therapy.

36 FIVE DRUG THERAPY OF SOLID TUMORS UTILIZING HIGH DOSE METHOTREXATE-LEUCOVORIN

M. Levitt, M.D., University of Manitoba, Dept. of Medicine, Winnipeg, Canada.

The following program of combination chemotherapy for solid tumors resistant to conventional therapy has been established: cyclophosphamide 600 mg/M^2 and vincristine 1.4 mg/M^2 by rapid i.v. injection at time 0; actinomycin D 700 micrograms and/or 5-fluorouracil 700 milligrams depending on histologic diagnosis at time 0, and methotrexate, 360 mg/M^2 over 30 hours followed by "Leucovorin Rescue" 60 mg/M^2 i.v. over 6 hours and 25 mg q.6.h. x 4, p.o. Of 20 patients 13 are male and 7 female, with a mean age of 59 (range 25 to 73). Seven have lung tumors (4 epidermoid, 2 oat cell, and 1 adenocarcinoma) 5, sarcomas, 2, breast tumors, and 5 others, (testis, nasopharynx, renal and 2 unknown primary adenocarcinomas). Nine have received 1 course, 8, 2 courses, 1, 3 courses, and 2, 5 courses on a monthly basis. Toxicity has included 1 day's nausea and vomiting per course in all patients, paralytic ileus in 1, alopecia in 3, reversible leukopenia as low as 1,000/mm^3 in 3, and mucositis in 3. There have been 4 objective and 2 subjective responses in the 11 patients who have had at least 2 courses of therapy.