Questions and Answers on Cancer

Adjuvant Chemotherapy for Gastric Cancer

A 69-year-old white male was found to have an ulcerating carcinoma of the gastric antrum measuring eight x 10 cm. with an ulcer crater measuring approximately five cm. in diameter. This was treated by a near total gastric resection with excellent results. The liver, adjacent viscera and tissues and the regional node filter were uninvolved.

Since the survival figures on gastric cancer are exceedingly poor, should adjuvant chemotherapy be instituted? Has any such chemotherapy been found worthwhile in cases of this type? Have there been any encouraging results in Stage I patients without local spread and which chemotherapeutic agents are advisable? I exclude, of course, situations in which gastric cancer has already become locally disseminated and favorable results from a combination of 5-FU and nitrosoureas are encouraging.

M.D., Louisville, Kentucky

Before responding to the specific questions regarding this particular patient, it is pertinent to comment on the prognosis of carcinoma of the stomach. It is quite true that the overall survival figures for gastric cancer are poor and are generally in the range of 10 percent five-year survival, if one considers all patients with gastric cancer entering an institution for diagnosis and treatment. On the other hand, data from several large institutions on patients with the specific findings described above are considerably better than the overall group. A patient with a distal gastric cancer that is free of regional lymphatic and other metastases has a 45-50 percent chance of five-year survival after adequate surgical resection. These figures leave much room for improvement, but they are more optimistic for patients like the one described than for the overall population of patients with gastric cancer.

Currently, there are a number of cancers treated primarily by surgery that seem to have improved treatment results when chemotherapy is given to combat possible occult or microscopic residual disease. In view of this, your question regarding the possible use of adjuvant chemotherapy for gastric cancer is very timely. Unfortunately, the answers to all the questions you have raised regarding adjuvant therapy for gastric cancer are negative, but merit some discussion from the standpoint of our future hopes.

Although the response rate from the combination of 5-FU and the nitrosoureas for recurrent gastric cancer is better than single agent therapy, there are no data from clinical trials of this combination used as an adjuvant to surgery. Actually, the clinical trials of even...
single drug therapy have focused more intensely on colorectal cancer, since a detectable difference achieved with adjuvant therapy would be more apparent in this disease than in gastric cancer. Single drug studies in colorectal cancer, particularly with 5-FU, have shown little or no benefit in all of the randomized prospective trials reported thus far. The future hope for improved results for all gastrointestinal cancer lies in the combination of agents, such as 5-FU and nitrosoareas. The improved results observed in the treatment of advanced disease for both colon cancer and gastric cancer do give some encouragement for the potential value of these adjuvants.

Past experience in many clinical trials has taught us, however, that the value of adjuvant chemotherapy must be established by prospective trials before it is advised for general use, in view of the failure of most programs to be of benefit, despite their rationale. The possibility always exists that the adjuvant therapy may have detrimental results, rather than beneficial ones, and this is an additional reason for insisting on scientific proof of their value before recommending their widespread use.

At this time, I believe that the patient should be followed carefully without additional therapy, although it is my hope that a similar patient in future years may be beneficially treated by some form of combination chemotherapy.

Walter Lawrence, Jr., M.D.
American Cancer Society
Professor of Clinical Oncology
Medical College of Virginia
Richmond, Virginia

Management of “Inflammation” on Pap Smears

What is the current treatment for a patient with a Pap smear that is “negative for tumor cells” but reveals a “mild,” inflammatory reaction? Is cryosurgery acceptable treatment when a repeat Pap smear comes back with mild inflammation after sulfa and/or Dienestrol creams are used for four-12 weeks?

Is it true that when cryosurgery is used on the cervix, the mucocutaneous junction, after healing, recedes further up the endocervical canal and frequently becomes inaccessible to routine Pap smear?

M.D., Louisville, Kentucky

It is important to determine the etiology of inflammation by wet smear and culture. The patient should be treated according to the diagnosis and a new Pap smear taken in two months. When available, colposcopy provides a valuable tool in the management of the patient since it is possible to immediately differentiate between inflammatory atypia and neoplasia.

I feel that in this situation, cryosurgery is categorically contraindicated. We have to recognize that negative cytology or Pap smear compatible with “mild inflammation” does not exclude the possibility of cervical neoplasia. The false-negative rate of a single Pap smear in a routine practice is around 20 percent. Before any cryosurgical procedure, the patient must be evaluated by all available diagnostic methods to exclude the possibility of invasive cancer. Cryosurgery without colposcopy is contraindicated.

Adolf Stafl, M.D.
Associate Professor
Department of Obstetrics and Gynecology
Medical College of Wisconsin
Milwaukee, Wisconsin

Pancreatic Ca Treatment

What is the present status of chemotherapy with and without associated radiation therapy for cancer of the pancreas?

M.D., Jacksonville, Florida

Chemotherapy for cancer of the pancreas is of uncertain value. There are no
completed controlled trials, although some are in progress. The familiar 5-fluorouracil (5-FU) has produced a beneficial response in about 25 percent of patients treated, but in different studies there has been a range of 0-67 percent responding. The effect on survival is unknown. A loading dose of 15 mg./kg./day for five days, followed by 7.5 mg./kg./every other day, has been the most popular regimen. Mitomycin C is equally effective but more toxic. A combination of 5-FU and BCNU (nitro-sourea) gave a response rate of 33 percent compared to 16 and 0 percent for the agents used alone.

Radiation through a 20 x 20 cm. port to deliver 3500-4000 rads, administered six days a week, plus 45 mg./kg. of 5-FU in divided daily doses on the first three days of radiotherapy, gave a mean survival of 10.4 months compared to 6.3 months for patients given radiation plus a placebo.

For more information on this, I recommend Carter’s recent article, “The Integration of Chemotherapy into a Combined Modality Approach for Cancer Treatment. VI Pancreatic Adenocarcinoma.” (Cancer Treatment Reviews 2:193-214, 1975).

Frank P. Brooks, M.D.
Professor of Medicine and Physiology
University of Pennsylvania
School of Medicine
Philadelphia, Pennsylvania

Stage I Hypernephroma: Treatment and Prognosis

In September, 1976 a 65-year-old man, otherwise in excellent health, underwent right radical nephrectomy for a hypernephroma. Preoperative scans of brain, bone, liver and lung, and tomograms of the lungs were all negative. His postoperative course has been uneventful. Pathological reports indicate no interruption of the capsule of the kidney and no invasion of the vena cava or lymphatics.

I would appreciate suggestions on a specific follow-up program for this particular patient, as well as estimated five-year survival rates given the sometimes unpredictable behavior of this tumor.

M.D., Encinitas, California

Renal adenocarcinoma is unpredictable at times. Perhaps it has been over-emphasized in individual cases and particularly in general series reporting. The histological grade, possibly the granularity of the cytoplasm and the clinical stage you describe in the inquiry, are important features and have prognostic significance, regardless of the type of therapy.

Most recently, the ectopic hormonal production by such tumors in man has been also found as an additional means of predicting clinical therapeutic response. Ectopic renin production is generally associated with a poor prognosis.

Your patient, as described, would be classified as Stage I and most experts would not recommend adjuvant therapy including chemotherapy at this time. The prediction for five-year survival is considerably above 50 percent, but how much above depends on other factors, such as histological grading, cytoplasmic granularity and ectopic hormone production. If these were known and were of an adverse status, perhaps some physicians would consider adjuvant therapy.

Undoubtedly, in forthcoming prospective trials, adjuvant chemotherapy will be used more widely, particularly for Stage II patients. When it comes to Stage III, multiple chemotherapy and other types of adjuvant programs are already underway.

Gerald P. Murphy, M.D.
Institute Director
Roswell Park Memorial Institute
Buffalo, New York
Postoperative Adjuvant Chemotherapy for Breast Cancer

A 57-year-old female was discharged from the hospital 16 months ago, after a modified radical mastectomy with metastases to one axillary lymph node that was cleaned out completely. The pathological diagnosis: infiltrating duct cancer of the right breast with metastases. No radiation was employed postoperatively. However, since the operation, the patient has been taking three tablets (6.0 mg.) of L-PAM, P.O. daily for one out of six weeks. Lately she has become allergic to the drug, and it has been discontinued. Recent bone scans, liver scans and chest X-rays were all negative. Should she receive a different form of chemotherapy? If so, please advise as to the dose and duration of use.

M.D., East Orange, New Jersey

In this case I see two options open to the physician. He can discontinue chemotherapy or continue with some different adjuvant drugs. I favor the first choice.

The patient with only one node involved following a thorough modified radical mastectomy has minimal risk beyond patients with no nodes involved. Furthermore, and of equal significance, there is no statistical evidence that the arbitrary two-year continuation of postoperative adjuvant chemotherapy for breast cancer is actually an essential time interval to achieve optimal results. There is a good possibility that the amount of chemotherapy that the patient has already received is sufficient to derive whatever benefit may be obtained by this modality.

Should the physician, however, wish to continue with an alternate form of chemotherapy, I would recommend the method of Bonadonna (Bonadonna, G. et al.: Combination chemotherapy as an adjuvant treatment in operable breast cancer. N. Engl. J. Med. 294:405-410, 1976). This protocol involves the use of cytoxan, methotrexate and 5-fluorouracil. Treatment under this regime consists of a 28-day cycle. The dosage schedule we use is cytoxan, 100 mg./m.² on days one through 14 by mouth, methotrexate, 40 mg./m.² I.V. on days one and eight and 5-fluorouracil, 600 mg./m.²1.V. also on days one and eight. Blood counts are obtained weekly for the first two courses and then just prior to day one of each additional course. Twelve courses are given.

Harry W. Southwick, M.D.
Professor and Chairman
Department of General Surgery
Rush Medical College
Chicago, Illinois

X-ray Therapy and Cancer of Other Sites

A 62-year-old male had superficial radiation to the face for acne at age 17. For the past 10 years he has had one or two basal cell carcinomas removed at different sites of his face. Is there any published material to indicate that such a patient will have a greater or lesser immunity to cancer of other organs?

M.D., Newark, New Jersey

There is to my knowledge no study which deals with the relationship between basal cell carcinoma of the skin due to X-ray radiation and the subsequent appearance of other cancers.

There are, however, two recent reports which relate indirectly to the question. Shore et al. (Follow-up study of patients treated by X-ray epilation for tinea capitis. Arch. Environ. Health 31:21-28, 1976) studied 2,000 individuals who were given X-ray therapy to the scalp for tinea capitis between 1940 and 1950. In this study there were no differences between the irradiated group and the non-irradiated control group in
the incidence of tumors other than those that occurred in the irradiated areas. Modan et al. (Radiation-induced head and neck tumors. Lancet 306:277-279, 1974) conducted a retrospective study of approximately 11,000 individuals whose scalps were irradiated for tinea capitis 12 to 23 years previously. There was an increased incidence of head and neck tumors including basal cell carcinomas. The authors observed other organ systems and noted no abnormal increase in neoplasms.

These studies indicate that basal cell carcinomas induced by superficial X-ray radiation are limited to the tissues absorbing the radiation and that distant cancers are not potentiated. In other words, there is neither greater nor lesser immunity induced.

The question gives no information as to the patient’s history of sun exposure. In the absence of this information and the absence of data regarding the X-ray dosage and filtration or shielding, it cannot be concluded that the basal cell carcinomas are due to the X-ray therapy alone.

J. Harry Katz, M.D.
Clinical Associate Professor of Medicine
Department of Dermatology
Cornell University Medical College
New York, New York

Actinic Keratosis

*What is the treatment of choice for the premalignant lesion, actinic keratosis, in a 40-year-old patient with blue eyes and red hair? Please discuss curettage, trichloroacetic acid, 5-fluorouracil and sun screens.*

M.D., Lancaster, California

Because of certain characteristics, which are probably inherited, patients with blue eyes and other fair-skinned people exposed to sunlight for prolonged periods, will often develop actinic keratoses, also called solar keratoses or senile keratoses. In our institution, the treatment of choice for this disease is 5-fluorouracil lotion applied once or twice daily for three weeks. Some physicians use one percent or two percent concentrations, but because it leads to a more complete response, I prefer the five percent concentration.

Our research has indicated that the action of 5-fluorouracil is related not only to its direct toxicity on malignant and premalignant cells, but also to induction of a selective hypersensitivity localized to the disease area. Major advantages of this mode of therapy are its simplicity, completeness of response and lack of scarring. If good patient cooperation and close supervision are maintained during treatment, successful removal may be expected in almost all patients.

When lesions are curetted, diseased cells are scraped away; however, curettage must be carried to a fairly deep level in order to remove all of the diseased area. Trichloroacetic acid acts by denaturing protein and coagulating all tissue with which it comes into contact. In both of these methods of treatment, normal as well as diseased cells are destroyed. Additionally, because both forms of treatment must be carried out to a fairly deep level, a certain degree of depigmentation and scarring results.

Since actinic keratoses result from exposure to the ultraviolet portion of sunlight, any good sunscreen that blocks out a significant amount of this radiation will prevent cutaneous damage. However, sun screens will not remove actinic keratoses, nor will they prevent formation of new lesions in cutaneous areas that have already been damaged. After therapy with topical 5-fluorouracil, sun screens should be used to prevent further damage and formation of new lesions in successfully treated areas.

Martin S. Litwin, M.D.
Professor of Surgery
Tulane University Medical School
New Orleans, Louisiana