**Questions and Answers on Cancer**

**Metastatic Malignant Melanoma**

*What is the latest chemotherapy for local metastatic malignant melanoma? The patient had local excision, and now has a recurrence at the same site; he had two courses of BCG plus DTIC. Is there a second line of drugs being used that might be helpful?*

M.D., Louisville, Kentucky

Local recurrence of cutaneous melanoma at the primary operative site, with or without clinically positive draining lymph nodes and with no evidence of distant metastases, is potentially curable surgically. The treatment of choice is wide excision of the recurrence, and a surgical approach to draining lymph nodes. The re-excision at the original operative site should include a five cm. rim of surrounding skin and dissection down to and including the underlying fascia. Lymphadenectomy is recommended if the primary draining lymph nodes (either clinically positive or clinically negative) can be anatomically identified. Subsequent adjuvant systemic therapy in patients at high risk for recurrence after curative surgery is presently under investigation.

If metastatic disease is present (aside from local recurrence and draining lymph nodes), the patient is not surgically curable. Systemic chemotherapy is therefore indicated; the treatment of choice being DTIC as a single agent. There is no prospective randomized Phase III trial in the literature which demonstrates any combination of chemotherapeutic agents to be superior to DTIC alone in the treatment of metastatic malignant melanoma. If the patient manifests progressive disease in spite of DTIC systemic therapy, the combination of BCNU plus vincristine is recommended.

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**Premarin for Postmenopausal Patient After Removal of Uterus**

A 54-year-old patient went through a smooth menopause at 45, and was given Premarin .6 mgm. for eight years and 1.2 mgm. ± for two years prior to August, 1975. Because of spotting, a D and C was done, which revealed a Grade I adenocarcinoma that had extended somewhat into the endocervix. After local radiation by implant, the uterus, tubes and ovaries were removed. Biopsy showed no viable malignant ac-
tivity. Postoperative recovery was slow but steady. She had no hot flashes, but felt that her general well-being was considerably reduced by the absence of Premarin.

Is restitution of 1.2 mgm. ± of Premarin contraindicated in this patient? The considerable current controversy does not treat conclusively postoperative patients where malignant disease would appear to have been eradicated by surgery and X-ray.

M.D., Denver, Colorado

The prognosis of early uterine cancer so treated is excellent. There is no data to indicate that small doses of Premarin produce breast cancer; in fact, Premarin appears to have an inhibitory effect on the appearance of future breast cancer. A symptomatic postmenopausal patient whose uterus has been removed can take Premarin in small doses with reasonable impunity since the cancricidal effect of Premarin appears to be directed at the endometrium.

Whether Premarin should be used to enhance “general well-being” is open to some question.

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Adjuvant Chemotherapy for Breast Cancer

What do the adjuvant therapy groups consider the best adjuvant chemotherapy for breast cancer when one or more nodes are involved? What single drug would be best to administer? Please specify the dosage and time intervals. Also, what combination of drugs is recommended?

M.D., Glendale, California

There is no definitive answer regarding the best adjuvant therapy for patients with positive nodes following radical mastectomy. Studies by Fisher¹ and Bonadonna² indicated the value of two different programs, one employing L-phenylalanine mustard (L-PAM) and the other a three drug combination of cyclophosphamide, methotrexate and 5-fluorouracil (CMF). Both of these regimens significantly delayed recurrences compared to surgery alone. However, survival data is not available to demonstrate conclusively whether survivorship was also increased. Other studies, which use other treatment programs, are in progress.³

However, if one accepts the premises that disease-free prolongation is a harbinger of better survival, and that patients with node-positive disease do not do well, then adjuvant therapy appears reasonable. In general, the CMF regimen has produced fewer recurrences. However, except in postmenopausal women, the results with L-PAM were almost comparable. To simplify the approach, I would suggest that CMF be used in postmenopausal patients and premenopausal women with four or more positive nodes. In the premenopausal patient with one to three positive nodes, L-PAM is a good choice.

The doses are:
L-PAM: 0.15 mg./kg. p.o. per day for five days repeated every six weeks for two years.
CMF: Cyclophosphamide: 100 mg./m² p.o. per day for 14 days.
Methotrexate: 40 mg./m² I.V. day one and eight.
5-fluorouracil: 600 mg./m² I.V. day one and eight.

Repeat every four weeks for 12 cycles.

Using both of these chemotherapy programs, it is essential that the dose be modified for toxicity and decreased for patients over the age of 65. I would recommend that these treatments be carried out in concert with competent medical
oncologists as the potential for severe toxicity is present in both.

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References
1. Fisher, B. et al.: L-phenylalanine mustard (L-PAM) in the management of primary breast cancer: A report of early findings. N Engl. J. Med. 292:117-122, 1975
2. Bonadonna, G. et al.: Combination chemotherapy as an adjuvant treatment in operable breast cancer. N. Engl. J. Med. 294:405-410, 1976
3. Carbone, P.P.: Chemotherapy in the treatment strategy of breast cancer. Cancer 36:633-637, 1975

Chemotherapy for Glioblastoma Multiforme?
A 32-year-old female patient was operated on for multiforme, Grade IV glioblastoma. Results were equivocal. After surgery, she received maximal radiation therapy, linear and cobalt. What is the chemotherapeutic agent of choice? Please explain dosage, method of administration and time intervals.

Are any new and promising drugs being tried at this time?
M.D., Pittsburgh, Pennsylvania

The Brain Tumor Study Group under the National Cancer Institute has carried out a strictly randomized study of glioblastoma multiforme over the last several years; the results seem to be promising.

Those patients who did best received 6000 rads to the whole head over a six to eight week period, combined with BCNU, 80 mg. per meter square, administered for three days every six to eight weeks.

The life expectancy of such patients was approximately double that of the patients who received only surgery without radiation or without BCNU.

Some of the patients who have been so treated in this way are still alive, and the results may appear better yet.

Other drugs being used at the present time include procarbazine and very large doses of methylprednisolone, given for a week at a time, one out of every three weeks. All of these forms of therapy are combined with radiation therapy, as noted above. Adriamycin has shown some promise and will undoubtedly be used in a multifaceted drug approach to these tumors in the future.

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Annual Sigmoidoscopy:
For All Patients Over 50

Is regular annual sigmoidoscopy advisable in asymptomatic as well as symptomatic patients?

What is the relationship between colorectal polyps and cancer? Please comment on the time required by these lesions to develop from initial changes to symptomatic cancer.

M.D., Philadelphia, Pennsylvania

While for "symptomatic" patients, regular annual exams would appear to be less than acceptable, for "asymptomatic" high-risk patients (for example, those over 50 years old) there is no question of the advisability.

As for the relationship between colorectal polyps and cancer, it is direct. The fact that it may take several years for these lesions to develop from initial changes to symptomatic cancer further emphasizes the importance of periodic proctosigmoidoscopy in the detection of earlier and more highly curable lesions.

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