The Use of Antioxidants with Chemotherapy and Radiotherapy in Cancer Treatment: A Review

Hal Gunn, M.D.[1]

Studies involving glutathione, selenium, beta-carotene, vitamin E, CoQ10, NAC, melatonin, 5-MTT and multiple antioxidants are reviewed.

Glutathione

Glutathione/colorectal cancer: Neuroprotective effect of glutathione on oxaliplatin-based chemotherapy in advanced colorectal cancer: A randomized double-blind, placebo-controlled trial

Fifty-two patients with advanced colorectal cancer were randomized to receive glutathione (1,500 mg/m2 over a 15 minute infusion period before oxaliplatin) or normal saline solution. At baseline, no patient suffered from clinical neuropathy in either arm. At the time of the second neurologic examination (four cycles), seven patients had grade 1 or 2 clinical neuropathy in the GSH arm (27%) vs. 11 patients in the control arm (42%). After eight cycles of chemotherapy, this increased to 9/26 vs. 15/26 (p=.04) in the treatment and control arms respectively. Grade 2-4 neurotoxicity was observed in only three patients in the GSH arm vs. eight in the placebo arm (p=.01). The response rate to chemotherapy was 26.9% in the glutathione arm and 23.1% in the placebo arm, showing no reduction in activity of oxaliplatin.

–Cascinu S et al. *J Clin Oncol,* 2002; 20(16): 3478-83.

Glutathione/Ovarian Cancer

Neurotoxicity of cisplatin +/- glutathione in first line treatment of advanced ovarian cancer

Several drugs have been proposed for chemoprevention from cisplatin-induced neurotoxicity. For the purpose of this study the effectiveness of reduced glutathione during cisplatin-based first-line chemotherapy was evaluated in a series of 54 patients affected by ovarian cancer. Patients were randomized to one of four treatment arms: 50 mg/m2 per week cisplatin +/- glutathione for nine courses or cisplatin 75 mg/m2 every three weeks +/- six courses glutathione (total dose of 450 mg/m2 in each arm). Neurotoxicity was assessed by clinical examination, vibrametry and neurophysiology before, during and after chemotherapy. First of all, it is noteworthy that glutathione co-treatment did not impair the effectiveness of chemotherapy. Non-neurological side effects were similar in both glutathione groups. They also showed a trend toward less severe neurotoxicity. Although neuroprotection was not complete, these findings are in agreement with previous data that support the view that chemoprevention with gluatathione should be considered in cisplatin treated patients. This study should be considered a pilot work as the low number of patients in each subgroup at the final evaluation prevented reliable statistical evaluation of the data.

–Bogliun G, Marzorati L, Marzorati M et al. *Int J Gynecol Cancer,* 1996; 6: 415-419.

Glutathione/Ovarian Cancer

Glutathione reduces the toxicity and improves quality of life of women diagnosed with ovarian cancer treated with cisplatin: results of a double-blind, randomized trial.

The objective of this trial was to determine whether glutathione would enhance the feasibility of giving six cycles of cisplatin without dose reduction due to toxicity. One hundred fifty patients with ovarian cancer (Stage I-IV) were

1. The Centre for Integrative Healing #200-1330 West 8th Ave., Vancouver, BC V6H 4A6

randomized to receive cisplatin alone or cisplatin plus glutathione. Glutathione produced a significant advantage in terms of the proportion of patients receiving six courses of cisplatin (58% vs. 39%, p=0.4)). Patients in the treatment group showed better creatinine clearance (74% vs. 62%, p=0.006), as well as a statistically significant improvement in depression, emesis, peripheral neurotoxicity, hair loss, shortness of breath and difficulty concentrating. Clinically assessed response to treatment demonstrated a trend towards a better outcome in the glutathione group (73% vs. 62%), but this was not statistically significant (p=0.25).

–Smyth JF et al: *Annals of Oncology,* 1997; 8: 569-573.

Glutathione/Head and Neck Cancer/non-small Cell Lung Cancer

Glutathione in the prevention of cisplatin induced toxicities: a prospectively randomized pilot trial in patients with head and neck cancers and non-small cell lung cancer.

Glutathione (GSH) has been shown to be an effective chemoprotector against cisplatin-induced toxicities in patients with ovarian cancer. This randomized controlled pilot study was conducted to determine its efficacy in the management of other solid tumors, in this case non-small cell lung cancer (NSCLS) and head/neck cancer. A total of twenty patients (n=6 NSCLS and n=14 head/neck) were randomized to receive 5 g of GSH immediately before chemotherapy or a control intervention of 2000 ml of electrolyte infusion. All patients received 80-mg/m2 cisplatin with etoposide or 5-flourouracil as standard treatment. Results showed that the intensity of hematologic toxicity was significantly less pronounced in the patients treated with GSH than in the control group, whereas in terms of non-hematologic toxicity no differences were observed. Objective remission occurred in six out of 11 patients from the GSH group and in four out of eight in the control group. There was no statistically significant difference in terms of response or overall survival. The results of this study suggest that application of GSH and cisplatin seem safe and feasible and the antitumoral efficacy of cisplatin in not impaired by the concomitant use of GSH in patients with solid tumors.

–Schmidinger M, Budinsky AC, Wenzwel C, et al. *Wien Klin Wochenschr,* 2000 Jul 28; 112(14): 617-23.

Glutathione/Gastric Cancer

Neuroprotective effect of reduced glutathione on cisplatin-based chemotherapy in advanced gastric cancer: a randomized double-blind placebo-controlled trial.

Fifty patients with advanced gastric cancer were randomized to receive either intravenous glutathione (1.5g/m2) immediately before cisplatin administration or a normal saline solution. At the ninth week, patients in the treatment group showed no clinically evident neuropathy, whereas 16 patients in the control group did. After the 15th week, four of the 24 assessable patients in the treatment arm suffered from neurotoxicity compared to 16 of 18 in the placebo arm (p=.0001). The use of glutathione also reduced transfusion requirements (32 vs. 62 transfusions) and treatment delay (55 vs. 94 weeks). The response rate to chemotherapy was 76% in the treatment group and 52% in the control group, suggesting that glutathione increases the clinical activity of cisplatin.

–Cascinu S et al: *J Clin Oncol,* 1995; 13(1): 3478-83.

Glutathione/Ovarian Cancer

A randomized double-blind placebo controlled trial assessing the efficacy of gluatathione as an adjuvant to escalating doses of cisplatin in the treatment of advanced ovarian cancer.

The efficacy of cisplatin in the treatment of epithelial ovarian cancer is dose dependent. This trial attempted to deter-

mine if glutathione could alleviate cisplatin toxicity with increased doses of cisplatin. This trial was closed early when it an interim analysis showed a highly significant survival advantage for those patients treated with a higher dose (100 mg/m2) of cisplatin. The toxic effects of the treatment were also significantly greater in the high dose arm. Three groups of 12 patients with advanced ovarian cancer were treated with cisplatin. In each group, six were treated with 1.5-g/m2 glutathione 15 minutes before each cisplatin treatment, and 6 were given a placebo. Group 1's treatment was for two successive days, group 2 for three days, and group 3 for four days, repeated every 4-weeks. Recruitment to the trial was stopped after eight patients had entered group 2. Ototoxicity was more common in Group 2, and 4 patients in this group were withdrawn when grade II toxicities were encountered. No patients were entered in group 3. Clinical assessments, laboratory tests and neurological and audiological examinations were performed on all treated patients, and no significant differences were noted between active (glutathione) and placebo groups. Ototoxicity was noted in both glutathione and placebo treated patients. The researchers believed that glutathione failed to significantly protect against cisplatin toxicity because cisplatin was administered over two hours. Glutathione has a short half-life, and it has been shown that 30-minute cisplatin infusions are optimal when combined with glutathione.

–Parnis FX, Coleman RE, Harper PG, Pickering D et al: *Eur J Cancer,* 1995; 31a: 1721.

Glutathione/Endometrial Cancer

Adjuvant radiotherapy of the pelvis with or without reduced glutathione: a randomized trial in patients operated on for endometrial cancer.

A randomized pilot trial was performed to evaluate the feasibility of administration of glutathione (GSH, 1200 mg, IV) as a protector in preventing diarrhea in patients operated on for endometrial cancer and submitted to adjuvant radiotherapy of the pelvis. Diarrhea occurred in 52% of patients in the untreated control group and only 28% of patients in the GSH-treated group. Preliminary data indicate that GSH administered before radiotherapy reduced the occurrence of diarrhea from oxidative damage to the intestinal mucosa.

–De Maria, D. et al, *Tumori,* 1992; 78:374-376

Glutathione/Solid Tumour Cancers

Evaluation of the neurotoxicity of cisplatin alone or in combination with glutathione.

The use of high doses of cisplatin in the treatment of solid tumors is often prevented by the onset of disabling sensory neuropathy. This prospective randomized study evaluated how cisplatin administration alone or in combination with gluathione affected 33 patients with relapsing ovarian cancer. The results of the neurophysiologic examinations performed before and immediately after chemotherapy suggest that combined glutathione/cisplain therapy is safe and effective in the treatment of ovarian cancer, and has extremely low peripheral neurotoxicity.

–Bogliun G, Marzorati L, Cavaletti G, Frattola L: *Ital J Neurol Sci,* 1992; Nov; 13 (8): 643-7.

Selenium

The protective role of selenium on the toxicity of cisplatin-contained chemotherapy regimen in cancer patients.

Forty-one patients with mixed cancer diagnoses were randomized into two groups in a cross-over trial. 4000 μg per day of selenium were administered from four days before to four days after chemotherapy for study cases. Results showed that WCB counts were better on day 14 after the initiation of chemotherapy for

the treatment group (3.35 vs2.31, p<0.05) and the amount of GCSF required was significantly less than it was for the controls (110.1 vs. 723.6, p<0.05). In addition, the volumes of blood transfusions were less (0 vs. 62 mL, p<0.05) and the nephrotoxicity of cisplatin was lower for the treatment group as compared to the controls. In sum, the results suggest that selenium can be used as an agent for reducing the nephrotoxicity and bone marrow suppression induced by cisplatin.
Hu Y et al: *Biological Trace Element Research,* Vol. 56: 331-341, 1997.

Beta-carotene
The modifying effect of beta-carotene on radiation and chemotherapy-induced oral mucositis.

Twenty patients with advanced squamous carcinoma of the mouth were randomized to receive standard diet with supplemental beta-carotene or standard diet only. Beta-carotene dosage started at 250 mg/day for 21 days and then 75 mg/day for the duration of the treatment (eight weeks in total). Evaluated in terms of patient weeks, a significantly (p<0.025) less severe oral mucosal reaction was measurable in the treatment group. Remission rate was not significantly different in the two groups of patients.
–Mills E. *British Journal of Cancer,* 1988; 57: 416-17.

Vitamin E (Tocopherol)
Neuroprotective effect of vitamin E supplementation in patients treated with cisplatin chemotherapy.

In this study, 27 people between the ages of 28 and 74 with different types of cancer were randomly assigned to receive either cisplatin chemotherapy alone or cisplatin chemotherapy with 300 IU of vitamin E per day. Those taking the vitamin E started approximately four days before the start of cisplatin chemotherapy and continued for three months following treatment. Participants taking vitamin E had significantly lower neurotoxicity scores at the conclusion of their treatment compared with those who only received cisplatin. More than 85% of those receiving cisplatin alone developed nerve damage, compared with only 31% of the vitamin E group (p<.01). The severity of neurotoxicity was significantly lower in patients taking vitamin E (2 vs. 4.7, p<01).
–Pace A, Antonella S, Picardo M et al: *J Clin Oncol,* 2003; 21:927-31.

Vitamin E/Radiation Induced Fibrosis

Randomized, placebo controlled trial of combined pentoxifylline and tocopherol for regression of superficial radiation-induced fibrosis.

Twenty-four women previously treated for breast cancer were randomized to one of four treatment arms: 1) 800 mg/day of pentoxyfilline (PTX) and 1000 IU of vitamin E; 2) PTX plus placebo; 3) placebo plus vitamin E, and; 4) placebo-placebo. The main end point measure was the relative regression of radiation-induced fibrosis (RIF) surface after six months. The results showed that mean susrface regresssin was significant combined vitamin E/PTX versus double placebo (60% ± 10%vs. 43%± 17%, p=0.38). Synergism between PTX and vitamin E is likely as treatment with each drug alone is ineffective. All treatments were well tolerated.
–Delanian S, Porcher R, Saida N, Lefaix J: *J Clin Oncol,* 2003; 21(13): 2545-50.

Vitamin E/Mucositis
Treatment of mucositis with vitamin E during administration of neutropenic antineoplastic agents. (Article in French)

Mucositis represents one of the most frequent complications during chemotherapy or radiotherapy. This study tested the efficacy of vitamin E in the treatment

of chemotherapy-induced mucositis in 20 patients with malignant heamopathies. Ten patients were treated with induction therapy for acute myelogenous leukemia and nine were treated with intensive therapy followed by autologous bone marrow transplantation. The severity of the mucositis was evaluated according to WHO classification. The results showed that vitamin E might be of therapeutic value in the prevention of mucositis especially during induction therapy for acute myelogenous leukemia.
–Lopez I, Goudou C, Ribrag V et al: *Ann Med Internes* (Paris) 1994; 145 (6):405-8.

Vitamin E/Mucositis

Vitamin E in the treatment of chemotherapy-induced mucositis

The purpose of this study was to determine the efficacy of vitamin E in the treatment of chemotherapy-induced mucositis in patients with malignancy. A randomized double blind, placebo-controlled study was performed with a total of 18 patients, 17 of whom had solid tumours, and one with acute leukemia. Lesions were assessed daily prior to and until five days after topical application of either vitamin E or placebo oil. Results found six of the nine patients receiving vitamin E had complete resolution of their oral lesions. In eight of the nine patients receiving placebo, complete resolution of their lesions was not observed. The difference was statistically significant (p=0.025). No toxicity was observed.
–Wadleigh RG, Redman RS, Grahman ML, et al. *Am J Medicine,* 1992; 92: 481-84.

Co-Enzyme Q10

Protective effect of CoQ10 administration on cardiac toxicity in FAC therapy. (Article in Japanese)

An unique combination treatment for cancer patients has been attempted in our department. The treatment consists of 500 rad irradiation of cobalt 60 on the first day and drip infusion of mixture of 50 mg adriamycin, 500 mg cyclophosphamide and 500 mg 5-fluorouracil on the next day. This combination therapy was repeated every three weeks. Myocardial toxicity may be a great problem in this therapy. Investigation was performed in 40 cancer patients in order to clarify if Coenzyme Q10 (CoQ10) could show any protective effect upon the possible myocardial toxicity. Patients were divided into two groups: one group of 20 patients who received 90mg/day CoQ10 orally and the other group of 20 patients who did not receive CoQ10. In the group without CoQ10, radiothoracic ratio (CTR) and pulse rate increased significantly in all patients. ECG low voltage of QRS complex was seen in two cases without CoQ10, changes of ST-segment, T-wave and appearance of arrhythmia were more than frequent in the group without CoQ10 than that with CoQ10. It is concluded that CoQ10 is effective for protecting the myocardium in this cancer therapy.
–Takimoto M, Sakurai T, Kodama K, et al: *Gan To Kagaku Ryoho,* 1982; Jan;9(1): 116-21. PMID: 7184359

N-Acetylcysteine

A randomized controlled trial assessing the preventions of doxyrubicin cardiomyopathy by n-acetlycysteine.

In animal studies, n-acetlycysteine (NAC) appears to protect against acute doxyrubicin (DOX) cardiac toxicity. The purpose of this trial was to assess whether NAC can protect patients from the chronic myocardiopathy associated with DOX use. Twenty-four patients treated with DOX were matched for age, sex and disease status to 30 control patients. Primary sites of disease were breast cancer, nodular lymphoma patients, and metastatic soft-tissue sarcomas. Patients were excluded is they had known heart disease or had received over 600 rad of cardiac irradiation. Patients received 75 mg/m2 I.V. of DOX every 4 weeks either alone or pre-

ceded by 5.5 gm/m2 NAC orally. Results found no significant protective effect for DOX induced cardiotoxicity in the NAC group compared to the controls. Researchers suggest that in light of the fact DOX induces a defect in cardiac free radical defenses for several days after a treatment, a single dose of NAC is not likely the most effective intervention. Patients reacted unfavorably to the taste and smell of NAC. The treatment group was found to have more diarrhea, slightly more hair loss, but somewhat less severe nausea.
–Myers C, Bonow R, Palmeri S et al: *Semin Oncol,* Suppl 1 March 1983;10 (1): 53-55.

Melatonin

Melatonin/non-small Cell Lung Cancer

Five-year survival in metastatic non-small cell lung cancer patients treated with chemotherapy alone or chemotherapy with melatonin: a randomized trial.

Numerous experimental data have documented the oncostatic properties of melatonin (MLT). In addition to its potential to direct antitumor activity, melatonin has proved to modulate the effects of cancer chemotherapy by enhancing its therapeutic efficacy and reducing its toxicity. The mechanisms responsible for this include its ability to prevent chemotherapy-induced lymphocyte damage as well as its antioxidant effect, which has been proved to amplify cytotoxic actions of the chemotherapeutic agents against cancer cells. The present study was done to assess the five year survival in metastatic non-small cell lung cancer patients. The study included 100 consecutive patients who were randomized to receive chemotherapy alone or chemotherapy plus 20 mg/day orally in the evening of MLT. Both the overall tumor regression rate and the five year survival ($p<0.001$) were significantly higher in patients concomitantly treated with MLT. In particular, no patient treated only with chemotherapy was alive after two years, whereas a five year survival was achieved in 3/49 (6%) of patients in the MLT group. As far as the toxicity of treatment was concerned, chemotherapy was better tolerated in the MLT group with regards to neurotoxicity (2/49 versus 9/51, $p<0.01$), thrombocytopenia (1/49 vs. 7/51, $p <0.01$), weight loss greater than 10% (3/49 vs. 21/51, $p< 0.001$), and asthenia (4/49 vs. 21/51, $p<0.005$).
–Lissoni P, Chilelli S, Villa S et al: *J Pineal Res,* 2003; 35: 12-15.

Melatonin/Solid Tumour Cancers

A randomized study with subcutaneous low-dose interleukin 2 alone vs. interleukin 2 plus the pineal neurohormone melatonin in advanced solid neoplasms other than renal cancer and melanoma.

The pineal hormone melatonin (MLT) has been shown to cause tumour regression in neoplasms that are generally non-responsive to IL-2 alone. Eighty patients with locally advanced or metastatic solid tumors were randomized to be treated with IL-2 alone or IL-2 plus 40 mg/day of MLT. A complete response was obtained in 3/41 patients treated with IL-2 plus MLT, but in none of the patients receiving IL-2 alone. A partial response was achieved in 8/41 patients treated with IL-2 plus MLT, and only 1/39 treated with IL-2 alone. Tumour objective regression rate was significantly higher in patients treated with IL-2 and MLT than in those receiving IL-2 alone (11/41 vs. 1/39, $p<0.001$). The survival at one year was significantly higher in patients receiving MLT (19/41 vs. 6/39, $p<0.05$), as was the mean increase in lymphocyte and eosinophil number. The treatment was well tolerated in both groups. This study shows that concomitant administration of MLT may increase the efficacy of low-dose IL-2 subcutaneous therapy.
–Lissoni P, Barni G, Tancini A, Ardizzoia A, et al. *Br J Cancer,* 1994; 69: 196-99.

Melatonin/Colorectal Cancer

Biomodulation of cancer chemotherapy for metastatic colorectal cancer: a randomized study of weekly low-dose irinotecan alone vs. irinotecan plus the oncostatic pineal

hormone melatonin in metastatic colorectal cancer patients.

The pineal hormone melatonin (MLT) has been proven to exert an effect on various chemotherapeutic drugs (cisplatin, anthracyclinces, 5-flouricil). This study assesses its possible influence on irinotecan (CPT-11) in the treatment of colon cancer. The study included 30 metastatic colorectal cancer patients progressing after at least one previous chemotherapeutic line containing 5-flouricil, who were randomized to be treated with CPT-11 alone or CPT-11 plus MLT (20 mg/day). No complete response was observed. A partial response was achieved in 2/16 patients treated with CPT-11 alone, and in 5/14 patients concomitantly treated with CPT-11 plus MLT. Stable disease was achieved in 5/16 patients treated with CPT-11 alone, and in 7/14 patients treated with CPT-11 and MLT. The percent of disease control achieved in patients concomitantly treated with MLT was significantly higher than those treated with chemotherapy alone (12/14 vs. 7/16, $p< 0.05$).

–Cerea G, Vaghi M, Ardizzioia A, et al. *Anticancer Res,* 2003 Mar-Apr; 23(2C): 1951-4.

5-MTT/Anemia/Metastatic Lung Cancer

Reduction of cisplatin-induced anemia by the pineal indole 5-methoxtryptamine in metastatic lung cancer patients.

The present study was performed to evaluate the pineal indole 5-methoxy-tryptamine (5-MTT) on red cell line and hemoglobin production. Twenty lung cancer patients treated with cisplatin and etoposide were randomized to receive either chemotherapy alone or chemotherapy plus 1 mg of 5-MTT/day. Hemoglobin significantly decreased in both groups of patients. However, the decrease in hemoglobin levels observed in patients treated with chemotherapy alone was significantly greater than that observed in patients concomitantly treated with 5-MTT. Moreover, the percent of patients who had no progressive disease on treatment was significantly higher in the 5-MTT group. Even though the low number of patients does not permit definite conclusions, these preliminary results suggest that the concomitant administration of 5-MTT may reduce cisplatin-induced anemia in cancer patients while enhancing the cytotoxicity of cancer chemotherapy.

–Lissoni P, Malugani F, et al: *Neuroendocrinol Lett,* 2003 Feb-Apr; 24(1-2): 83-5.

Melatonin/Non-small Cell Lung Cancer

A randomized study of chemotherapy with cisplatin and etopisode versus chemoendocrine therapy with cisplatin, etoposide and the pineal hormone melatonin as a first-line treatment of advanced non-small cell lung cancer patients.

Seventy advanced non-small cell lung cancer patients were randomized to receive chemotherapy (cisplatin and etoposide) alone or chemotherapy plus melatonin (20 mg/day orally). The tumour response rate was higher in the patients receiving melatonin (11/34 vs. 6/35). The percent of one-year survival was more than double in patients treated with melatonin (15/34 vs. 7/36, $p<0.05$). In addition, patients in the treatment group experienced less chemotherapy-induced toxicity.

–Lissoni P et al. *Journal of Pineal Research,* 1997; 23 (1): 15-19.

Melatonin/Solid Tumour Cancers

Treatment of cancer chemotherapy-induced toxicity with the pineal hormone melatonin.

This study involved 80 patients with metastatic solid tumours (lung, breast and gastro-intestinal) in poor clinical condition. Patients were randomized to receive chemotherapy alone or chemotherapy plus melatonin (20 mg/day). Thrombocytopenia, malaise and asthenia were significantly less frequent in the melatonin group. Stomatitis and neuropathy were also less frequent in the treatment group, although not statistically significant.

–Lissoni P et al. *Supportive Care in Cancer,* 1997; 5 (2): 126-9.

Melatonin/Glioblastoma

Increased survival time in brain glioblastomas with use of a radioneuroendocrine strategy with radiotherapy plus melatonin compared to radiotherapy alone.

Brain tumour biology has suggested that brain tumour growth is partly mediated by neuroendocrine factors, primarily opiod peptides and pineal substances. On this basis, 30 patients with glioblastoma were randomized to receive either radiotherapy alone or radiotherapy plus 20 mg/day orally of melatonin (MLT) until disease progression. The percent survival at one year was significantly higher in the patients treated with radiotherapy plus MLT than those receiving radiotherapy alone (6/14 vs. 1/16, $p<0.02$). The survival curve observed in the MLT group was significantly longer than that seen in patients treated with radiotherapy alone ($p<0.05$). Moreover, radiotherapy or steroid-related toxicities were lower in patients concomitantly treated with MLT. This study suggests that radiotherapy plus the pineal hormone MLT may prolong the survival time and improve the quality of life of patients affected by glioblastoma.

–Lissoni P, Meregalli S, Nosetto L et al. *Oncology,* 1996: 53: 43-46.

Multiple Antioxidants

Multiple Antioxidants/non-small Cell Lung Cancer

The role of vitamins along with chemotherapy in non-small cell lung cancer.

Sixty-five patients with squamous cell carcinomas were randomized to be treated with paclitaxel and carboplatin alone or with multiple antioxidant vitamins. The multiple vitamin regime was beta carotene 60 mg/day, vitamin E (α-tocopherol) 1025 mg/day and ascorbic acid 6100 mg/day. The overall response rate was higher in the treatment arm and survival at one year was 54% in the treatment group compared to and 33% in the control group. Although there was a trend towards increased survival in the multipole antioxidant treated group, the difference was not statistically significant possibly due to the small number of patients in this study.

–Puthak AK, Singh N, Guleria R et al. Presented at the *International Conference on Nutrition and Cancer,* October 3-5, 2002; Montevideo, Uruguay.

Multiple Antioxidants/Breast Cancer

Nutritional and high dose antioxidant interventions during radiation therapy for cancer of the breast.

Forty-eight patients with stage 0-lll breast cancer were randomized prior to initiating radiation therapy (RT) to receive high-dose antioxidant vitamins and follow a 10% fat diet during their treatment or the control arm (no special diet or vitamins). Patients were followed for a minimum of 14 months post-RT. All patients were matched for age, stage, T-stage, receptor positivity, chemotherapy, hormonal therapy and surgery. Local recurrence, skin reaction, vitamin levels, quality of life and cholesterol levels were measured at six months and one year for both groups. There were no statistical differences between the groups in terms of skin reaction, quality of life. One patient in the control group developed a new cancer in the opposite breast. There was a significant improvement in the cholesterol levels of the control group before and after treatment ($p=0.0106$). Compliance in the treatment group was high (93%). The addition of high dose antioxidant vitamins during RT for breast cancer has no increased risk for local recurrence or new cancers one year after treatment.

–Walker E, Ross D, Pegg J, et al. Presented at the *International Conference on Nutrition and Cancer,* October 3-5, 2002; Montevideo Uruguay.