According to a report in the *British Journal of Cancer* (2002;86:1854-1857), replacing the body’s pool of carnitine might help reduce fatigue in some patients receiving chemotherapy.

“Fatigue is a very common side effect of chemotherapy and radiation therapy,” said Terri Ades, RN, MS, AOCN, Director of Quality of Life and Health Promotion Strategy for the American Cancer Society. “Different treatments are needed for the different causes of fatigue,” Ades said. “Since the exact cause is not always known, more research is needed to help us better understand fatigue and how best to treat it.”

Previous studies have found chemotherapy regimens that include either ifosfamide or cisplatin sometimes deplete pools of carnitine, a metabolite produced in the liver and kidneys and stored in skeletal muscle, where it is used as an energy source. These two drugs may disrupt the normal production of carnitine and increase the amount released in urine.

“After chemotherapy, many patients have low levels of carnitine in their blood and we think that’s one of the reasons they feel so exhausted,” said first author Francesco Graziano, MD, of the Medical Oncology Unit at Urbino Hospital in Urbino, Italy. “It seemed logical that boosting carnitine levels with a dietary supplement might restore that lost energy.”

Graziano and colleagues studied the effect of levocarnitine (LC) as a dietary supplement using four grams per day for one week in 50 patients with either lung, gastric, ovarian, or pancreatic cancer. Patients with low carnitine levels, who felt fatigued during chemotherapy with either ifosfamide or cisplatin, were eligible to participate. Those with other conditions that could cause fatigue, such as anemia, were excluded.

On average, the patients’ blood carnitine levels rose 50 percent and returned to within the normal range in all patients. Scores on the Functional Assessment of Cancer Therapy-Fatigue scale improved for 45 patients, remained stable in three, and worsened in two. The most common benefit cited among the 45 patients was increased strength in their legs. Hemoglobin levels did not change significantly during that period of time. Also, the LC supplements had no apparent negative impact on the effectiveness of the chemotherapy.

“Carnitine is widely available as a dietary supplement in pharmacies and health food stores, and is often used by those without health problems to boost...
athletic performance or lose weight,” said Andrew Vickers, PhD, of the Integrative Medicine Service at Memorial Sloan-Kettering Cancer Center. “Though the balance of evidence is that if you are healthy, carnitine cannot make you more so, there are increasing data from randomized trials suggesting that carnitine can be of benefit to patients with poor physical function due to serious illness such as intermittent claudication, congestive heart failure, or diabetes.”

Ades warned, even though these results may be promising; “Because this is a very early study, there are still many questions to be addressed with more research before a recommendation can be made about the use of carnitine as a treatment for fatigue.” The authors agreed that their “…data should be looked at with caution due to potential biases and limitations inherent to the study itself…despite its limitations, the findings of this study are intriguing and open new perspectives for future clinical trials.”

**PC-SPES STORY NOT OVER YET**

Until recently, PC-SPES was a popular over-the-counter herbal preparation used by many men with prostate cancer. Men reported it helped them feel better, and clinical studies demonstrated PSA (prostate-specific antigen) responses and even some responses measurable by imaging studies. But then several lots of PC-SPES capsules were found to contain DES, which might account for its clinical activity. PC-SPES was removed from the market, and the future of this controversial herbal product appeared bleak indeed.

Now in a report from *Cancer Research* (2002;62:3920-3924), Michael Bonham and colleagues from the Fred Hutchinson Cancer Research Center and the University of Washington in Seattle have shown that PC-SPES alone may be active against prostate cancer, and that its herbs act by mechanisms that differ from those of DES.

Using cDNA microarrays, Bonham looked at the effects of PC-SPES (carefully checked and found to be free of DES) on expression of more than 3,000 genes in prostate cancer cell cultures. The same methods were also used to determine the effects of DES on gene expression.

PC-SPES increased the activity of 144 genes, and decreased the activity of 175 other genes. Many of these genes are thought to have a part in the growth and regulation of prostate cancer cells. The researchers found that, for the most part, PC-SPES and DES acted on different prostate cancer-related genes.

David Rosenthal, MD, Professor of Medicine at Harvard Medical School and Medical Director of the Zakin Center for Integrative Therapies at the Dana-Farber Cancer Institute in Boston was encouraged by the results of this study. “There is something different and valuable here,” said Rosenthal, who is also Chair of the American Cancer Society’s Alternative and Complementary Methods of Cancer Management Advisory Group.

The example of PC-SPES illustrates the need for proper manufacturing and testing of herbal products, said Rosenthal. “We didn’t study this the right way at the beginning. We should have studied it first, then done the clinical trials. We have learned something from PC-SPES.”

Peter Nelson, MD, a medical oncologist at the Fred Hutchinson Cancer Research Center and co-author of the report, said that he was first interested in PC-SPES when he became aware that many of his prostate cancer patients were taking the herbal supplement. Now he believes there may be something in PC-SPES that is unique to the compound and works against prostate cancer. “There is really something in that mixture that has activity against prostate cancer,” said Nelson.
ST. JOHN’S WORT INTERFERES WITH IRINOTECAN

St. John’s Wort is an herb commonly used around the world as a treatment for depression. Just because it is “natural” doesn’t mean it doesn’t have risks when it comes to treating cancer patients, according to an article and editorial in the August 21 issue of the Journal of the National Cancer Institute (2002;94:1247-1249;1187-1188).

The research, conducted in the Netherlands, was based on previous observations that St. John’s Wort increases levels of enzymes that can cause certain drugs to be processed more quickly than normal, weakening their effect.

Because irinotecan is processed through one of these enzyme systems, R. H. J. Mathijssen and his colleagues from the Department of Medical Oncology at the Daniel den Hoed Cancer Center in Rotterdam examined blood levels of irinotecan in patients who received this chemotherapy drug either with or without previous treatment with St. John’s Wort.

When the patients were given St. John’s Wort, the amount of irinotecan in the blood was decreased by 42 percent. The researchers also found that the reduction in the drug levels was greater the longer the patients had been taking St. John’s Wort. “Overall, our findings suggest that irinotecan metabolism and toxicity are altered by St. John’s Wort, and that the two agents cannot be given safely in combination without compromising overall antitumor activity,” wrote the authors.

They concluded that “until specific dosing guidelines are available, it is strongly recommended that patients receiving chemotherapeutic treatments with such agents refrain from taking St. John’s Wort.”

In an editorial that accompanied the article, Patrick J. Mansky, MD, and Stephen E. Straus, MD, from the National Center for Complementary and Alternative Medicine at the National Institutes of Health in Bethesda, MD, echoed the concerns of the study’s authors. “That herbal medicines may have adverse pharmacologic properties has come as a surprise to those who assumed that natural products must be safe,” wrote Mansky and Straus. They noted that cancer patients and their doctors must be aware that no matter how helpful some herbal treatments may appear, they are not all safe.

Major cancer centers, such as Memorial Sloan-Kettering Cancer Center (MSKCC) in New York, have been aware of the problems with herbal treatments for some time. Barrie Cassileth, PhD, who is the Chief of MSKCC’s Integrative Medicine Service and a member of the American Cancer Society’s Alternative and Complementary Methods of Cancer Management Advisory Group, said the message is clear. “We have to be careful about taking botanicals with radiation therapy, surgery, and chemotherapy,” said Cassileth. “At Memorial, we tell our patients to stop all herbal remedies during and for two weeks before treatment.”

Cassileth stressed the importance of doctors, nurses, and other health care workers telling patients about the need to stop herbal remedies before receiving treatments or undergoing surgery. “We tell patients to stop aspirin and vitamin E. We should also tell them to stop herbal remedies,” she said. What’s important to remember, concluded Cassileth, is that these recommendations are not the result of a bias against herbal remedies. This is a crucial issue, and the recommendations we make are based on hard data,” she said. “Herbs can be helpful, but they can also be very harmful.”

EFFORTS TO STOP TEEN SMOKING ARE PAYING OFF

Newly-released data, reported in the July 17 Morbidity and Mortality Weekly Report (2002;51:409-412), indicated smoking among high school students peaked in the late 1990s, and is now declining. The data are from the Youth Risk Behavior Survey, a biennial Centers for Disease Control and Prevention (CDC) survey
of the prevalence of health risk behaviors among high school students.

The CDC report shows that the percentage of these students who have ever tried tobacco was stable throughout much of the 1990s, then fell from 70.4 percent in 1999 to about 63.9 percent in 2001.

The percentage of high school students who smoked on one or more days in the 30 days before the survey dropped from 36.4 percent in 1997 to 28.5 percent in 2001. In 1999, 16.8 percent of high school students described themselves as frequent smokers (smoking on 20 out of the 30 days before the survey), but that fell to 13.8 percent in 2001.

“When the tobacco companies lost the lawsuit that made them pay for the disease tobacco has caused, they passed the costs of their legal problems onto smokers, raising the cost of cigarettes out of the reach of many young people,” said Ron Todd, MSEd, Director of Tobacco Control for the American Cancer Society. And some states have raised tobacco taxes in recent years, said Todd.

Some states have used the money they got from the tobacco settlement to expand programs to educate young people on the dangers of tobacco and to prevent their using it, said Todd, and that has also helped.

**QUITTING SMOKING ADDS YEARS TO YOUR LIFE, REGARDLESS OF AGE**

People who stop smoking can live a lot longer, regardless of the age at which they quit, according to a report in the *American Journal of Public Health* (2002;92:990-996). The study found that younger people benefit the most, but even those who are 65 can add years to their life by quitting.

“What's unique about this study is that it gives some hope even to 65-year-olds who smoke,” said Donald Taylor Jr., PhD, at Duke University in Durham, NC. “A man would add between 1.4 and 2 years to his life. That's a tangible benefit you can get even late in life from stopping smoking.”

According to the study, women who were 65 years old added between 2.7 and 3.7 years to their lives when they quit compared with continuing smokers. But the greatest benefits were seen by the youngest people in the study. Male smokers who quit at age 35 could expect to live between 6.9 and 8.5 years longer than continuing smokers. The benefit for 35-year-old women was between 6.1 and 7.7 years.

**Largest Study of Its Kind**

In order to calculate the benefits of quitting, researchers from Duke University and the American Cancer Society analyzed data from 877,243 respondents in the ACS Cancer Prevention Study II, an ongoing prospective mortality study begun in 1982. They compared data on smokers, former smokers, and those who had never smoked. The national scope and large sample size of the Cancer Prevention Study II permitted use of modeling techniques that could estimate the benefits of cessation more accurately than had been done before.

“With 47 million smokers in the United States, the message that it’s never too late to quit is an important one,” said Michael Thun, MD, ACS Vice President for Epidemiology and Surveillance Research. “Quitting is the only proven approach by which a smoker can avoid much of the increased risk of lung and other cancers, heart disease, stroke, chronic obstructive lung disease, and other disorders caused by smoking. The benefits of quitting smoking are much larger than the benefits from treating these diseases, once they occur.

“Quitting is difficult, but it is possible. For most smokers, tobacco dependence is comparable in severity to the dependence caused by opiates, amphetamines, or cocaine. Research clearly shows that clinicians can help their patients quit, but these counseling and pharmacological interventions are, unfortunately, underutilized.”