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EXERCISE & NUTRITION during/after* **CANCER**

CURRENT PEER-REVIEWED MEDICAL LITERATURE and EXPERT COMMENTARY
from **RELIABLE SOURCES** and **DR. BLEYER**

*Studies on cancer prevention are included if they have special relevance to cancer survivors

November 2009

The 12 months of 2008 *E&N News* are now available as a **year summary** for downloading, either for exercise or nutrition (with each including reports on the combination of exercise and nutrition) at www.defeatcancer.info. Both versions include executive summaries and are indexed and bookmarked.

E&N News is now listed as **one of 7 resources recommended by MD Anderson Cancer Center** in the *Complementary Therapies, General* category and endorsed by the Cancer Patient Education Network of the National Cancer Institute. The MD Anderson Cancer *Complementary/Integrative Medicine Educational Resources* resource (www.mdanderson.org/departments/CIMER) is rated #1.

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DIET | EXERCISE | FAMILY | EDUCATION | ATTITUDE | THRIVING

▶ **Exercise and Nutrition**

Obesity causes 100,000 US cancer cases, group says [Prevention]

[The latest estimates from research linking diet, physical activity and fatness indicate that from 9% to 49% of common cancers could be prevented if Americans stayed slender](#)

Reuters - Nov 5, 2009

Reporting by Maggie Fox; Editing by Alan Elsner

WASHINGTON (Reuters) – Obesity causes more than 100,000 cases of cancer in the United States each year -- and the number will likely rise as Americans get fatter, researchers said on Thursday.

Having too much body fat causes nearly half the cases of endometrial cancer -- a type of cancer of the uterus -- and a third of esophageal cancer cases, the **American Institute for Cancer Research** said.

Cancer is the second-leading cause of death in the United States after heart disease. The American Cancer Society projects that 1.47 million people will be diagnosed with cancer this year and 562,000 will die of it.

More than 26 percent of Americans are obese, defined as having a body mass index of 30 or higher. BMI is equal to weight in kilograms divided by height in meters squared. A person 5 feet 5 inches tall becomes obese at 180 pounds (82 kg).

Additionally, nearly a third of Americans are overweight, defined as having a BMI of 25 to 30.

The study combined findings from AICR research linking diet, physical activity and fatness with cancer risk with national surveys on obesity and cancer incidence.

"We then worked out the percentage of those specific cancers that would be prevented if everyone in the United States maintained a healthy weight," the group said in a statement.

Here are some of its estimates of cancer types that could be prevented annually if Americans stayed slender:

* **Esophageal - 35 percent of cases or 5,800 people**

* **Pancreatic - 28 percent or 11,900**

* **Gallbladder - 21 percent or 2,000**

* **Colon - 9 percent or 13,200**

* **Breast - 17 percent or 33,000**

* **Endometrium - 49 percent or 20,700**

* **Kidney - 24 percent or 13,900**

In July, federal and other researchers estimated that obesity-related diseases account for nearly 10 percent of all medical spending in the United States or an estimated \$147 billion a year.

Dr. Bleyer:

The numbers continue to increase, with obesity-related breast and uterus cancer accounting for more than half of the cases (53,700 or 100,000)

As indicted in the report, this problem will only get worse before it can get better

Staying ahead of the curve

[The Bulletin health reporter interviewed three experts on physical fitness as a function of age and how older adults can regain physical fitness](#)

By Markian Hawryluk / The Bulletin / November 12, 2009

You're approaching age 45. You have a healthy body mass index. But are you more likely to sit on the couch and watch TV or are you going for a run, riding your bike and generally staying active? The answer may make a difference in the future.

When it comes to fitness and athletics, even the most hardened enthusiasts realize at some point they're over the hill. Who knew the hill begins to crest by age 45?

A new study published last month in the Archives of Internal Medicine found that cardiovascular fitness in both men and women begins to decline sometime in the fifth decade of life and that the drop speeds up as you get older.

Experts disagree on whether that means the rate of decline is inevitable or whether a commitment to physical fitness can flatten out the curve. But there is widespread agreement that what you do now will have a profound effect on your fitness and your health in the latter decades of life.

Many researchers believed that the decline in fitness levels pretty much followed a straight line, that individuals lost a standard amount of cardiovascular fitness every year. But **Dr. Andrew Jackson, an exercise physiology professor** at the **University of Houston**, said that notion came mainly from cross-sectional studies. Those types of studies tested athletes at different ages at one point in time, then compared fitness levels.

“If you use longitudinal data, people who have been measured several times, then what you're getting is a better measure of change within the individual,” Jackson said.

Jackson and his colleagues examined data from the Aerobics Center Longitudinal Study that tested the fitness levels of more than 20,000 men and women between two and 23 times over the course of 32 years.

They calculated results from the treadmill tests in metabolic equivalents, or METs, a measure of how much oxygen the body is using or how much energy the body is expending. One MET represents the amount of energy used when a person is at rest.

At age 40, the men in the test averaged just over 12.6 METs. (METs convert to VO2 Max, another common measure of aerobic capacity, by multiplying by 3.5. So 12.6 METs is equivalent to a VO2 Max of 44.)

Between the ages of 40 and 50 the average MET for men dropped by a half point; between ages 50 and 60 it dropped by a full point; and between 60 and 70 it dropped by two points. Women had a less steep decline but started at a lower level, about 10.6 METs.

“Essentially after about age 40 to 45, you start to lose your aerobic capacity, and that accelerates over time,” Jackson said.

“If they are, like a lot of people in Oregon, active lean people, their aerobic capacity at 45 is going to be considerably higher than somebody who isn't, and if they continue that lifestyle, they're going to in the same sense go down, but they'll maintain that difference,” Jackson said. “This is one reason why you can have 70- or 80-year-old men running marathons. They've been doing it all their lives, and they've got the aerobic capacity of maybe somebody that's 50.”

In other words, **the higher your fitness level, the more you have to lose and the longer you can stave off the consequences of a low level of fitness.**

Previous research has established that **once men fall below a fitness level of 8 METs and women below 7 METs, their risk of health problems — including hypertension, diabetes, heart disease, cancer and death — increase.** And it's less likely they'll be able to live independently.

The Social Security Administration, for example, uses a VO2 Max of 18, or just over 5 METs, as the standard for disability.

“We're talking about the ability to carry on an active life,” Jackson said. “They would have trouble with daily life, climbing up stairs, walking and so on.”

Peak performance

Although the study group involved a higher percentage of active people than the general population, it did include many sedentary people. Other research has shown that active individuals may be able to maintain a high level of fitness longer.

“There are these small measurable declines that happen. There are real physiologic changes that happen with aging,” said **Dr. Vonda Wright**, a professor of orthopedics at the **University of Pittsburgh**. “They don't always translate into athletic performance.”

Wright studied results from the 2001 National Senior Olympic Games, comparing the winning times for different age groups. She found that the senior athletes showed an average 3.4 percent decline per year from age 50 to 85. Men showed the same decline in both sprint and endurance events, while women showed a greater decline in sprint than in endurance events. Results dropped slowly from age 50 to 75, then there was a marked drop-off in performance after age 75.

“So what that means is the 50-year-old runs his mile in 4:34 and the 70-year-old runs his mile in 7 minutes. That's faster than many couch potato 30-year-olds,” Wright said.

Eventually, the cumulative effect of wear and tear on the body takes its toll, she said. Cardiovascular capacity drops off, muscles tighten and lose flexibility, affecting stride length, and other effects of aging take over.

The drop-off in fitness levels even among elite athletes is evident locally with the record times for the **Pilot Butte Challenge**. The race held annually in September times runners up the 1.2-mile route to the top of the 490-foot butte in Bend.

The record time for men, 7:10, was set by Lars Flora at age 31. Results for each age group after 45 get progressively slower. For women, results are more varied in the younger age groups but show the same progressive decline in times past age 45.

But the record times, which are posted at the start of the Pilot Butte trail, show that new records for various age groups are set each year. Of the 17 age groups, the record time was set in the past three years for eight of the men's groups and 10 of the women's groups. There is even a record time for the 90 and older age group for men, set by Bill Lauderback at 18:17. While historical results aren't posted, it's likely that some of the current age group record times are faster than previous records for younger age groups.

It's a trend that's evident throughout the world.

"The older athlete is redefining what normal aging is and what's possible for people who are middle age or older," said **Dr. Michael Joyner**, an anesthesiologist with the **Mayo Clinic** in Rochester, Minn.

Joyner said athletes of all ages continue to improve record times because of better training methods, equipment and medical care.

"Your VO2 Max typically starts to decline in your 30s, but a highly trained athlete can delay that decline until they are in their later 30s or even early 40s," Joyner said. "An average sedentary person loses about 10 percent per decade starting at about age 30, but for someone who is able to continue to train very hard into their 40s or 50s, they only lose about half that much, primarily due to the fact they continue to train hard."

Wright, who authored the book "Fitness After 40," said **older adults can keep fitness levels high, but they have to change the way they exercise.**

"People continue to try to train like they're 20 years old," she said. "The runners just go out and run. They don't do anything else. But that's not good for a 40-year-old body."

She recommends that men and women after age 40 adopt a program that includes stretching, aerobics, resistance training and balance work.

- **Stretching:** "Aging muscles and tendons get tighter and tighter every day you don't stretch," she said. "What that does is decreases your stride length, it decreases your range of motion, it causes back pain, and it throws your biomechanics off." She suggests a slow, 30-second stretch of every major muscle group in the body. While that sounds ominous, she said, it can be done fairly quickly.
- **Aerobics:** Most older athletes focus on aerobic work, but Wright said sometimes they overdo it. "It makes no sense to be intense every single day because you don't give your body time to recover, and our recovery capacity is slower as we age," she said.
- **Resistance training:** Wright doesn't talk about weight lifting as much because she believes functional resistance training has more real-life benefit. "When we're running and doing athletics, we don't sit on a chair, and haul weight around," she said. "I like weight lifting to be done through a functional range of motion, using a variety of different resistance methods: bands, kettlebells, medicine balls. And there is room for iron weight, but not how we've always envisioned these things."
- **Balance:** At age 20, our balance starts to decline, Wright said. Any sort of balance training can help you maintain function longer. "Balance and equilibrium are totally retrainable," she said. "You just have to do it every day."

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Dr. Bleyer:

- ☑ Although this article by a *The Bulletin* health reporter does not address cancer specifically, it has direct relevance to cancer patients and survivors, to say nothing about its applicability to Central Oregon as mentioned by the interviewees and reference to the Pilot Butte Challenge
- ☑ Since more than 90% of cancer patients are older than 40 years when diagnosed, the recommendations for how to exercise and become fit after age 40 are particularly relevant since, as the Professor of Orthopedics, a female by the way, points out, what works for the younger adult doesn't work for the over-40 body
- ☑ Stretching, aerobics, resistance training and balance work are for older adults and it's good to know that balance and equilibrium can be relearned at an older age if these attributes had been lost prior to a diagnosis of cancer

► Exercise

Randomized controlled trial of the effects of aerobic exercise on physical functioning and quality of life in lymphoma patients

A new randomized clinical trial shows that patients with lymphoma receiving aerobic exercise training, compared with patients receiving usual care only, also benefit in physical function and quality of life, including striking improvement in fatigue, happiness, depression, general health, cardiovascular fitness, and lean body mass

Kerry S. Courneya, Christopher M. Sellar, Clare Stevinson, Margaret L. McNeely, Carolyn J. Peddle, Christine M. Friedenreich, Keith Tankel, Sanraj Basi, Neil Chua, Alex Mazurek, Tony Reiman

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Purpose Lymphoma patients commonly experience declines in physical functioning and quality of life (QoL) that may be reversed with exercise training.

Patients and Methods We conducted a randomized controlled trial in Edmonton, Alberta, Canada, between 2005 and 2008 that stratified **122 lymphoma patients** by major disease type and current treatment status and **randomly assigned them to usual care (UC; n = 62) or 12 weeks of supervised aerobic exercise training (AET; n = 60)**. Our primary end point was patient-rated physical functioning assessed by the Trial Outcome Index-Anemia.

Secondary end points were overall QoL, psychosocial functioning, cardiovascular fitness, and body composition.

Results Follow-up assessment for our primary end point was 96% (117 of 122) at postintervention and 90% (110 of 122) at 6-month follow-up. Median adherence to the supervised exercise program was 92%. At postintervention, **AET was superior to UC for patient-rated physical functioning (mean group difference, +9.0; 95% CI, 2.0 to 16.0; P = .012), overall QoL (P = .021), fatigue (P = .013), happiness (P = .004), depression (P = .005), general health (P < .001), cardiovascular fitness (P < .001), and lean body mass (P = .008)**. Change in peak cardiovascular fitness mediated the change in patient-rated physical functioning. **AET did not interfere with chemotherapy completion rate or treatment response. At 6-month follow-up, AET was still borderline or significantly superior to UC for overall QoL (P = .054), happiness (P = .034), and depression (P = .009) without an increased risk of disease recurrence/progression.**

Conclusion AET significantly improved important patient-rated outcomes and objective physical functioning in lymphoma patients without interfering with medical treatments or response. Exercise training to improve cardiovascular fitness should be considered in the management of lymphoma patients.

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Dr. Bleyer:

- ☑ With only 60 patients in the exercise regimen and 62 in the control group, the relative improvement in general health, happiness, depression, cardiovascular fitness, and lean body mass each were dramatic, with a less than one in 200 chance the benefit was not due to exercise
- ☑ This dramatic effect was accomplished within 3 months, whether or not the patient was on chemotherapy
- ☑ The beneficial effect lasted at least 6 months after the completion of the exercise regimen, especially for happiness and lack of depression
- ☑ This is a landmark study that extends previously demonstrated benefits of exercise in patients with other types of cancer to those with lymphoma, which when treated with chemotherapy usually requires aggressive, toxic and mainly intravenous, treatment

Moderator effects in a randomized controlled trial of exercise training in lymphoma patients

The authors of the above cited study report what characteristics of patients influenced how much they benefited from an exercise regimen, finding that those in poor health and physical shape or with the more advanced cancer had the greatest benefit

Courneya KS, Sellar CM, Stevinson C, et al

University of Alberta; Cross Cancer Institute, Edmonton, Alberta, Canada; Alberta Cancer Board, Calgary, Alberta, Canada; and Manchester University, Manchester, United Kingdom
Cancer Epidemiol Biomarkers Prev 2009;18(10):2600–7

Background: The Healthy Exercise for Lymphoma Patients trial showed that aerobic exercise training improved important health outcomes in lymphoma patients. Here, we examine potential moderators of the exercise training response.

Methods: Lymphoma patients were stratified by major disease type and current treatment status and randomly assigned to usual care (n = 62) or aerobic exercise training (n = 60) for 12 weeks. Endpoints were quality of life, cardiovascular fitness, and body composition. Moderators were patient preference for group assignment, age, sex, marital status, disease stage, body mass index, and general health.

Results: Patient preference did not statistically moderate the effects of exercise training on quality of life (P for interaction = 0.36), but the interaction effect of 7.8 points favoring patients with no preference was clinically meaningful. Marital status (P for interaction = 0.083), general health (P for interaction = 0.012), and body mass index (P for interaction = 0.010) moderated the effects of aerobic exercise training on quality of life with **better outcomes for unmarried versus married patients, patients in poor/fair health versus good-to-excellent health, and normal weight/obese versus overweight patients.** Disease stage (P for interaction = 0.056) and general health (P for interaction = 0.012) moderated the effects of aerobic exercise training on body composition with **better outcomes for patients with advanced disease versus early disease/no disease and patients in good health versus very good-to-excellent health.** No variables moderated intervention effects on cardiovascular fitness. Findings were not explained by differences in adherence.

Conclusions: Clinically available variables predicted quality of life and body composition responses to aerobic exercise training in lymphoma patients. If replicated, these results may inform future randomized trials and clinical practice.

Dr. Bleyer:

- ☑ That those in the worst shape had the most benefit has to be encouraging to this group
- ☑ The corollary conclusion to the finding that those most in need had the greatest benefit is that those in the best shape (with the least need) already had benefited from the exercise and nutrition they had maintained before cancer
- ☑ That being unmarried also identified a group with the most benefit is hard to explain; it may mean that being married is more likely to have kept the patient/survivor on a better nutrition and exercise regimen before cancer
- ☑ Either way, **DEFEATcancer** submits that nutrition is undoubtedly also a modifying factor that the investigators did not study (and should)

For lymphoma patients, vigorous exercise found safe, effective during chemotherapy

[Further commentary, including an interview of the primary author, on the afore-cited report that shows aerobic exercise training benefits patients with lymphoma](#)

By Carlson, Robert H.

Oncology Times: 25 November 2009 - Volume 31 - Issue 22 - pp 60-62;
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Numerous studies have shown that vigorous exercise benefits cancer patients, both physically and psychologically.

A new randomized clinical trial shows now that this is also true in patients with lymphoma receiving aerobic exercise training, compared with patients receiving usual care only.

What makes this study unusual is that patients in the intervention group benefited equally whether or not they were undergoing chemotherapy at the time of exercise.

The entire exercise group showed an approximate 20% improvement in measurements of physical functioning as well as in quality of life.

The trial, published in the September 20 issue of the Journal of Clinical Oncology (2009;27:4605-4612), was conducted at the University of Alberta between 2005 and 2008 and led by Kerry S. Courneya, PhD, Professor and the Canada Research Chair in Physical Activity and Cancer there.



Kerry S. Courneya, PhD

In addition to the changes patients noticed in quality of life and fatigue, we were also able to show it was the changes in their objective fitness parameters that really mediated or predicted how much better they felt from the exercise intervention. The fitter they felt, the less fatigue they reported

Lymphoma patients from the Cross Cancer Center in Edmonton were randomly assigned to usual care (62 patients) or aerobic exercise training (60 patients). The primary endpoint was patient-rated physical functioning assessed by the Trial Outcome Index-Anemia. Secondary endpoints were overall quality of life, psychosocial functioning, cardiovascular fitness, and body composition.

The authors said that to the best of their knowledge this is the first randomized controlled trial assessing exercise in lymphoma patients.

After 12 weeks of aerobic exercise training on a recumbent or upright cycle ergometer three times a week supervised by an exercise physiologist, there was a 20% improvement in peak oxygen consumption, as well as patient-reported improvements in physical functioning, happiness, and general health, and relief of depression and lymphoma symptoms.

Dr. Courneya and his colleagues credited the improvement in peak cardiovascular capacity as key to the changes in patient-rated physical functioning.

Importantly, aerobic exercise training did not interfere with chemotherapy completion rate or treatment response.

At 24 weeks of follow-up after the completion of exercise training, overall quality of life was still borderline or significantly superior for exercise versus usual care, without an increased risk of disease recurrence or progression.

The authors concluded that aerobic exercise training significantly improved important patient-rated outcomes and objective physical functioning in lymphoma patients without interfering with medical treatments or response.

Exercise training to improve cardiovascular fitness should be considered in the management of lymphoma patients, the researchers concluded.

Lymphoma Has Been Understudied in Terms of Exercise

In an interview, Dr. Courneya explained that exercise intervention studies in lymphoma are by nature different from other cancer types.

The vast majority of exercise studies have been done in early-stage breast cancer patients with good prognosis, and there are also a growing number of studies in prostate cancer relative to androgen deprivation, said Dr. Courneya, a kinesiologist. Lymphoma is understudied because of the many treatments to reduce the burden of disease and the slow progress of the disease, and there are lots of psychological and functional issues about preparing a patient to be repeatedly on and off treatment, possibly for many years.

Kinesiology studies on exercise and disease in the past have focused mainly on cardiovascular disease, diabetes, and obesity, he said. Only over the past 10 years or so have the exercise-science people become interested in the role of exercise in cancer patients and cancer survivors.

He said an improvement in fitness and increase in lean body mass, aerobic capacity, and cardiovascular fitness is a very important outcome in almost any population, and known to be a very good predictor of mortality. We did not look at mortality in this study, but our hunch is that cardiovascular fitness is a very good predictor of mortality in this population, so there is a very good possibility of survival benefits, despite existing disease and the fact that half of the patients were on therapy at the time.

Battling Fatigue

Dr. Courneya said the objective measures of physical conditioning underlie the important changes in overall functioning of patients.

In addition to the changes patients noticed in quality of life and fatigue, we were also able to show it was the changes in their objective fitness parameters that really mediated or predicted how much better they felt from the exercise intervention. The fitter they felt, the less fatigue they reported.

He called fatigue a profound and overwhelming symptom that interferes with all parts of a cancer patient's life. If you can intervene and change fatigue, you can change a lot of aspects of the patient's life. There are no drug treatments or other interventions shown to improve fatigue, but exercise has a potentially unique role to play in management of fatigue in cancer patients—that's one of the most important findings in the literature.

Dr. Courneya noted that this was a fairly sophisticated exercise program that progressed over time and used interval training. Patients exercised at 50% to 60% of their aerobic capacity, and then, for very short intervals, really hammered hard on the exercise bikes to maximum capacity.

Off Chemo vs On

The study showed no difference in the results by treatment status. In breast cancer [studies] we saw bigger exercise benefits if patients were off chemotherapy than on, and kind of expected the off-treatment group here also to have a little better exercise response than the chemotherapy group, he said. But we saw no difference—the 20% in fitness and the big gains in quality of life also happened for patients who were actually on chemotherapy at that time. That's a very exciting finding.

The study did not look at disease outcomes or the effect of exercise on the risk of relapse or mortality. That's probably the million-dollar question: What is the role of these lifestyle factors in actually managing disease and living longer? The data suggest that big improvements in fitness are a very powerful predictor of mortality in many different diseases.

We cannot say that lymphoma patients who exercise will live longer or reduce the likelihood of relapse, Dr.

Courneya continued. But even if it delayed or helped lymphoma patients prepare for the next round of treatment-

which they know is coming a year or a few years down the road, the fitter they are, the more likely they will be able to endure successive rounds of treatment and benefit from the treatment.

He noted that studies are now under way looking at weight training in lymphoma patients, which in prostate cancer patients on anti-testosterone therapy has had notable effects. Also in breast cancer patients: Those who did weight training completed more of their therapy.

And the Challenge trial just launched in Canada and Australia will study exercise training in an expected 962 colon cancer patients immediately after chemotherapy. Exercise intervention with disease outcomes is the primary endpoint.

LLS

Barton Kamen, MD, PhD, Executive Vice President and Chief Medical Officer of the Leukemia and Lymphoma Society, said that studies in leukemia and lymphoma patients are beginning to validate bigger studies in prostate, breast, and lung cancers showing that patients with a good quality of life do better through their chemotherapy.



Barton Kamen, MD, PhD, praised the study but among his caveats were that this early work needs to be revisited in five years after patients are off therapy to assess comorbidity. We know that in pediatric patients 25% to 50% of patients will have a medical issue later on, and in one third it will be significant to life-threatening. So if you stay healthy with the right attitude through the short term, do you also protect against late effects such as cardiac disease, pulmonary disease, and end organ disease?

I was pleased to see that what seems good in patients with the more common cancers who usually are not in the hospital that much also benefits patients with lymphoma. He said AML remains fairly unique in terms of the amount of time of initial hospitalization.

Dr. Kamen said some recent work is also showing that the body is capable of adapting and healing itself, as seen when exercise reduces levels of the pro-inflammatory cytokine interleukin-6 and raises levels of the anti-inflammatory IL-10.

And encouraging as much physical activity and normalcy as possible just makes sense, so I'm glad these papers are validating this, he said.

There are limitations to this paper, though, Dr. Kamen pointed out. Although more than 1,300 patients were screened, only 122 met the strict eligibility requirements.

So we don't know how biased that was, because many participants said they didn't want to do it, and a lot said they didn't have time. The researchers also excluded a lot of patients with preexisting illnesses such as high blood pressure, so that [those in the study] were not the sickest of the sick.

Dr. Kamen said he was delighted to see that lymphoma patients benefited equally from exercise therapy whether off or on chemotherapy, but he said studies in other cancers might not see this because of the wide age range in the Canadian study. Patients here were age 18 and older, he said. You're not going to have 18- or 20-year-olds in a prostate or breast cancer group.

Dr. Kamen said this early work needs to be revisited in five years after patients are off therapy to assess comorbidity.

We know that in pediatric patients 25% to 50% of patients will have a medical issue later on, and in one third it will be a significant to life-threatening issue. So if you stay healthy with the right attitude through the short term, do you also protect against late effects such as cardiac disease, pulmonary disease, and end organ disease?

No Valet?

Dr. Kerry Courneya and the rest of his Canadian team maximized patient adherence to the aerobic exercise training by incorporating behavioral support techniques, including an attractive exercise facility, telephone follow-up after missed sessions, positive reinforcement of staff, variation in exercises, and paid parking. Parking can be outrageous in a major city, he said.

Dr. Bleyer:

- ☑ The interview of the primary author underscores that the treatment team was aggressive in assuring that patients adhered to the exercise regimen, including provided free parking
- ☑ The limitations of the study are appropriately characterized by the consulting expert (Dr. Kamen) and indicate that some of the striking results were probably due to highly motivated patients who "survived" the rigorous selection criteria to be eligible to participate in the study
- ☑ Nonetheless, the randomization of the eligible subjects eliminated most of the biases, not the least of which is that the control group was equally motivated, of the same age, and had the same overall good health

▶ **Nutrition**

Glutamine as indispensable nutrient in oncology: experimental and clinical evidence

Glutamine, a non-essential human amino acid that is preferentially consumed by a variety of types of cancer cells, appears to be supplementable in a patient's diet without stimulating cancer growth or recurrence

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Eur J Nutr. 2009 Nov 21 [Epub ahead of print]

Background: In hypermetabolic situations, glutamine is intensively used by rapidly dividing cells such as enterocytes, lymphocytes, and fibroblasts as nitrogen source and/or alternative energy fuel. It is hypothesized that in cancer patients the increased glutamine demands of the host increase the capacity of endogenous production resulting in a strong glutamine deprivation with detrimental effects on organ functions. In long-term periods of cancer cachexia, an adequate nutrition support including glutamine can essentially contribute to cover glutamine needs and, thus, to spare energy reserves of the host and to retard severe complications such as multi-organ failure. Due to the early in vitro knowledge that cancer cells preferably consume glutamine, oncologists often refuse to supply glutamine to the tumor-bearing host to avoid any potential risk. An objective evaluation whether supplemental glutamine supports tumor growth in vivo is, however, still lacking.

Purpose: The present review evaluates in vivo experimental and clinical data with respect to potential effects of glutamine administration in tumor-bearing hosts and draws conclusions for the use of glutamine supplements in clinical oncology.

Methods: Experimental and clinical intervention studies were identified in a systematic review of MEDLINE Database (last entry: June 2008) using key search terms and review articles. These studies were supplemented with reports identified through manual searches and other studies previously known by the authors. **Results:** Numerous experimental studies (rat/mouse model) show that oral/enteral or intravenous glutamine supports metabolism of the tumor-bearing host and can ameliorate gastrointestinal toxicity of therapeutical measures. Within the last two decades, **36 (24 oral/enteral, 12 parenteral) clinical studies** evaluating the tolerance, safety and effects of glutamine in various patient groups have been published. In the great **majority of these clinical studies, glutamine supplementation in cancer patients improves host metabolism and clinical situation without increasing tumor growth**. Potential mechanisms of glutamine effects include maintenance of mucosal integrity, improved immune competence, inhibition of cell proliferation, increased apoptosis rate, increased synthesis of glutathione, induction of heat shock protein synthesis, and increased synthesis of glucagons-like peptides.

Conclusions: In various clinical situations, appropriate exogenous glutamine supply is safe and can beneficially contribute to diminish risks of high-dose chemotherapy and radiation. In addition, there is some evidence that adequate glutamine availability can beneficially affect outcome, especially in patients undergoing bone marrow transplantation.

Dr. Bleyer:

- ☑ Many antidotes to chemotherapy and radiation toxicities also stimulate cancer growth or interfere with the effectiveness of chemotherapy or radiation in destroying the cancer, such as antioxidants, the anemia-reversing drugs (Aranesp, Procrit, Epogen), and folic acids (Leucovoin)
- ☑ It's always good to learn that a popular over-the-counter supplement like glutamine does not stimulate cancer growth
- ☑ Glutamine is in clinical trial to determine whether or not it can reduce the peripheral neuropathies (hand and foot tingling) of chemotherapy drugs like vincristine, vinblastine, taxotare, taxol, cisplatin and liposomal adriamycin

Improving outcome of chemotherapy of metastatic breast cancer by docosahexaenoic acid: a phase II trial

An uncontrolled study suggests that breast cancer cells can be rendered more susceptible to certain chemotherapy agents when with an oral lipid

Bougnoux P, Hajjaji N, Ferrasson MN, Giraudeau B, Couet C, Le Floch O.

Br J Cancer. 2009 Nov 17. [Epub ahead of print]

'Nutrition, Croissance et Cancer', Henry S. Kaplan Cancer Center, University Hospital Bretonneau, University François Rabelais, Tours, France.

Background: Breast cancer becomes lethal when visceral metastases develop. At this stage, anti-cancer treatments aim at relieving symptoms and delaying death without resulting in additional toxicity. On the basis of their differential anti-oxidant defence level, tumour cells can be made more sensitive to chemotherapy than non-tumour cells when membrane lipids are enriched with docosahexaenoic acid (DHA), a peroxidisable and oxidative-stress-inducing lipid of marine origin.

Methods: This open-label **single-arm phase II** study evaluated the safety and efficacy (response rate), as primary end points, of the addition of 1.8 g DHA daily to an anthracycline-based chemotherapy (FEC) regimen in breast cancer patients (n=25) with rapidly progressing visceral metastases. The secondary end points were time to progression (TTP) and overall survival (OS).

Results: The objective response rate was 44%. With a mean follow-up time of 31 months (range 2-96 months), the median TTP was 6 months. Median OS was 22 months and **reached 34 months in the sub-population of patients (n=12) with the highest plasma DHA incorporation**. The most common grade 3 or 4 toxicity was neutropaenia (80%).

Conclusion: DHA during chemotherapy was devoid of adverse side effects and can improve the outcome of chemotherapy when highly incorporated. DHA has a potential to specifically chemosensitise tumours.

Dr. Bleyer:

- ☑ The evidence for benefit is indirect in that all patients received the oral agent and only those with the highest incorporation of the agent (DHA) into cells had the longest survival
- ☑ The benefit likely applies only to those chemotherapy regimens that include daunorubicin (Adriamycin®) or epirubicin (as used in Europe where this investigation took place), the cellular uptake of which may be promoted by DHA
- ☑ At the very least, this study shows that DHA is well tolerated and when given in combination with the breast cancer chemotherapy agents used in this study

The European prospective investigation into cancer and nutrition [Prevention]

[This exhaustive set of reports, primarily on cancer etiology and prevention, that has relevance for cancer patients/survivors](#)

Note: the entire November supplement of the European Journal of Clinical Nutrition [63, S1-S238 (4 November 2009) doi:10.1038/ejcn.2009.77] contains multiple reports from the *European Prospective Investigation into Cancer and Nutrition*. This exhaustive set of reports, primarily on cancer etiology and prevention, has relevance for cancer patients/survivors.
