Dietary Fat Manipulations to Lower Cancer Risk Are Under Close Scrutiny

New approaches for lowering cancer risk through dietary fat manipulation are still preliminary, rely primarily on laboratory or animal results, and most are not yet ready for clinical trials. But scientists agree that new research tools are giving them insights into the molecular mechanisms by which dietary fats affect cell growth and development, and that understanding these mechanisms may ultimately lead to new prevention strategies.

"There are no easy answers when it comes to diet and cancer, but there are answers," said Marilyn Gentry, president of the American Institute for Cancer Research. AICR, a charitable organization that supports research on diet, nutrition, and cancer, held its 6th annual research conference in Washington, D.C., in late August.

Diet to Control Disease

One question under scrutiny is whether to put women at high risk of breast cancer recurrence on a low-fat diet to try to control any residual disease from spreading. Women with advanced breast cancer who eat a diet very low in fat show changes in the composition of their breast fat that may reduce their chances of recurrence, according to a study from the Revlon/University of California at Los Angeles Women’s Cancer Research Program.

The Revlon/UCLA study is thought to be the first to show alteration of fatty acids in breast tissue. Principal investigator Stefani Capone, M.D., a hematology/oncology division fellow at the UCLA School of Medicine, presented preliminary data at the AICR meeting on the first 15 patients enrolled in the study — all of whom have undergone high-dose chemotherapy/bone marrow transplantation and have an estimated breast cancer recurrence risk of between 30% and 40%.

After 3 months on a diet consisting of 15% of calories from fat, the women showed a marked change in the ratio of omega-3 to omega-6 polyunsaturated fatty acids (PUFAs). The ratio of omega-3, which is thought to inhibit cancer cell growth and is found in seafood, to omega-6, which is thought to promote cancer cell growth and is found in vegetable oils, increased in serum samples more than five-fold during the 3-month diet. The ratio also increased to some extent in breast fat.

"What we’ve shown is that we can change the PUFA ratio," said Capone. "We’re hoping that this will translate into a decreased risk of cancer recurrence." The very low-fat diet is supplemented with 60 grams of powdered soy protein per day and 10 fish-oil capsules, said Capone. Patients are allowed a 2-ounce portion of fish or chicken a day, but no red meat.

So far, 38 patients have completed the study and only nine have dropped out, four because their breast cancer progressed. "We got good compliance primarily because our patients are highly motivated," said Capone. "Most of them are coming to us, asking ‘What can I do now?’"

The five patients who dropped out, but whose breast cancer did not progress, did so not because they couldn’t tolerate the low-fat diet but because of travel, work, or family complications, said Capone. Study participants — whose average age is 47 — receive intensive weekly counseling on their individualized low-fat diets and are monitored through their food diaries. They will be followed for life.

Tumor Dormancy

A low-fat diet may help to maintain cancer dormancy, theorized Steven Clinton, M.D., Ph.D., clinical associate at the Dana-Farber Cancer Institute. He defined cancer dormancy as maintenance of tumor size without any additional growth for a defined period of time. "Tumor dormancy represents a delicate balance between a nascent tumor and the host," said Clinton.

Based on preliminary animal studies of aggressive cancer, Clinton proposed the concept of a link between diet and angiogenesis, the process by which a cancerous tumor develops new blood vessels to sustain its growth. He noted that metastasis is dependent both on angiogenesis and on a nutrient supply, and said that it might be possible to hold the cancerous tumor in check through dietary re-
strictions combined with an anti-
angiogenesis agent.

Clinton noted that the high-fat, affluent western diet leads to high levels of estrogens, insulins, and insulin growth factors, all of which might contribute to cancer cell growth. He suggested that dietary therapy to maintain tumor dormancy might be effective in prostate cancer, for example.

"There's enough data to say that an affluent diet is linked to prostate cancer risk," he said, adding that a dietary strategy aimed at delaying the age of onset could theoretically have a major impact on incidence because many older men would die of something else first. "We should be able to impact that curve to some degree."

Conference speakers said the link between dietary fat and cancer is strongest for breast, prostate, and colorectal cancer. Although the concept of using a low-fat diet to prevent cancer is deemed attractive, the speakers hypothesized that it might be necessary to intervene before puberty, an especially difficult time to study an anticancer diet.

"A high-fat diet in childhood could lead to early menses and a higher risk for breast cancer," said Laurence N. Kolonel, M.D., Ph.D., professor of public health at the University of Hawaii. "The problem is that it's very hard to assess."

Clinton agreed. "It's hard enough to do this in consenting adults," he said. But he said the "next opportunity" for lowering cancer risk may be in the young adult age group. While "We can't say that reducing fat by 30% is going to reduce your tumor incidence by 40%," he said, enough data now exist on the possible cancer risk of an affluent diet to educate young people on the need for healthy eating patterns for life.

In this regard, "Genetics is going to play right into the hands of nutrition and chemoprevention," said Clinton. He noted that the increasing availability of cancer tests to identify high-risk groups may give scientists increasing opportunities for dietary intervention with defined population groups.

For example, he cited the recently identified androgen receptor polymorphism that puts males at higher risk of prostate cancer (see News, July 17). "It's a very exciting possibility that with polymorphisms like that, as well as other genetic risk factors, we may be able to define groups that should be advised a little more vigorously on what we know about diet and nutrition," he said.

But for scientists to do just that, Clinton said, society needs to catch up with science. "Who wants to get a genetic test when you're 13 years old [that may later jeopardize your chances of a job or health insurance]?" he asked.

— Peggy Eastman

**BCPT Drops Enrollment Target**

Last month, researchers running the Breast Cancer Prevention Trial announced that they would need only 13,000 women at increased risk for breast cancer instead of 16,000 to determine if tamoxifen can prevent the disease. The need for fewer participants arose because the women self-selecting to get involved in the study have about twice the "minimum" level of increased breast cancer risk needed to participate.

"When designing the trial and calculating the number of participants we would need, we estimated that most women would have a certain increased likelihood of developing breast cancer," explained Norman Wolmark, M.D., chairman of the National Surgical Adjuvant Breast and Bowel Project, the National Cancer Institute-sponsored research network conducting the trial. "But the women who are entering the study are at a much greater projected risk."

The minimum risk calculates to 17 of each 1,000 women participants developing breast cancer within 5 years. But because the actual study population is at a greater risk than this minimum, and therefore more likely to develop breast cancer, the scientists can determine, with fewer participants overall, whether tamoxifen can reduce the risk of breast cancer, heart disease, and osteoporosis in this group of women ages 35 and older.

About 12,000 women have volunteered for the study, and Wolmark estimates the rest can be enrolled in about a year. Results could come in 5 to 6 years, if not sooner. Regular review of interim data takes place every 6 months, and any adverse or beneficial effect deemed strong enough could cause the trial to be halted at any point.

— Kara Smigel