

Regular, moderate-to-vigorous aerobic exercise significantly reduces markers of increased colon-cancer risk in men

SEATTLE — Sept. 12th, 2006 — Regular, moderate-to-vigorous aerobic exercise significantly reduces a risk factor associated with the formation of colon polyps and colon cancer in men, according to a study led by researchers at Fred Hutchinson Cancer Research Center. The findings, from the first randomized clinical trial to test the effect of exercise on colon-cancer biomarkers in colon tissue, appear in the September issue of *Cancer Epidemiology, Biomarkers and Prevention*.

"In men who met the study's exercise prescription of an hour of aerobic activity per day, six days a week for a year, we saw a substantial decrease in the amount of cellular proliferation in the areas of the colon that are most vulnerable to colon cancer," said lead author Anne McTiernan, M.D., Ph.D., an internist and epidemiologist who directs the Hutchinson Center's Prevention Center. "However, we found that even four hours or more of exercise weekly was enough to produce a significant benefit," she said.

Specifically, the researchers saw a decrease in the number of actively dividing cells, or cellular proliferation, within the colonic crypts — tiny tube-like indentations in the lining of the colon, or epithelium, which help regulate the absorption of water and nutrients. "A certain amount of cellular proliferation at the bottom part of the crypt is normal. But when these cells start dividing too quickly, they can migrate up the sides of the crypt to the surface and eventually form a polyp," she said. While most polyps are benign, over time some types can become malignant.

The researchers found an inverse relationship between the amount and intensity of exercise and the levels of cellular proliferation, as measured by

how far the migrating cells traveled from the base of the crypt and up the sides toward the surface of the epithelium.

A significant decline in cellular proliferation was observed among men who worked out an average of four hours a week or more and in those whose cardiopulmonary fitness was most robust. The greatest decrease in cellular proliferation was seen in men who exercised more than five hours a week. No such decrease was seen among sedentary men or those who exercised infrequently.

"Proliferation in the upper section of the colon crypt decreased among those exercising for a mean 250 minutes per week or greater, which is important because this pattern of proliferation is most associated with risk for colon cancer," the researchers reported.

Body weight did not appear to have an impact on the effect of exercise on cellular proliferation. "These effects were independent of weight. Vigorous exercise was helpful for men of any size, as long as they worked out nearly every day," said McTiernan, a member of the Public Health Sciences Division at the Hutchinson Center and a faculty member at the University of Washington.

So while men of all shapes and sizes seemed to benefit from frequent, vigorous workouts of at least four hours a week, the investigators saw no notable changes in markers of cellular proliferation in their female counterparts. "This finding supports previous epidemiological studies that also have suggested that regular exercise reduces the risk of colon cancer in men more than in women," McTiernan said. "It's not a finding that we really wanted to see, but at least our results are consistent with those of previous population-based, epidemiological studies."

The mechanism behind the null effect in female exercisers is unknown. Possible explanations, the researchers hypothesize, include the fact that exercise lowers the level of naturally occurring estrogen, a hormone that protects the colon. Another possible explanation is that the men worked out more vigorously and more often than did the women. "On average, the men in the study met their physical-activity goal of an hour a day, six days a week,

whereas the women met about 80 percent of their goal. Also, the men spent more time jogging or running compared to the women," McTiernan said.

"The women still did very well in this exercise intervention, but it may not have been enough to protect the colon."

The study, which was funded by the National Cancer Institute and the National Institutes of Health, involved 202 healthy, sedentary Seattle-area men and women between the ages of 40 and 75. All had undergone a colonoscopy within three years of participating in the year-long intervention to confirm the absence of colon cancer. Before and after completion of the study, the participants also underwent a flexible sigmoidoscopy, a procedure that allows for visual inspection of the rectum and lower colon, and the collection of tissue samples from the mucosal lining of the colon.

Half of the participants were randomly assigned to an exercise group and half were randomly assigned to a comparison, or control group. The exercisers were asked to engage in moderate to vigorous activity six days a week for a year, both on their own and at a one of several exercise facilities (including one located at the Hutchinson Center). They were also asked to maintain their regular eating habits for the duration of the study. Those in the control group were asked to maintain their current activity level and diet for a year, after which they had an opportunity to exercise for two months at no cost with a personal trainer at one of several study facilities. The Seattle Foundation and Precor Inc. of Bothell donated exercise equipment for the state-of-the-art Hutchinson Center exercise facility.

Adherence to the program was excellent, as indicated by daily exercise logs; 80 percent of the exercisers met more than 80 percent of their six-hour-a-week goal.

A major strength of the study was its randomized, controlled, clinical-trial design, which enabled the researchers to minimize the impact of confounding factors, document exercise activity and examine the direct effects of exercise on colon tissue.

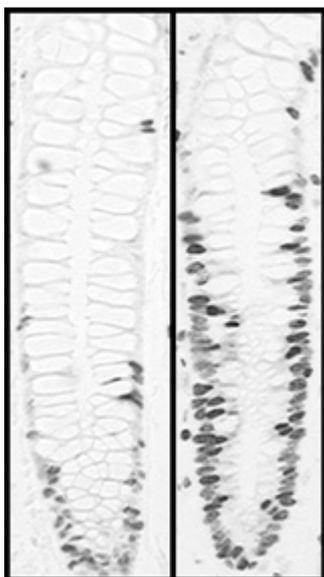
"I think that this study really underscores the new activity recommendations from the USDA and the Institute of Medicine, both of which advise people to

exercise an hour a day, six days a week for weight control and general health," McTiernan said.

Researchers from the University of Washington School of Medicine, Veterans Affairs Puget Sound Health Care System and Virginia Mason Medical Center in Seattle collaborated on the study.

Note for media only:

To obtain an embargoed copy of the paper, "Effect of a 12-month exercise intervention on patterns of cellular proliferation in colonic crypts: A randomized controlled trial," or to arrange an interview with McTiernan or a study participant, please contact Kristen Woodward, (206) 667-5095 or <http://www.fhcr.org/about/ne/news/2006/09/12/kwoodwar@fhcr.org>.



Cellular proliferation in colon crypts: active vs. sedentary people

Left: This U-shaped colon crypt contains darkly stained spots that represent the nuclei of proliferating cells. Cellular proliferation in the lower regions of the colon crypt, as shown in this example, was more often observed in people who exercised vigorously.

Right: The darkly stained nuclei in this example extend extensively into the upper regions of the crypt. Proliferation in the upper regions of the crypt was

more often observed in sedentary individuals.

Image courtesy of Paul Lampe, Ph.D., Fred Hutchinson Cancer Research Center

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