SCIENCE NEWS of the week

Fat Chance: Predicting Breast Cancer's Course

The quest to link breast cancer definitively to diet continues, amid new evidence showing a relationship between dietary fat and the severity of the disease. Dietary fat consumed in the year prior to diagnosis may affect the growth and spread of breast cancer, according to a study by Canadian researchers. Among 666 women with newly diagnosed breast cancer, René Verreault and Jacques Brisson of Laval University in Quebec City found a significant association between the amount of dietary fat consumed and lymph-node involvement, which is a measure of the severity of the breast cancer.

In addition, they report, the relationship varied with the type of fat consumed: High intake of saturated fat correlated to more frequent node involvement in older women, while high intake of polyunsaturated fat was associated with less frequent node involvement in both younger and older women. Many studies have assessed breast cancer risk in relation to diet, but few have looked at the effect of diet on prognosis. This is the first study, the scientists say, to examine the effect of both kinds of fat on women in pre- and postmenopausal age groups. The report appears in the Aug. 3 JOURNAL OF THE NATIONAL CANCER INSTITUTE.

The women, interviewed in the six months following their diagnosis, answered questions about their medical history and completed a food-frequency questionnaire covering 114 food items, estimating their intake of various foods in the year preceding discovery of their cancer. The researchers made adjustments for age, body weight and total energy intake.

In the group consuming the most saturated fat, 51 percent had node involvement, while in the group consuming the least saturated fat, 41 percent were affected. Conversely, in the group consuming the least polyunsaturated fat, 55 percent had node involvement, while among the group *highest* in polyunsaturated-fat consumption, 45 percent had the complication.

"It's puzzling," Brisson told SCIENCE NEWS. "We did the study because we thought maybe total fat was important. We were surprised at the effect of polyunsaturated fat." Studies of rats, Verreault points out, have consistently shown that polyunsaturated fat is related to greater incidence of mammary tumors. "We tried to think of all sorts of biases and errors and couldn't find anything to explain such a nice, neat pattern," Brisson says. "It just shows that we really have to look into this area further."

James R. Hebert of the American Health Foundation, in New York City, calls the findings "interesting and provocative." Although the distribution of dietary fat in the study group was very narrow — the percent of fat as a total of calories varied only from 33 to 39 percent — Hebert says the study "is a step in the right direction, as far as the kind of evidence we need. The researchers see an effect, and it will be important to see if others can replicate it."

Many scientists do not believe a link exists between fat intake and the growth rate of cancer, says David Byar of the National Cancer Institute (NCI) in Bethesda, Md., citing this as the major reason the NCI's vast breast-cancer prevention trial has been discontinued.

Controversy over the Women's Health Trial, which ended July 31 after more than three years, swirled around three major issues, according to an editorial by NCI's Peter Greenwald, in the same issue of the journal. In addition to doubts about the dietary fat/breast cancer hypothesis, the estimated potential reduction in breast cancer risk in the women, aged 45 to 69 over the projected 10 years, was revised from 50 to 25 percent. Thus, in order to achieve statistically significant results, the study group would have required expansion well beyond the 32,000 originally planned and the original cost of $90 million. Third, scientific advisers questioned the success of a trial depending on long-term compliance with a diet radically different from the U.S. norm.

So researchers have gone back to the drawing boards to design a new low-fat trial with emphasis on total cancer incidence — including breast cancer — and coronary heart disease as well. — *C. Eron*

Disease evolution plagues scientists

In the 14th century, the black plague stormed through Europe, killing at least one-quarter of its inhabitants. Then, as mysteriously as it had come, it disappeared. Now molecular biologists have found a clue that may help explain why diseases like the plague rise and fall — and rise again.

The researchers base their conclusions on studies of two strains of bacteria, *Yersinia pestis*, which causes plague, and *Yersinia pseudotuberculosis*, which confers resistance to plague but causes only mild symptoms. Hans Wolf-Watz of the University of Umeå, Sweden, with Roland Rosqvist and Mikael Skurnik of the Swedish Defense Research Establishment, first examined two genes believed to help *Y. pseudotuberculosis* invade cells. The genes code for invasin and Yop1, proteins found at the surface of *Y. pseudotuberculosis*. *Y. pestis* contains altered forms of the genes that do not produce proteins. The scientists mutated the *Y. pseudotuberculosis* genes for invasin, for Yop1 or for both proteins and administered bacteria containing the altered genes to mice. They then measured the bacteria's virulence by counting the number of mice that died.

The results show that a mutation in one or the other of the two genes barely changes the bacteria's virulence, but mutations in both genes make the bacteria remarkably more deadly. Apparently, the presence of invasin and Yop1 results in a mild, controlled infection but their absence allows bacteria to ravage cells and cause disease, the researchers say.

Next, the scientists closely examined the Yop1 genes of *Y. pestis* and *Y. pseudotuberculosis*. They found only one small genetic difference between the two strains. This difference and one in the invasin gene account for *Y. pestis*' virulence, they conclude.

Finally, in a sort of reverse of the first experiment, they transplanted the Yop1 gene from *Y. pseudotuberculosis* into *Y. pestis*. Confirming expectations, *Y. pestis* became notably less virulent.

In the Aug. 11 NATURE, the researchers propose that plague epidemics may have come and gone when nearly harmless strains like *Y. pseudotuberculosis*, with a flick of two genes, became *Y. pestis* and then, with another switch, mutated back to a nonvirulent form. But an evolutionary hypothesis cannot be based on genetics alone, says evolutionary biologist Richard Lenski of the University of California, Irvine. In an editorial accompanying the report, Lenski says other variables, such as the size of the host population, can determine the course of a disease. In a large population, many mutant forms of bacteria can exist, he explains, but when the host population is small, only the less virulent strains survive.

Lenski also mentions that similar environmental variables may be affecting the course of the AIDS-causing human immunodeficiency virus (HIV). But this possibility is highly speculative, he hastens to add. "I deliberately left the section on HIV vague," he says. — *M. Hendricks*