Does Vitamin A Prevent Cancer?

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Millions of Americans believe that vitamins—vitamin A in particular—may prevent cancer. Although this belief is still unproved, scientists and medical professionals, as well as laypeople, are acting on it. Several cancer researchers at Roswell Park Memorial Institute in Buffalo dose themselves with vitamin A tablets each day in the hope of preventing cancer. About 50 percent of nurses surveyed by a group of Harvard scientists take daily multivitamin pills, partly for their presumed anticancer effect. The National Cancer Institute is funding 16 studies of the use of vitamin A and related compounds to prevent cancer, at a cost in 1983 of $3,121,000. But, as was evident at a recent workshop at the National Institutes of Health on vitamin A and cancer,* the evidence and logic behind this hypothesis is shakier than many persons outside the field realize.

Practically the only clear-cut and indisputable evidence linking vitamin A and cancer are experiments showing that vitamin A and its derivatives can prevent some tumors in laboratory animals—particularly squamous cell cancers, which are derived from skin cells. From there, however, the story gets murky. It might be predicted, for example, that the more vitamin A that people consume, the lower their incidence of cancer. Such is not the case. A number of groups of investigators asked cancer patients and matched controls about their diets and found that the cancer patients consumed the same amount of vitamin A in the years before they were diagnosed as the controls. Major sources of vitamin A in the diet are meat, dairy products, eggs, liver, and vitamin pills.

Since vitamin A is carried in the blood, researchers thought that perhaps they could detect differences between cancer patients and matched controls by looking at blood levels of vitamin A. The amount of blood vitamin A is tightly regulated so that, in each individual, it remains nearly constant. Perhaps, it was thought, persons susceptible to cancer regulate their vitamin A metabolism differently so that they, as individuals, have less of the vitamin in their blood and so carry too little of it to their tissues.

At first, the experiments looking at vitamin A in blood seemed promising. Two groups of investigators reported that persons with low levels of vitamin A were at increased risk for cancer. But more recent studies have failed to confirm these earlier ones. In fact, when Curtis Hames of the Cardiovascular Epidemiology Unit in Evans County, Georgia, and his associates went back and looked again at a population from Evans County that had initially seemed to show a correlation between low vitamin A and high cancer risk, they no longer found a relationship. The public health implications of an association between low levels of vitamin A and cancer would have been enormous, says DeWitt Goodman of Columbia University's College of Physicians and Surgeons. However, he sadly notes, the relationship, "doesn't appear to be holding up."

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But, the cancer researchers reasoned, "pre-formed" vitamin A is not the only source of this substance. People also get vitamin A from carotenes, which are found in vegetables and are largely broken down to vitamin A in the gut. And some of the same epidemiological studies that showed no difference in the vitamin A content of diets of cancer patients and controls, *did* show that cancer patients tended to eat fewer vegetables in the years before their disease was diagnosed.

But the increased risk associated with low fruit and vegetable consumption is not terribly impressive—the relative risks tend to be less than 2. And the carotene hypothesis has other difficulties as well. Researchers who looked, including Walter Willett and Charles Hennekins of Harvard Medical School, saw no difference in the carotene levels in the blood of persons who subsequently got cancer and those who did not. Unlike vitamin A levels, the levels of carotene in the blood vary with diet.

Moreover, there is virtually no evidence that carotenes prevent cancer in animals. One of the only published studies is a recent one by Micheline Mathews-Roth of Harvard Medical School, in which she fed mice 30 times the normal amount of carotenes and was able to prevent skin cancers. What this means for people is unclear. Goodman explains that scientists just have not been very interested in giving carotenes to animals because a number of laboratory animals, including rats and pigs, do not absorb the substance and because vitamin A and its derivatives "are much more active."

A major reason investigators are so intensely interested in carotenes is because these substances are broken down into vitamin A. But, as several investigators at the conference mentioned, the association between fruit and vegetable consumption and what may be a slight decrease in cancer risk by no means demonstrates that the carotenes in vegetables should get the credit. "Something about vegetables does seem beneficial, but there are lots of possibilities besides carotene," says Willett. People who eat lots of vegetables and fruits also consume more fiber, for example. And the more vegetables that people eat, the less fat they tend to consume. Still, five of the 16 intervention studies being funded by the NCI involve carotene and two more involve both carotene and vitamin A. Hennekins, whose study of nearly 22,000 U.S. physicians is the largest, describes the carotene hypothesis as "soft."

If the confusing tale of the search for a "chemopreventive agent," in the NCI's words, leads to any conclusion, it is a negative one. As Willett says, "There is no basis now for proposing that vitamin A protects against human cancer and there is almost zero evidence to justify taking vitamin A." The meeting closed with the usual nostrum: More research is needed.—**Gina Kolata**

*The Vitamin A and Cancer Prevention Conference was sponsored by the Malnutrition Panel, United States–Japan Cooperative Medical Science Program, and the National Cancer Institute. It was held on 28 and 29 February 1984.