Vitamin A and cancer: A mixed review

Previous research has suggested that eating foods rich in vitamin A reduces the risk of cancers of the lung, larynx, stomach and esophagus. Recently, however, some epidemiologists have begun looking more closely at vitamin A's protective effect by singling out the effects of carotene, a vitamin A precursor, from retinol, the primary form of vitamin A. Carotene is found in such foods as carrots, tomatoes, broccoli, spinach and peaches. Retinol comes from animal products such as high-fat meats, liver, butter, whole milk and egg yolks.

A retrospective study of 178 men and women diagnosed with esophageal cancer in western New York suggests that people who eat foods rich in retinol have a risk of that cancer up to three times greater than those eating low-retinol diets. The researchers also found that the risk of esophageal cancer decreased with increasing consumption of foods containing carotene, but not significantly. The study by Saxon Graham of the State University of New York at Buffalo and co-workers, reported in the March AMERICAN JOURNAL OF EPIDEMIOLOGY, confirms earlier findings of the different effects of carotene and retinol in cancers of the lung, mouth and larynx.

To eliminate the effect of possible diet and lifestyle changes due to a diagnosis of cancer, the patients were asked about their eating habits and frequency of cigarette smoking and alcohol consumption before their symptoms appeared. The researchers found that the risk of esophageal cancer increased with increasing consumption of foods known to contain retinol, with calories and fat, and with nutrients found in dairy products – calcium, riboflavin and vitamin D. But when the researchers examined the risk of retinol separate from the risk of these other factors, they found that retinol alone increased the risk of esophageal cancer. The study also confirms earlier findings that esophageal cancer risk increases with cigarette smoking and alcohol consumption. Esophageal cancer strikes about 10,000 people in the United States annually.

Pinning down the Lyme disease antibody

Half the people with Lyme disease fail to show its characteristic red rash, which makes diagnosing it difficult. Worse, some of these people don't test positive for the disorder on standard diagnostic tests, which detect antibodies to the bacterium *Borrelia burgdorferi*, the cause of Lyme disease that infects people through the bite of a tick.

Researchers now report they apparently have found the cause of the negative tests in infected people: antibodies to the disease often completely bind to antigens on *B. burgdorferi* and routine testing doesn't detect them, says Patricia K. Coyle of the University of New York at Stony Brook, co-author of the report published in the Feb. 10 LANCET. In most infectious diseases, extra, unbound antibodies circulate in the blood and can be detected by a laboratory test.

The researchers analyzed blood samples from 10 subjects who had symptoms of the disease, including the rash, but had negative antibody tests. They found that all 10 patients had bound antigen-antibody complexes. The researchers used a laboratory test that split apart the antigen-antibody complex, releasing the bound antibody so it could be detected. Coyle says this may one day become a routine second test for people with Lyme disease symptoms but negative antibody tests.

The researchers used three control groups to confirm their findings: 21 of 22 subjects who tested positive for the disease also had the antigen-antibody complex; all 19 controls with other diseases did not have the complex, and four of 12 controls with no rash but with other symptoms, and who tested negative for the disease, had the antigen-antibody complex. Apparently the other eight either weren't infected or had such low antibody levels that they couldn't be detected yet, Coyle says.

Uncommon ICAM blocks common cold virus

When the space shuttle Atlantis finally blasted off last week, a full week behind schedule, NASA estimated the delay had cost the agency a whopping $2.7 million. Several factors contributed to the five launch postponements, but the first and perhaps most frustrating among them was the common cold that left crew commander John Creighton too congested to fly.

Most colds don't have such dire consequences. But virologists Steven D. Marlin, Vincent J. Merluzzi and their colleagues couldn't have asked for a more timely backdrop as they published their latest research in the March 1 NATURE describing a way to block infection by cold-causing viruses.

Working at Boehringer Ingelheim Pharmaceuticals Inc. in Ridgefield, Conn., the researchers mass-produced slightly altered versions of a protein receptor that normally serves as the nasal-passage docking site for rhinoviruses – the kind of virus that causes about 50 percent of common colds. Using cultured human cells that bear the rhinovirus receptor, called ICAM-1 (SN: 3/18/89, p.165), the researchers showed that when they flooded the cells with synthetic ICAM-1s, the decoy receptors sopped up more than 90 percent of the rhinoviruses before the viruses had a chance to infect the cultured cells. This level of protection, if achieved in people, could feasibly prevent the onset of some colds, the researchers suggest.

In theory, the approach has several benefits over those employed by other antiviral drugs, Marlin and others note. Most important, since the virus absolutely requires the ICAM-1 receptor to initiate infection, researchers need not fear the virus will mutate into a form that lacks an affinity for the synthetic decoys. "The virus has no other way of binding to cells," Marlin says. "If they mutate such that they don't bind to ICAM-1, they're dead viruses."

But several hurdles remain. For one, scientists remain uncertain what kind of ill effects may follow if they repeatedly flood the nasal passages with large quantities of the synthetic receptor, which in its natural form has important duties beyond serving as a welcome mat for rhinoviruses. For example, ICAM-1 plays a key role in both triggering immune responses and in shepherding immune-system cells from the circulatory system into surrounding tissues.

Marlin says there are reasons to believe that extra copies of ICAM-1 may not cause serious problems in the body. However, he adds, "The only way to find out is to try it." Since no other animal suffers from this common human ailment, that means trying it on people. But clinical trials are probably still a few years away, Marlin says.

First gene therapy in humans proposed

Researchers at the National Institutes of Health (NIH) in Bethesda, Md., have filed the first formal request to inject into humans genetically engineered cells custom-designed to treat an inherited disease. The cells will produce an enzyme – adenosine deaminase, or ADA – missing in children suffering from a hereditary disorder called severe combined immunodeficiency. Because these children are incapable of mounting a proper immune response against disease-causing microorganisms, they must live in sterile environments and rarely live beyond their first few years.

R. Michael Blaese, Kenneth Culver and W. French Anderson submitted their proposal to the NIH Feb. 23. The experimental protocol builds upon ongoing experiments by some of the same researchers, in which genetically engineered cells are being used not to cure patients but to learn more about naturally occurring cancer-fighting cells (SN: 5/27/89, p.324).

Federal officials will review the proposal at a series of meetings during the month of March. Approval or rejection isn't expected until at least June.