Cancer Vaccine Trials in Monkeys Hold Promise

Scientists working with a rare breed of primate have developed a vaccine that appears to protect the animals against a virus-induced cancer that may also strike humans. The vaccine's success in animal trials puts researchers "in sight of" related tests on people, says M. Anthony Epstein of the University of Bristol, England.

The vaccine provokes an immune response against Epstein-Barr virus (EBV)—which Epstein co-discovered 20 years ago — a microbe that causes infectious mononucleosis and is strongly associated with two human cancers, Burkitt's lymphoma and nasopharyngeal carcinoma. If the vaccine protects people against these cancers, it would offer proof that the virus plays a direct role in initiating a human tumor. "It would be a phenomenal breakthrough," says Gary Pearson of the Mayo Clinic in Rochester, Minn., who is collaborating with another group doing EBV vaccine research.

A vaccine against another suspected human tumor virus that causes hepatitis B and is linked with hepatocellular carcinoma has already been tested on people, but hasn't yet been shown to prevent cancer associated with the virus, either in humans or animals, says Pearson. A mass immunization in China to see if it will prevent cancer is being planned.

While EBV vaccine is not ready for human trials, it has performed well in animal tests. Epstein, who spoke last week at the National Institutes of Health (NIH), described how he and his colleagues purified a glycoprotein they call gp340, which is a component of EBV membranes and the membranes of EBV-infected cells. Gp340 is recognized by antibodies that disable EBV. In early experiments, mice injected with gp340 packaged in artificial liposomes (oil droplets) produced antibodies that attacked Epstein-Barr virus.

In order to test whether gp340 could protect against EBV infection, the scientists established a colony of cottontop tamarins, a rare New World monkey that is particularly susceptible to cancer induced by the virus. Epstein and colleagues have developed a system for infecting this exotic animal with EBV so that within two to three weeks, the tamarins are riddled with tumors. "It's a very dramatic disease which you cannot miss," Epstein says.

In the most recent experiment, four uninfected tamarins were vaccinated with gp340, given time to develop their own antibodies to the molecule, and then injected with Epstein-Barr virus. Two other monkeys were not vaccinated, but were also inoculated with EBV.

Epstein announced at the NIH lecture, "I can tell you that on Monday, when I examined these animals, the two unprotected animals were developing lesions (tumors) and the four immunized animals were not." He cautioned that "we have to wait before a final conclusion," but added that he thinks "we are justified in believing that this is going to hold up."

Pearson, who has pursued EBV vaccine research on owl monkeys, predicts tests on humans are about two years away. First, new methods for producing gp340 must be developed because the glycoprotein is currently stripped from the membranes of EBV-infected tumor cells and may be contaminated. As one researcher puts it, "no one would like to see that material go into humans." Furthermore, the purification procedure Epstein and others use, which depends on antibodies to latch onto and separate gp340 from other membrane components, is currently too expensive for large-scale production, Pearson told SCIENCE NEWS.

Among the best solutions to both the contamination and expense problems is to make the vaccine by recombinant DNA techniques, according to Pearson, who is collaborating with scientists at the University of Chicago who have isolated and are studying the expression of the gene that codes for gp340. Once they've gotten genetically engineered bacteria carrying the gene to make a protein that can induce EBV-neutralizing antibodies in animals, work can begin on producing large enough quantities for human tests, he says.

College students will likely be the first human guinea pigs, explains Epstein, because young adults who have never been infected with EBV are at risk for infectious mononucleosis. Students lacking antibodies against EBV—and who therefore haven't been infected — could be vaccinated and watched to see if they get mono. Next, children at risk for Burkitt's lymphoma, one of the most common childhood cancers in Africa, should be vaccinated, he says. The effects of that immunization could be judged just five to ten years later.

Logistical problems could complicate such a program, says Werner Henle, a virologist at the University of Pennsylvania in Philadelphia, because infants would have to be immunized during the short time—perhaps as little as a month—after they've lost their maternal antibodies and before they become naturally infected.

—G. Morse

Infection in the elderly: Who's on second?

Though it is known that the body's ability to fight infection declines with age, it is not known why. Research on elderly rats, presented at the American Gastroenterology Association meeting this week in New Orleans, suggests that a class of disease-fighting molecules called IgA don't get to where they're needed in the digestive system. And while the researchers are quick to note that application of the finding is a long way off, it may explain why, despite sufficient levels of IgA in the blood, the elderly digestive tract is more prone to infection and cancer.

The primary defense of the respiratory and gastrointestinal tracts is their mucosal lining. The lining provides a physical barrier as well as IgA, which serves as a sentinel for bacteria or viruses that shouldn't be there. Researchers from the University of California at San Francisco initially found that livers in older rats secrete fewer IgA molecules into the digestive tract than younger rats' livers. Now they report that a problem develops in the liver cells themselves. The way a baseball goes from a fielder to second base to first base in a double play, an IgA molecule gets passed from the blood to a liver cell to the bile duct.

The researchers found that in older rats, each liver cell has three to four times fewer IgA receptors, so fewer of the vital molecules get into the digestive tract — if the second baseman catches fewer balls, fewer double plays get made. "It may be a partial explanation of the observed decline in mucosal immune response in the elderly," says Douglas L. Schmucker, one of the researchers.

"Most of the data and dogma suggest that the immune system itself — the [immunoglobulin-producing] lymphocytes — are less able to function in the elderly," he says. "This may be true, but there may be an added problem ... IgA may be in the system but it can't get to the site where it is needed on the mucosal surfaces."

The next question is to delineate the mechanism associated with the decline. "We know that sixfold less [IgA] gets across," says Schmucker. "We're trying to figure out why." What is needed now is more detail on the changes in the liver cell receptors, observes Peter Holt of St. Luke's-Roosevelt Hospital in New York, who chaired the session at which the data were presented. "The physiological implication of the work at the moment is very important," he says, "but the application to human diseases is more remote." ***— J. Silberner***