Here's the Skinny on Painless Vaccines

Parents with a child needing vaccinations might one day pick up shampoo from the pharmacy rather than drag the kid to a physician for a painful shot. This futuristic scenario stems from the unexpected finding in mice that a novel kind of vaccine, a simple solution containing DNA, works when applied directly to skin—as long as the skin has hair on it.

If the new result holds up, DNA-loaded skin patches or shampoos could replace injectable vaccines, lowering medical costs and making immunization more practical in developing countries. Some scientists are skeptical of the new work, reported in the September NATURE BIOTECHNOLOGY, but others express optimism.

"This is a very preliminary report, but it's an exciting, logical progression towards the idea of much simpler and more effective vaccines," comments Stephen A. Johnston of the University of Texas Southwestern Medical Center at Dallas, who pioneered research on DNA vaccines.

Vaccination in the future?

Such vaccines have been called the third revolution in vaccine science. The first came more than a century ago, when scientists found that injections of a dead or weakened pathogen can confer protection against the disease it causes. In the second revolution, scientists over the past 2 decades have found that they can immunize people with just a single protein from a pathogen.

DNA vaccines now extend and simplify the latter strategy: Scientists inject the gene for the immune-stimulating protein rather than the protein itself. Some of the body's cells then take up the gene and make the protein. Although researchers still aren't sure why, a DNA vaccine often stimulates more effective immunity than the corresponding protein inoculation.

Investigators normally inject DNA vaccines into muscle or the blood. The assumption that such vaccines require injection, in fact, led to the latest findings. Hongran Fan and her coworkers at the Veteran Affairs Palo Alto (Calif.) Health Care System and Stanford University School of Medicine planned to demonstrate the effectiveness of intramuscular gene injections by comparing them with simply dripping a DNA vaccine solution onto the skin of mice.

They noticed, however, that skin cells also absorbed the gene in the dripped DNA vaccine. Curiously, this didn't work on a strain of hairless mice. "We finally realized we were seeing gene transfer, and it was dependent upon hair," says Paul A. Khavari, a colleague of Fan's.

Subsequent experiments showed that cells within hair follicles take up and make protein from the DNA-vaccine gene, the team reports. This triggers an immune response in which the mice make antibodies and immune cells specific for the gene's protein. Facing a constant onslaught from infectious microbes, the skin has evolved means to efficiently generate an immune response, the researchers speculate.

Khavari and his colleagues have not yet shown that a skin application of a DNA vaccine protects animals from a virus or bacterium. In fact, in a test using a gene from the hepatitis B virus, the immune response was about one-third as strong as that produced by a commercial injected-protein vaccine. "We're looking at ways to boost the immune response," Khavari says.

While a California biotech firm called Maxygen has licensed the rights to Khavari's DNA-vaccine approach, some researchers remain skeptical. "Many people have had problems reproducing their findings," says De-chu Tang of the University of Alabama at Birmingham.

Tang says his group has shown that infecting skin with a cold virus carrying the gene for a flu-virus protein protects mice against influenza. However, merely applying the gene for that protein to the skin doesn't stimulate immunity, he says. Other genes may more effectively arouse the immune system, Tang admits. —*J. Travis*

Fewer gallstones arise in active women

Gallbladder attacks requiring surgery occur less often in women who exercise regularly than in inactive women, a new study shows. A job that keeps a woman on her feet helps, too.

Researchers studying the lifestyles of 60,290 nurses assessed the benefit of exercise by dividing the women into five roughly equal groups according to the extent of their typical exercise programs. The scientists calculated activity based on questionnaire responses detailing how many hours a week a woman did aerobic exercises, ran, swam, hiked, or participated in other sports that required at least moderate exertion.

Over roughly 10 years, those in the most active group, who exercised moderately for at least 2 to 3 hours a week, were only 69 percent as likely to undergo gallbladder removal surgery as the least active women were, scientists report in the Sept. 9 NEW ENGLAND JOURNAL OF MEDICINE. After accounting for differences in body weight, the exercise appeared to cut the risk to 79 percent, says study coauthor Michael F. Leitzmann, an epidemiologist at Harvard School of Public Health and Brigham and Women's Hospital in Boston.

Approaching the lifestyle question from another angle, Leitzmann and his colleagues asked women how many hours they spent each week watching television, sitting at work, and driving a car as part of a daily commute.

The researchers found that watching a lot of TV coincided with a one-third-greater incidence of gallbladder surgery. The women who delegate more than 40 hours a week to sitting at work and driving to it reported nearly 1 1/2 times the number of these gallbladder surgeries as the most active did.

The researchers "went to great lengths to examine the effects of confounding variables, such as age, obesity, and recent change in weight, and the results were the same despite adjustments for these factors," Kenneth J. Vega and David E. Johnston of the University of New Mexico Health Sciences Center in Albuquerque note in the same journal issue.

Leitzmann and his colleagues last year reported a similarly elevated risk of gallstones in sedentary men. Despite these and other gallbladder studies, the biological effect of exercise remains obscure. Exercise might limit stone formation by cutting blood concentrations of LDL cholesterol, the so-called bad cholesterol, Leitzmann says.

High triglyceride concentrations in blood result in the liver adding cholesterol to bile—a digestive juice stored in the gallbladder. There, the saturated bile can form stones of hardened cholesterol, sometimes blocking bile's exit and causing pain. Gallstones necessitate nearly all gallbladder removal surgery. —*N. Seppa*