



The DMS COOP Project, a network of private physicians established in 1972 to do practice-improvement studies, is the oldest practice-based primary-care research network in the U.S.

Researcher calls vaccine results “stunning”

Diane Harper, M.D., M.P.H., was busy at her computer as usual one recent afternoon. There was a palpable electricity in her small office, however. The day before, *The Lancet* had published the results of an international clinical trial she'd led, testing a vaccine against two strains of human papillomavirus, HPV-16 and HPV-18, viruses that cause 70% of cervical cancer. Harper has studied the HPV-cervical cancer connection for 20 years.

Randomized: “The results of this trial are actually stunning,” Harper says. The vaccine increased the body's immune response to the viruses to 80% to 100%. Conducted between 2000 and 2003, the study included 1,113 women aged 15 to 25 from the U.S., Canada, and Brazil. In the double-blind, randomized trial, 560 received the vaccine and 553 received a placebo. Participants got three vaccinations over a period of six months and follow-up testing for 27 months.

“Among ‘the perfect people,’” Harper says—that is, women who got all three injections and all follow-up tests—“the vaccine was 100% effective against persistent HPV-16/18 infections.” Even among less-than-perfect subjects—those who got one or two injections—it was 91% effective. “Usually the data aren't so good for the

group that doesn't fully comply with the protocol,” she observes, “but even this group saw a significant benefit.”

HPV is transmitted by skin-to-skin contact, usually through sexual activity. Of the more than 100 strains of HPV—most of which do not cause serious health problems—about 30 are linked to cancer of the cervix. Most HPV infections, even from high-risk strains, are resolved by the body's immune system, but some progress to cancer. Worldwide, 230,000 women die of cervical cancer annually—the vast majority in developing countries, where screening and treatment are not widely available. Even in the U.S., more than 13,000 women are diagnosed with the disease and 5,000 die of it each year.

The vaccine tested in the study—a virus-like particle (VLP)—was designed by GlaxoSmithKline Biologicals of Belgium to prevent infections, cell abnormalities, and precancerous lesions, all of which can advance to cancer. The VLPs, Harper explains, are “little hollow globes, a coating with nothing inside.” Scientists are able to snip out a piece of the HPV DNA that contains the genetic code without the virus. This is used to create the VLPs, which mimic the virus but contain nothing harmful. When the particles are injected, the body sees them as HPV and begins producing antibodies.

Phase III: Harper and her colleagues are now beginning a Phase III trial, which will enroll 15,000 women worldwide, including 300 at DHMC, and run through 2009. If all goes as expected, the vaccine could be available in the U.S. by 2010.

She receives no money from GlaxoSmithKline, Harper adds. “The study and its protocols were planned by independent physicians,” she says, though she feels industry has a role to play in “excellent science that can be translated into improved clinical care.”

CATHERINE TUDISH

Country fare

“We need to think about veterans who live in rural settings as a special population,” explains DMS psychiatrist William Weeks, M.D. Weeks and colleagues at the White River Junction, Vt., Veterans Affairs Outcomes Group conducted the first nationwide comparison of the health status of rural versus urban VA patients. The study, published in the *American*



Journal of Public Health, found that

rural veterans are in much poorer health than their suburban and urban counterparts. The authors had some advice for policy makers: establish more clinics in rural areas and coordinate VA services with Medicare.

Water, water, everywhere . . .

A new federal standard for arsenic in drinking water—set to take effect in 2006—is 10 parts per billion. That may still be too high, according to a team of DMS researchers that has been examining the effects of arsenic on rat cells. Led by physiologist Jack Bodwell, Ph.D., the team published its findings in *Chemical Research in Toxicology*.

The researchers described how arsenic disrupts hormone signaling and regulation—causing reproductive problems and other abnormalities—and confirmed that even concentrations of arsenic well below the new standard can cause such problems.



JON GILBERT FOX



Diane Harper led a worldwide HPV vaccine trial.