

HPV Vaccine Acceptance Deemed Too Low

BY KATE JOHNSON

EXPERT COMMENTARY FROM THE ANNUAL MEETING OF THE SOCIETY OF OBSTETRICIANS AND GYNAECOLOGISTS OF CANADA

MONTREAL — Uptake of human papillomavirus vaccination is too slow, say some experts, while others still question whether enough is known about the risk-benefit ratio to deem the vaccine truly necessary.

In an industry-sponsored symposium held during the meeting, Dr. William Fisher, a consultant to Merck & Co., strongly urged physicians to make HPV vaccination a routine part of their practice. There are about 100 strains of HPV virus, with 15 considered oncogenic. HPV strains 16 and 18 are responsible for about 70% of cervical cancer, while strains 6 and 11 are responsible for genital warts. Merck's Gardasil vaccine targets all four strains, while Cervarix (GlaxoSmithKline PLC) targets the oncogenic strains 16 and 18.

"HPV vaccine would seem to be a very reasonable form of protection for both men and women who may be sexually active in an environment characterized by a very high level of HPV and in which infection is very common," as the infection may have serious health consequences for the individual and his or her partner, said Dr. Fisher, professor of psychology and of obstetrics and gynecology at the University of Western Ontario, London.

To illustrate the prevalence of HPV infection, Dr. Fisher noted a 25% rate of infection with high-risk oncogenic strains of HPV among Canadian teenage girls, aged 15-19 years, in a low-risk family practice setting who were negative for HPV the previous year (CMAJ 2003;168:421-5). Similarly, among a group of 621 university-age women tested every 6 months for 2 years, the rate of newly acquired high- and low-risk HPV strains was 13% at 1 year, and 29% and 24% at 2 years (Cancer Epidemiol. Biomarkers Prev. 2003;12:485-90).

"We couldn't be talking more clearly about a socio-sexual epidemic," he said. "This is a social disease on steroids," said Dr. Fisher, who is also with the center for health, intervention, and prevention at the University of Connecticut, in Storrs.

In a recent study involving young Canadian couples, HPV was present in 64% of new couples and the oncogenic HPV-16 strain was the most common strain found at baseline.

Concordance of strains was 41% at baseline and grew to 68% at 6 months, he said (Epidemiology 2010;21:31-7). "There's no doubt in new relationships that HPV is rapidly becoming part of the sociocultural landscape," Dr. Fisher said. While there is a well-established link between high-risk HPV and gynecologic cancers, HPV-related head and neck cancers are "probably the newest sexually transmitted infections on the radar," he said.

In a Swedish study, the prevalence of oncogenic HPV strains in head and neck cancer biopsies was found to have increased from 23% in the 1970s to 77% by 2005 (Int. J. Cancer 2009;125:362-6).

In addition, a 2010 study shows that the risk of HPV-related head and neck cancer, while increased with six or more coital partners (odds ratio, 1.25), more than triples with more than four oral-genital partners (OR, 3.36). "Oral-genital sex is the new handshake, and it is actually likely that people have more oral-genital partners than coital partners," Dr. Fisher added.

Yet while Canadian and U.S. authorities recommend HPV vaccination in young girls and women, and school-based vaccination programs are offered across Canada, such recommendations have not resulted in mass vaccination, he said. A recent study suggests that only about one-third of American girls, aged 13-17 years, have been vaccinated (Am. J. Prev. Med. 2010;38:525-33).

Dr. Marie Plante, president of the Society of Gynecologic Oncologists of Canada, said that as a gynecologic oncologist she sees the downside of such low vaccination rates. "We treat women with cervical cancer. ... I've got several of them in their 20s and early 30s and it ruins their lives, and they can't have children sometimes. So we see the frustrating part because it could have been prevented," said Dr. Plante, chief of the gynecologic oncology division at Laval University in Quebec City. She estimated that about 50% of cervical cancer cases she sees are in women whose regular screening had failed to identify the disease.

"As much as I am very critical of the push from the companies [to market their vaccines], I will tell you that honestly I think the vaccine is safe," Dr. Plante continued. However, "it is not necessary," she said. "It does not guarantee 100% protection. It's an option you have to reduce the chances that you develop precancerous cells. In most cases this will be treated quickly and won't take your life away." Importantly, the vaccine

also reduces the potentially significant burden of genital warts, the experience of which is "amazingly negative"—it's "terrible and painful," she added.

Last year a prominent editorial and article in JAMA questioned the medical arguments for vaccination, as well as the ethics of aggressive marketing campaigns from pharmaceutical companies (2009;302:795-6, 781-6). "If the potential benefits are substantial, most individuals would be willing to accept the risks. But the net benefit of the HPV vaccine to women is uncertain. Even if persistently infected with HPV, a woman most likely will not develop cancer if she is regularly screened," wrote Dr. Charlotte Haug, editor-in-chief of the Journal of the Norwegian Medical Association.

In their article, Sheila Rothman, Ph.D., and David Rothman, Ph.D., of Columbia University, New York, noted that in 2006, Merck's Gardasil "was named the pharmaceutical 'brand of the year' for building a 'market out of thin air.'"

Alan Cassels, a drug policy researcher at the University of Victoria (B.C.), was critical. "It's not a slam dunk that if you get the HPV vaccine you'll be prevented from developing cancer," he said in an interview. He compared the vaccine to cholesterol-lowering drugs. "Yes, we can prove that a drug lowers cholesterol, but the question is whether it prevents heart attacks and strokes. So, while the HPV vaccine may prevent transmission of the virus, will that really result in [fewer] cancers? We won't know for 10 or 20 years down the road."

Given the uncertainty of benefit, or the duration of efficacy, Mr. Cassels cautioned that the risks of any intervention should be minimal, which is not the case with the HPV vaccine.

As of Jan. 31, 2010, there were 49 U.S. reports of death among females who had received Gardasil, according to the Centers for Disease Control and Prevention. Twenty-eight of these reports have been confirmed and 21 remain unconfirmed. In the 28 confirmed reports, "there was no unusual pattern or clustering to the deaths that would suggest that they were caused by the vaccine," according to a CDC statement. ■

Disclosures: Merck sponsored the symposium. Dr. Fisher disclosed that he has been a consultant for Merck, Boehringer Ingelheim, and Bayer. Dr. Plante reported having no conflicts of interest.

Combo MMRV Vaccine Tied to Higher Febrile Seizure Risk

BY ROXANNA GUILFORD-BLAKE

FROM PEDIATRICS

Children aged 12-23 months old are at increased risk of febrile seizures 7-10 days after vaccination with the combination measles-mumps-rubella-varicella vaccine, compared with separate administration of the measles-mumps-rubella vaccine and the varicella vaccine, according to surveillance data from the United States.

The use of the combination measles-mumps-rubella-varicella (MMRV) vaccine instead of separate measles-mumps-rubella and varicella (MMR+V) vaccines accounted for one additional febrile seizure for every 2,300 MMRV vaccines administered—a nearly twofold increased risk, Dr. Nicola P. Klein of Kaiser Permanente Vaccine Study Center, Oakland, Calif., and her colleagues reported.

The researchers issued their preliminary findings to the Centers for Disease

Control and Prevention's Advisory Committee on Immunization Practices (ACIP) in February 2008.

ACIP subsequently changed its recommendations from a stated preference for MMRV to no preference for either MMRV or separate MMR+V vaccination.

"We analyzed [more than] 459,000 12- to 23-month old children vaccinated with either MMRV or separate MMR and varicella vaccines and found the MMRV vaccine to be associated with increased fever and seizures 7-10 days after vaccination," they wrote (Pediatrics 2010 June [doi:10.1542/peds.2010-0665]).

Researchers compared seizure risk following MMRV to that following MMR+V using regression analyses and by incorporating chart-reviewed febrile seizure cases.

They looked at Vaccine Safety Datalink (VSD) data on 83,107 MMRV vaccine recipients and 376,354 MMR+V recipients from 2000 to 2008. VSD's surveillance system monitors for potential

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Major Finding: In the 7- to 10-day postvaccination period, use of MMRV was associated with 4.3 additional febrile seizures per 10,000 doses, compared with separate administration of MMR and varicella vaccine.

Data Source: Vaccine Safety Datalink data on 83,107 MMRV vaccine recipients and 376,354 MMR+V recipients in 2000-2008.

Disclosures: Study funding came from the VSD contract with America's Health Insurance Plans, funded by the Centers for Disease Control and Prevention. Dr. Klein and Dr. Baxter have reported research support from Merck & Co, Novartis, GlaxoSmithKline, Wyeth, and Sanofi-Pasteur. The other authors reported no conflicts of interest.

associations between specific vaccines and adverse events using weekly data and sequential statistical analysis, according to investigators.

In the 7-10 days post vaccination, the MMRV vaccination was associated with 4.3 additional seizures per 10,000 doses. It was not associated with significantly elevated seizure risks during any of the five intervals outside that period, Dr. Klein and her colleagues said.

"Our study results show that both MMRV and MMR vaccines, but not vari-

cella vaccine alone, are associated with increased outpatient fever visits and seizures 7-10 days after vaccination, with MMRV vaccine increasing fever and seizure twice as much as the MMR plus varicella vaccines," the investigators reported.

"Providers who choose to use the combination vaccine should be aware of and clearly communicate this increased risk to the families and caregivers of their patients," Dr. Klein and her colleagues said. ■