

Making the Case for Universal HPV Vaccination

BY DOUG BRUNK
San Diego Bureau

CALGARY, ALTA. — As an epidemiologist whose research focuses on the prevention of cervical cancer, Dr. Eduardo L. Franco spends a lot of his time dispelling arguments and protests from other health care professionals and patients that more research is needed before universal human papillomavirus vaccination can be recommended worldwide.

"Although clinical experience has just passed 6 years, the evidence base is one of the strongest in disease prevention," Dr. Franco said at the annual meeting of the Society of Obstetricians and Gynaecologists of Canada. "The standard of proof is far more rigorous than that used in evaluation of candidate vaccines of the past. It may be the most scrutinized vaccine by the public and the media concerning need and safety."

Prophylactic HPV vaccines include a quadrivalent form made by Merck & Co. that was licensed in the United States in June 2006 and a bivalent form made by GlaxoSmithKline that was submitted to the FDA in March 2007.

Dr. Franco, director of the division of cancer epidemiology at McGill University, Montreal,

shared several examples of arguments against HPV vaccination that he encounters, followed by his counterargument for each.

One chief argument he hears is that the vaccine is too costly and unaffordable where it's most needed. However, he said, procurement programs such as the CDC's Vaccines for Children Program, the Global Alliance for Vaccines and Immunization, and the Pan American Health Organization's revolving fund should help to lower the cost. "Historically," he added, "prices decline with time since deployment."

Other common arguments against HPV vaccination include the following:

► **There are no data on long-term duration of protection.** In fact, to date, studies demonstrate a sustained antibody response with no indication that humoral immunity will wane before 10 years. "Even with lowered antibody titres, postvaccination protection has continued unabated," said Dr. Franco, who also is a professor of epidemiology and oncology at McGill. "We did not wait for such proof before deploying other vaccines."

► **Protection is limited; vaccines cover only two oncogenic types.** In fact, protection is against the

two most important types (HPV 16 and 18), which translates into a protective fraction of 70% of all cervical cancers. That protection "is likely to be expanded via cross-protection," he said. "In combination with tailored screening strategies, it may achieve unprecedented lifelong protection."

► **Screening will continue to be needed.** True, Dr. Franco said, but recent progress on new technologies such as HPV testing with Pap triage "will permit extending screening intervals safely and cost effectively. Proper integration of primary and secondary prevention strategies is likely to reduce costs and improve cervical cancer control."

► **There is a risk of type replacement, which occurred with the pneumococcal vaccine.** In fact, Dr. Franco said, type replacement is unlikely to occur because there is no epidemiologic proof that HPV types compete for specific niches. "Several studies have tested this hypothesis," he noted. "The fraction of the population not exposed to HPV 16 or 18 is always high; exposure to HPV 16 or 18

does not constrain the pool of susceptible individuals who could acquire other HPVs."

► **We should not vaccinate preteens and teens; there are no efficacy data on patients aged 9-14 years.** This age group is not at risk for lesions and monitoring

cancerous lesions is an acceptable end point," he explained.

► **There is no cervical cancer epidemic.** Dr. Franco asserts that the health costs, morbidity, and mortality associated with cervical cancer are sufficiently important to justify action and that the HPV vaccination is likely to exert protection against other neoplastic diseases such as oropharyngeal cancer and benign genital warts.

► **More research is needed on safety.** Dr. Franco responds to this argument by noting that the safety data on the HPV vaccine "are among the most well documented for any new vaccine. There was no waiting period for the adoption of other vaccines with lesser standards of proof. Inaction has a high cost in terms of morbidity and mortality that could have been averted."

Dr. Franco disclosed that his entire research program has been funded by the Canadian Institutes of Health Research (CIHR), the National Cancer Institute of Canada, and the National Institutes of Health. He has received a Distinguished Scientist salary award from the CIHR and has served as an occasional adviser to several companies with products related to cervical cancer prevention. ■



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them "would be unethical and unproductive," Dr. Franco said. "Immunobridging" studies show that vaccine-induced humoral response in preteens is the highest among all groups, "which is sufficient justification for expectation of benefit," he said.

► **There is no proof yet that vaccination can reduce the risk of invasive cancers.** Dr. Franco counters this notion by pointing out that absence of evidence is not evidence of absence. "Sensible judgment based on understanding of the natural history of HPV infection and cervical cancer indicates that prevention of pre-

Consider EBV in Patients With Genital Ulceration

BY SHARON WORCESTER
Southeast Bureau

DESTIN, FLA. — Since Epstein-Barr virus is known in rare cases to initially present as severe, painful genital ulcerations without other clinical or laboratory evidence of acute disease, this infection should be considered in the differential diagnosis of patients who present with such lesions.

"You won't see it presenting this way very often, but ... if you have young patients presenting like this, remember to test for EBV," Dr. Bari Cunningham said at a meeting sponsored by the Alabama Dermatology Society.

Dr. Cunningham, of the University of California, San Diego, described the case of a 15-year-old girl who presented with extremely painful vaginal lesions.

"Of course, sexually transmitted diseases were first and foremost on everybody's mind," she said, noting that the patient, who was adamant that she was not sexually active, was traumatized by the constant questioning about her sexual history and by the fact that no one believed her.

When the cultures came back negative, the differential was broadened, and Behçet's syndrome, systemic lupus erythematosus, pyoderma gangrenosum, and inflammatory bowel disease were among the diagnoses considered. The girl's conditioned worsened. She became sicker and



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stopped eating, and more skin surfaces became involved. She was noted to have a swollen liver.

All cultures up to that point were negative and a complete blood count was unremarkable; however, mild elevations on liver function tests, which developed during hospitalization, were noted, and the test for EBV immunoglobulin M came back positive.

Several cases of EBV presenting in this manner have been reported in the literature, Dr. Cunningham said. ■

Reimbursement Is Physicians' Top Concern on HPV Vaccine

BY ALICIA AULT
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NEW ORLEANS — Getting reimbursed is the top concern for physicians who offer the human papillomavirus vaccine, according to a survey conducted by researchers at Brigham and Women's Hospital, Boston.

Using a Web-based tool, Brigham resident Emily M. Ko and her colleagues surveyed 1,488 physicians who practiced with the Partners HealthCare System from May to July 2007. The survey included physicians practicing in tertiary and community settings.

Overall, 424 physicians participated. Of these, 87 (21%) were ob.gyn.s, 196 (46%) were internists, and 104 (25%) were pediatricians. The remainder came from various specialties, including infectious disease, geriatrics, endocrinology, and emergency medicine, Dr. Ko reported in a poster at the annual meeting of the American College of Obstetricians and Gynecologists.

Among participants, 80% said they offer the HPV vaccine. That included 92% of pediatricians, 81% of ob.gyn.s, and 78% of internists. According to the researchers, male physicians were 54% less likely to provide the vaccine than were female physicians. The survey did not ask questions that would determine why some physicians might be less likely to offer the vaccine, Dr. Ko said in an interview.

However, in citing barriers to vaccination, she noted that male physicians were six times more likely than female physicians to say that vaccination would keep patients from getting routine gynecologic exams or Pap smears.

Physicians based in community hospitals were twice as likely to offer the vaccine as were their colleagues at tertiary care facilities. Primary care physicians were 14 times more likely than specialists to offer the shot.

Overall, survey participants cited reimbursement as the No. 1 hurdle to offering the vaccine.

In all, 95% of physicians said the vaccine would not promote promiscuity or decrease the use of condoms. Of the remainder, 3% were neutral on the issue, and 1.4% said that the vaccine might promote promiscuity, according to Dr. Ko.

There was no difference between genders or among specialties on the promiscuity issue. However, 7% of physicians said that parents might fear that vaccination would promote sexuality and promiscuity. This was not reported as one of the biggest barriers to vaccination, said Dr. Ko. But among pediatricians, 19% said that parental fear was a barrier, making it the third biggest obstacle to vaccination.

Dr. Ko reported no conflict of interest disclosures. ■