

HPV Vaccine Marketing Practices Questioned

BY DIANA MAHONEY

Women at the highest risk for human papillomavirus infection were among the least likely to get the message that there is a vaccine that can protect them, editorialists said in a special communication published in JAMA.

Sheila M. Rothman, Ph.D., and David J. Rothman, Ph.D., of Columbia University, New York, contend that Merck & Co. promoted its quadrivalent human papillomavirus vaccine Gardasil as an anticancer agent, maximizing the threat of cervical cancer and minimizing the sexual transmission of the virus.

"Rather than concentrating on populations in geographic areas with excess cervical cancer mortality, including African Americans in the South, Latinos along the Texas-Mexico border, and whites in Appalachia, the marketing campaign posited that every girl was at equal risk," Dr. Rothman and Dr. Rothman wrote (JAMA 2009;302:781-6).

Further, Merck's marketing strategy included awarding "sizeable educational grants" to professional medical associations in adolescent and women's health

and oncology to encourage these organizations to undertake or intensify vaccination activities, according to the authors.

In an interview, Pamela Eisele, a spokeswoman for Merck, denied the claims. "We did not require any reporting or review of any materials developed," Ms. Eisele said. "Merck provides independent grant support to professional medical associations that develop and distribute their own educational information about HPV and cervical cancer to broad audiences."

"We value our relationships with these groups and conduct our interactions with strict adherence to the Pharmaceutical Research and Manufacturers of America Code on Interactions with Healthcare Professionals," said Ms. Eisele. "Merck closely follows the standards for commercial support of continuing medical education established by the Accreditation Council for Continuing Medical Education."

Dr. Rothman and Dr. Rothman charged that the role of several professional medical associations in the marketing of

the HPV vaccine "is cause for concern."

One recipient of Merck funding, the American Society for Colposcopy and Cervical Pathology (ASCCP), used the grant money to create a day-long program to educate its

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members on vaccine use. Further, the society developed a Gardasil-specific speaker support center that included a registry of members who completed the educational program and a database of when and where they presented, Dr. Rothman and Dr. Rothman said.

The ASCCP's member clinicians "have little occasion to recommend or deliver immunization," and could potentially see a negative economic benefit from a successful vaccination effort, yet "ASCCP leaders perceived vaccine promotion as an opportunity to turn a potential financial liability into an asset," and to re-energize its society,

according to Dr. Rothman and Dr. Rothman.

"That is not the case," Dr. L. Stewart Massad, chair of ASCCP's Practice and Ethics committees, said in an interview. "We have long recognized that the current [cervical cancer] prevention system is

flawed. Although prevention based on Pap testing, colposcopy, and destruction of precursors is effective, it is expensive, intrusive, insensitive,

and nonspecific, and it results in the overtreatment of thousands of women each year."

Given the potential for conflicts of interest associated with an industry-supported educational program, "we set up internal systems to evaluate the materials for bias, and I reviewed all of the materials independently," Dr. Massad said, noting that he accepts no financial support or grant money.

Merck also gave grant money to the Society of Gynecologic Oncologists (SGO) and the American College Health Association.

Dr. Rothman and Dr. Rothman wrote that the SGO was

concerned about its future as a subspecialty and perceived the HPV marketing opportunity as a way to springboard from a surgically-based to a medically-based discipline. The organization used the funding from Merck and other companies to create an education campaign, which was overseen by a panel that included some members with financial ties to Merck.

The materials created by the SGO panel "omitted cautionary qualifications," according to Dr. Rothman and Dr. Rothman. Further, the materials "did not include data on disparities in cervical cancer incidence and outcomes," nor did it include questions about the vaccine's history and efficacy, whether the risks outweigh the benefits, or a discussion of the continued need for Pap tests.

The ACHA used grant money to create an HPV Vaccine Toolkit for clinicians that includes talking points, sample e-mail messages, sample press releases, and public service announcements—none of which mention funding, according to the Dr. Rothman and Dr. Rothman. ACHA officials could not be reached for comment. ■

Chikungunya Fever: Could an Outbreak Happen Here?

BY BRUCE JANCIN

VAIL, COLO. — Chikungunya fever is a tropical disease few American physicians are familiar with—but that could change quite suddenly, as physicians in temperate northern Italy discovered.

This mosquito-borne disease marked by sudden high fever, arthralgia and myalgia, prominent skin rash, and headache occurs in sub-Saharan Africa and Asia. At least, that was true until August 2007, when an outbreak of 254 cases—1 fatal—struck out of the blue in the Ravenna province of northeastern Italy.

The traditional vector of Chikungunya virus is the *Aedes aegypti* mosquito. But when the virus underwent a mutation in a gene coding for a viral envelope protein, the mutant strain became at least 100-fold more infective for the *A. albopictus* mosquito, also known as the Asian tiger mosquito. The virus essentially jumped aboard a more competent vector.

Transmission by *A. albopictus* was responsible for a 2005-2006 outbreak of 500,000 cases of Chikungunya fever in the Reunion Islands off the eastern coast of Africa. The outbreak then spread to India and Sri Lanka, where it caused more than 1.3 million cases, Dr. Kenneth L. Tyler explained at a conference on pediatric infectious diseases sponsored by The Children's Hospital, Denver.

"This would all be sort of a weird and

remarkable event occurring in an out-of-the-way part of the world if it weren't for a cautionary development in Italy," added Dr. Tyler, professor of neurology, medicine, and microbiology at the University of Colorado.

The disease was imported to northern Italy by a traveler from India who arrived June 21, 2007, got sick 2 days later, and somewhere along the line was bitten by the *A. albopictus* mosquitoes endemic in that area. The virus quickly established itself in the regional *A. albopictus* population. The Italian outbreak ensued.

Could something similar occur in the United States? As it happens, *A. albopictus* is endemic throughout the southeastern United States. The mosquito is thought to have arrived in 1985 via the port of Galveston, Tex., in a shipment of tires from Southeast Asia and has since gradually spread through much of the south. And 37 U.S. cases of Chikungunya fever imported from the Indian Ocean outbreak have been documented, including 5 viremic patients. Two of those five returned to Louisiana and South Carolina, states where *A. albopictus* is endemic. So perhaps a U.S. outbreak was a near-miss.

Chikungunya fever is a dengue fever-like illness characterized by 2-5 days of sudden-onset high fever and chills, and a petechial or maculopapular rash, mainly on the trunk. This is followed by arthralgia disease that can last



A public health billboard in Barcelona sends a warning about the Asian tiger mosquito.

weeks or months. Indeed, the root of the word "Chikungunya" in Tanzania, where the virus was first isolated in the early 1950s, comes from a verb for "to become contorted" in local dialect, reflecting the severe joint symptoms.

Neurologic manifestations of Chikungunya fever in children include en-

cephalitis, meningitis, and febrile seizures. In adults, meningitis and encephalitis can occur early, during the acute febrile stage of the disease, with acute neuropathy and myelitis occurring later.

Dr. Tyler offered Chikungunya fever as an example of an emerging CNS viral infection moving into new geographic regions as a result of expanded vector competence. But he noted that just as new viral diseases can emerge, once-familiar and important ones can recede or submerge, for unexplained reasons.

Case in point: Western equine encephalitis, which has mysteriously disappeared from the U.S. scene in recent years. In fact, there hasn't been a single reported case since the turn of the century.

"The virus still circulates. It doesn't seem to be less virulent in mouse studies. It just doesn't seem to be an important cause of human encephalitis anymore—and why it was but isn't now we don't know. The virology doesn't seem to provide an explanation," he observed. "It makes one a little bit uncomfortable, because just like things can disappear they can reappear." ■