HPV Vaccine Cost Makes Some Doctors Hesitate

Private providers could pay between $10,000 and $15,000 in vaccine inventory per month.

BY PATRICE WENDLING
Chicago Bureau

KANSAS CITY, MO. — In the rush to mandate the human papillomavirus vaccine, several implementation issues, not the least of which is cost, remain unresolved, Dr. Howard Backer said at the National Immunization Conference sponsored by the Centers for Disease Control and Prevention.

Private providers can expect to pay between $10,000 and $15,000 in vaccine inventory per month when adding in the human papillomavirus (HPV) vaccine approved for use in girls and women aged 9-26 years.

For a multiprovider practice with five to six physicians who provide childhood vaccines, inventory costs could add up to about $100,000 a month.

"A lot of them aren't willing to put out that much money up front when it may take months before they're reimbursed," said Dr. Backer, immunization branch chief, California Department of Health Services in Sacramento, and chair of the Association of Immunization Managers.

The American Medical Association and American Academy of Pediatrics are working on ways of addressing this. But for now, it means a lot of providers aren't jumping into HPV vaccinations.

"They thought it was a good idea until they looked at what it really meant to buy that much vaccine for their practice[s]," he said.

In addition, reimbursement for vaccine administration costs, which include staff time, storage equipment, injection supplies, and possibly even insurance against vaccine loss, is woefully inadequate. It is often about $5-$10 per administered dose, and probably should be at least 20%-25% above vaccine cost, which is approximately $120 per dose, with three doses required over 6 months.

Private providers can sign up with the federal Vaccines for Children (VFC) program, which allows clinicians to receive free vaccines for qualified individuals up to age 18.

But this leaves two problem populations—women ages 19-26 years, and the underinsured, whose insurance may not cover vaccinations.

Dr. Backer presented a recent Association for Immunization Managers survey of 50 program managers that shows 72% of states provide HPV vaccine to VFC-eligible children. About half (53%) of the program managers use Medicaid funds to cover vaccinations for women ages 19-26 years, whereas very few cover the underinsured in the private (22%) or public (30%) settings.

"It's a challenge to fund this vaccine across the spectrum of girls and women for whom it is recommended," he said in an interview. "The numbers are increasing as the states add funding or pass insurance mandates, but I doubt it will reach 100% coverage for 9- to 26-year-old females."

Many private insurance companies have not yet decided if they will cover the vaccine, and some states have been hesitant to commit beyond the 11- to 12-year-old age group until they receive the necessary state appropriations and are reassured they will have enough vaccine for the VFC population.

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DR. BACKER

Still, a number of new nontraditional vaccine providers such as STD clinics, family planning offices, and pharmacies are expressing interest in the vaccine. Although enthusiastic, many have a poor understanding of vaccine implementation issues and lack the necessary office infrastructure, Dr. Backer said.

"Quality assurance is a major issue," he said. "I would submit … that our standard VFC AFIX [Assessment, Feedback, Incentive, eXchange] visit is not going to work for these nontraditional providers."

Moreover, some of the new partners, such as ob.gyns., want to provide only the HPV vaccine. Under VFC rules, providers are supposed to offer all vaccines for which the patient is eligible.

"I think we can get gynecologists to give HPV, but it's probably too much to tell them to give Tdap and meningococcal and other vaccines at the same time, at least until they get their program up and running," he said.

It is unclear whether an exemption will be made for these new partners. Currently, permission is granted on an individual basis by the CDC to states that want to obtain exemptions or add new rules to the VFC program requirements.

It's also unknown whether new VFC requirements can be added to ensure that HPV immunizations given by nontraditional providers are entered into an immunization registry or whether notification of the vaccinations will be sent to primary care providers. Finally, Dr. Backer questioned whether the emergence of nontraditional HPV vaccine providers would jeopardize the medical home model, upon which the VFC program was based, if patients opt to bypass their physician's office in favor of their local pharmacy. ■

Consider Newer Therapies to Treat New Strain of *C. difficile*

BY JOHN R. BELL
Associate Editor

STOWE, VT. — Although *Clostridium difficile*–associated diarrhea is now more severe and more drug resistant than before, because of the evolution of a recently identified and more robust strain, a variety of new agents are in the pipeline.

And in some patients, several current treatments can effectively eliminate the organism, according to Dr. Samuel Pegram, who spoke at an emergency medicine update sponsored by the University of Vermont.

C. difficile, first identified in 1935, has evolved from a fairly benign bacterium to a multidrug-resistant pathogen that is responsible for an increasing portion of pediatric and adult cases of severe diarrhea, known as *C. difficile*–associated diarrhea or disease (CDAD), said Dr. Pegram, professor of medicine at Wake Forest University, Winston-Salem, N.C.

Currently, the pathogen is present in up to 30% of patients who have antibody-associated diarrhea, he said, and up to 65% of patients with antibody-associated colitis test positive for the bacterium. He cited a recent study that found that among children presenting to an emergency department with diarrhea, 47% had a bacterial pathogen, and nearly 7% were infected with *C. difficile* (Clin. Infect. Dis. 2006;43:807-13).

Moreover, a new strain is responsible for greater symptom severity and is resistant to many traditional therapies. This strain is known by various names, including BI, NAP1, ribotype 027, and toxinotype II, depending on what type of analysis is used to identify it in a particular laboratory. This new variant produces 16 times the amount of toxin A as prior strains and 23 times the amount of toxin B as toxinotype 0 strains, said Dr. Pegram, who is also the director of the Infectious Diseases Specialty Clinic at the university. In addition, the new subtype shows resistance to fluoroquinolones, including ciprofloxacin.

Several new treatments are in the developmental pipeline, however. They include tolevamer, a nonantibiotic toxin-binding polymer expected go on the market this year, and the antibiotic ramoplanin (Oscient Pharmaceuticals), which is in phase III trials, as is the novel macrocycle OPT-80 (Optimer Pharmaceuticals). An antibiotic called Rifalazil (ActivBiotics Inc.) is in phase II development, along with a monoclonal antibody to toxin A and B (Medarex Inc.). In addition, a toxoid vaccine is in phase I development (Acambis).

Yet the mainstream therapies for infection are still viable in many patients, though they have various abilities to overcome recurrence and come with a wide range of treatment costs, Dr. Pegram noted.

The least expensive treatment, at $18 for a 10-day course, is generic metronidazole 500 mg orally three times daily, he said, although a brand formulation also exists (Flagyl, Pfizer Inc.), costing $147 for the same treatment duration. Vancomycin (Vancocin, Viropharma Inc.), for which no generic exists, costs $611 for 10 days. Dr. Pegram estimated recurrence rates to be 20%-25% with metronidazole or vancomycin. Toxin-binding resins currently available include cholestyramine and colestipol.

Other weapons in the physician's arsenal are the oral antibiotic rifaximin (Xifaxan, Salix Pharmaceuticals), approved for *E. coli*–associated traveler's diarrhea in patients at least 12 years old, and nitazoxanide (Alinia, Romark Laboratories), approved for treatment of diarrhea caused by *Giardia lamblia* or *Cryptosporidium parvum*.

Probiotic agents including yogurt, yeast, and oral lactobacillus may also be effective, he noted. Brands of lactobacillus include Lactinex (Becton Dickinson) and Culturelle (Kirkman). Yeast products include *Saccharomyces boulardii* and Florastor (Biocodex Inc.), which he said can be given in a dosage of two 250-mg capsules daily for 4-6 weeks.

In addition to pharmacologic and probiotic therapy, there remains the option of fecal transplantation to replenish the decimated gut flora, Dr. Pegram said. This can be done by collecting 30-50 g of fresh stool from a healthy donor and delivering it in a saline vehicle via either an enema or a nasogastric tube. Despite the perhaps unsettling nature of this treatment, "it certainly has worked," Dr. Pegram said, although it carries a risk of transmitting other pathogens to the recipient. Thus, this option "is less desirable," he said.

Intravenous immunoglobulin is also an option, he said. "Half the people sitting in this audience will have detectable antitoxin to toxins A and B," said Dr. Pegram. Thus "pooled intravenous immune globulin might work. You give it as a one-time dose—a large dose and very expensive—400 mg/kg. And it's actually proven to be a very valuable asset when adding on therapy to the very sick patient."

He noted that research is underway to develop a "hyper–immune globulin" by using plasmapheresis to cull these antibodies from persons with high antibody levels.

Dr. Pegram also noted that the Centers for Disease Control and Prevention has outlined steps that health care providers can take to prevent the spread of *C. difficile*. Perhaps most surprising is the admonition to use soap and water instead of alcohol-based sanitizers—which, he pointed out, can kill other hardy bacteria, such as methicillin-resistant *Staphylococcus aureus*, but not *C. difficile*.

A polymerase chain reaction test for detection of *C. difficile* toxin will likely be introduced this year, Dr. Pegram said. ■