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Health Care Worker Pertussis Shots New Standard of Care for Hospitals

SPECIAL FEATURE

By Gary Evans

This article originally appeared in the April 2006 issue of Hospital Infection Control.

Gary Evans reports no financial relationships relevant to this field of study.

Travel Medicine providers often advise health care workers and volunteers headed for the developing world. There they are certain to encounter many pediatric patients. One should consider administering a single dose booster for health care providers using the new tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis vaccine (Tdap), recently approved for people between the ages of 11 and 64.

HEALTH CARE WORKERS WHO CARE FOR INFANTS YOUNGER THAN 12 months old should be the first in line to receive the new pertussis vaccine, the Centers for Disease Control and Prevention recommends.

"They would be first, then all other health care workers that have direct contact with patients would be the second priority," says Trudy Murphy, MD, a medical epidemiologist with the CDC national immunization program.

The CDC's Advisory Committee on Immunization Practices (ACIP) recently issued the recommendation to protect health care workers and their patients, particularly neonates who would not be indicated for pertussis vaccination but may be vulnerable to complications after infection.

"Hospitals should determine where their pertussis exposures take place," says William Schaffner, MD, chairman of the department of preventive medicine at the University of Vanderbilt Medical Center in Nashville, TN, and a liaison member of ACIP representing the National Foundation for Infectious Diseases. "Virtually all of ours take place in our children's hospital. We anticipate that the leadership of our children's hospital will want to provide [pertussis] immunization for literally everyone who works there as quickly as possible."

Beyond such priority areas, hospitals are expected to phase in the recommendations by targeting new hires and using other strategies to gradually add the pertussis vaccine to their employee immunization regimen.

"The ACIP workgroup did not anticipate that—absent an outbreak of pertussis in the community—hospitals would conduct crash programs to implement this," he says. "But they want all hospitals to note this as a new obligation."

CDC cost estimates project an overall savings for hospitals implementing the immunization program but, regardless, immunizing workers for pertussis is a new standard of care.

"[The cost savings] argument is helpful, but you are always asking an administration to lay out money now in anticipation of future savings," Schaffner explains. "If budgets are tight, then that is a harder argument to make. But this is now going to be a new standard of care for institutions and their employees, so it will be very important."

Questions remain on PEP

However, an unresolved issue is the administration of post-exposure prophylaxis (PEP) to vaccinated workers exposed to a pertussis case. Additional studies need to be done to determine whether immunized workers could forego PEP antibiotics after exposure to pertussis-infected patients. "If we can learn in the near future that PEP is not needed if a health care worker is vaccinated, additional cost savings could be possible," Murphy says.

One would anticipate that the vaccine would be protective, but there is a dearth of data to support that assumption. "Let's say we immunize everyone at our children's hospital," Schaffner says. "Now we get a pertussis exposure. Do you have to work up that exposure and give—according to current indications—certain personnel antibiotic prophylaxis anyway? The problem is that there are not any compelling data."

The standard of care in pediatric practice is that PEP should be administered following "close and prolonged" contact even if the exposed child has been immunized, he notes. "We're still working on the exact wording, but [ACIP] will say that if an immunized person is exposed to pertussis, there are 2 ways the hospitals can handle this, and they are both acceptable," Schaffner explains. "One is to give antibiotic prophylaxis. The other [approach] is put that person under surveillance and permit them to continue to work if they don't develop symptoms. The unit manager or someone in occupational health could check in with them on a daily basis for the incubation period of pertussis. If they then develop symptoms, immediately offer them treatment and excuse them from work. Both are acceptable strategies."

ACIP is going to give infection control professionals the option, "but you can't just do nothing," he stresses. "You have to at the very least put your exposed person under surveillance, and that's because we don't have any data in this kind of setting to provide assurance to hospitals that they don't have to worry about it."

In a unanimous vote described as a slam-dunk by one committee member, ACIP approved the recommendation at a Feb. 22 meeting in Atlanta. The provisional recommendation now awaits finalization by the CDC, which is expected to approve it and make it an official employee health guideline.

"This will be perceived as a new challenge, but the recommendations are strong, the scientific basis is accurate and we look forward to helping institutions implement it," Schaffner says. "I know our institution is planning to do so."

Nosocomial outbreaks disruptive, costly

Large outbreaks of pertussis have occurred in health care facilities through failure to recognize and isolate infected infants and children, failure to recognize and treat disease in staff members, and failure to institute infection control measures rapidly.[1] Expensive and time-consuming follow-up in such cases may include work furloughs

for some workers and PEP with antibiotics. While droplet spread is considered the primary mode of transmission, several well-described hospital outbreaks have occurred in which *Bordetella pertussis* was thought to be transmitted to or from health care workers in a manner suggesting airborne transmission.[2] Most hospital outbreaks have involved pediatric patients. No prolonged carrier state has been identified, and transmission is most likely associated with active symptoms, particularly coughing.[3,4] The use of air samplers and polymerase chain reaction analysis has shown that *B. pertussis* DNA can be found in the air surrounding patients with *B. pertussis* infection, providing further evidence of airborne spread.[5]

Pertussis infection control changed dramatically last year with licensure of a tetanus toxoid, reduced diphtheria toxoid (Td), and acellular pertussis vaccine (Tdap), which is designed as a single dose booster vaccine for people 11-64 years of age. It provides protection against tetanus, diphtheria, and pertussis. Although most children are protected against pertussis by vaccination during childhood, immunity wanes over time and leaves adults unprotected. In 2004, US adults 19-64 years of age accounted for 7008 of 25,827 (27%) reported pertussis cases. The true number of cases among adults 19-64 years is likely much higher, estimated at 600,000 each year, ACIP reports.

Similarly, many nosocomial cases are likely flying under the radar as well. "One [problem] is simply education and awareness," Schaffner says. "Adult practitioners virtually never think of pertussis. Awareness is one thing, and the other is that it is very difficult to make the diagnosis because we do not have a readily available diagnostic test. We are all waiting for the FDA to act on a blood test that would help us diagnose pertussis."

The clinical presentation of pertussis in adults ranges from mild cough illness to classic pertussis (ie, prolonged cough characterized by paroxysms, posttussive emesis, and inspiratory whoop), ACIP reports. Complications include rib fractures resulting from severe cough and pneumonia requiring hospitalization.

The recommendation approved by ACIP states: "Health care personnel who work in hospitals or ambulatory care settings and have direct patient contact should receive a single dose of Tdap as soon as feasible if they have not previously received Tdap. Priority should be given to vaccination of health care personnel with direct contact with infants aged younger than 12 months old. An interval as short as 2 years from the last dose of Td is recommended for the Tdap dose. Other health care personnel (ie, those who do not work in hospitals or ambulatory care settings or who do not have direct patient contact) should receive a single dose of Tdap according to the routine recommendation and interval guidance for use of Tdap among adults. However, these personnel are encouraged to receive the Tdap dose at an interval as short as 2 years following the last Td. Hospitals and ambulatory care facilities should provide Tdap for health care personnel and use approaches that maximize vaccination rates such as education about the benefits of vaccination, convenient access, and provision of Tdap at no charge."

Contraindications to Tdap include a history of serious allergic reaction (ie, anaphylaxis) to vaccine components or a history of encephalopathy (eg, coma, prolonged seizures) not attributable to an identifiable cause within 7 days following administration of a pertussis vaccine. Pregnancy is not a contraindication to Tdap or Td vaccination. However, guidance on the use of Tdap during pregnancy is under consideration by ACIP. Currently, pregnant women who received the last tetanus toxoid-containing vaccine fewer than 10 years earlier should receive Tdap after delivery, according to routine recommendations for vaccinating adult contacts of infants younger than 12 months of age. Women who received the last tetanus toxoid-containing vaccine more than 10 years earlier should receive Td during pregnancy in preference to Tdap. Pregnant women who have not received the primary 3-dose vaccination series for tetanus should begin the Td series during pregnancy. If Td is indicated during pregnancy, vaccinating during the second or third trimester is preferred when feasible.

Precautions and reasons to defer Tdap include Guillain-Barré syndrome within 6 weeks after a previous dose of a tetanus toxoid-containing vaccine, moderate to severe acute illness, unstable neurological condition, or a history of Arthus hypersensitivity reaction to a tetanus toxoid-containing vaccine administered within the last 10 years.

A jump-start for hospitals

In essence, the vast majority of health care workers would be covered by a previously approved general recommendation to immunize adults younger than 65 years old, but ACIP is trying to jump-start the issue in hospitals.

"There is now a provisional recommendation, as of October 2005, that all adults [younger than 65] receive a dose of the Tdap vaccine to replace the next tetanus booster that they would be scheduled to have," Murphy says. "What this recommendation says is that we want hospital health care workers to get this vaccine as soon as possible—if at least 2 years has passed since their last tetanus and diphtheria booster—in order to protect them from pertussis and any patients they might expose."

The aforementioned 2-year time frame is based on the fact that the pertussis vaccine is a combination formula

with tetanus and diphtheria, and shots for the latter 2 may have been recently administered. "The issue has to do with a small concern about safety," Schaffner says. "If you got Td and then got Td again as part of Tdap, would you get more of a local reaction? There are data to support the notion that you can give Tdap as early as a year and a half or two years after your previous Td."

Most hospitals not routinely using Td

The issue is not likely to be a major complication because most hospitals are not routinely immunizing workers with for tetanus and diphtheria. "It was the sense of the ACIP working group that the majority of hospitals are not providing Td as an employee benefit," he says. "They may be providing it to some people, certainly after an injury in terms of injury management, but not as an ongoing preventive immunization. So for those hospitals that are not already doing that it will clearly take some getting used to gear up for that."

Indeed, that raises the question about how to implement the recommendations in a timely fashion. "The ACIP working group spent a fair amount of time talking about the feasibility issues," says Schaffner. "There are 2 ways to think about it. The first is to assess [and immunize] all new hires, and in a gradual fashion assess all of your current personnel according to some system. Then provide Tdap as needed and appropriate and gradually fold this in over a period of time—a year, 2, or 3 years."

The ACIP approved the recommendation unanimously with relatively little discussion, which primarily centered on cost issues for hospitals and assurances that workers would not be charged for the vaccine.

"Whenever a recommendation is made that increases a hospital's cost, people will want good evidence that they will benefit from it," Murphy says. "In this case, we are quite certain that there will be benefits for the health care worker and for preventing transmission to others in the health care setting. At this time, because we do not have any studies to demonstrate it, we can't predict what the cost savings will be for hospitals implementing these programs, but our modeling [studies] suggest that there will be cost savings."

CDC projected cost benefits indicate that every dollar invested in pertussis vaccine will reap $2.40 for the institution in prevented infections, exposures, and infection control measures. The CDC model is based on a recently published study of 17 symptomatic cases of pertussis among health care workers that resulted from exposure to an infant who was later confirmed to have pertussis.[6] The health care workers in turn had 307 close contacts, so the hospital had to implement extensive infection control and follow-up measures. Investigators determined costs by interviewing infection control and hospital personnel, reviewing billing records, and surveying symptomatic workers. They calculated the benefits and costs of a vaccination program for health care workers using a model to estimate the number of pertussis exposures that would require control measures annually. The cost the outbreak was $81,382, including costs incurred by health care workers of $6512.

"A Tdap vaccination program in health care workers could have a substantial impact in reducing hospital-acquired pertussis morbidity by reducing the number of annual [pertussis] exposures by 46%," said Ismael Ortega-Sanchez, PhD, a researcher in the national immunization program at the CDC. "Benefits or savings from Tdap vaccination could be sizeable for hospitals even after they cover program costs." ■

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CME Objectives

The objectives of Travel Medicine Advisor are:

• To present the latest data regarding the diagnosis and treatment of various travel-related diseases;

• To present new data concerning recommended precautions and prophylaxis for patients traveling to specific areas of the world; and

• To alert the readers to recent disease outbreaks and epidemics. ■

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Reversal of Atherosclerosis Via Intensive Statin Therapy

Aggressive LDL lowering with statins, so-called "very intensive statin therapy," leads to reversal of coronary atherosclerosis, according to a new study. The ASTEROID (A Study to Evaluate the Effect of Rosuvastatin on Intravascular Ultrasound-Derived Coronary Atheroma Burden) trial, a perspective, open label, blinded end-points trial, utilized the potent statin rosuvastatin in evaluating whether very intensive statin therapy resulting in LDL cholesterols in the low 60s associated with increases in HDL cholesterol could reverse atherosclerosis. Five hundred and seven patients were initially evaluated with intravascular ultrasound (IVUS) to determine baseline atheroma burden. Patients were then treated with intensive statin therapy with rosuvastatin 40 mg daily for 24 months, which resulted in an average LDL cholesterol of 60.8 mg/dL (mean reduction, 53.2%) and increased HDL cholesterol by 14.7%. IVUS was performed again at 24 months. The mean change in atheroma volume in the most diseased 10 mm sub segment was -6.1 (10.1) mm^3, with a median of -5.6 mm^3 ($P < .001$ vs baseline). Change in total atheroma volume showed a 6.8% median reduction. Adverse events were infrequent. Specifically there were no cases of rhabdomyolysis.

The authors conclude that lowering LDL-C to levels below currently accepted guidelines, when accompanied by significant increases HDL-C, can regress atherosclerosis in coronary disease patients, and is indicated for high-risk patients with established coronary disease (*JAMA*. 2006;295:1556-1565). An accompanying editorial notes that the study had several limitations, including lack of a control group or a comparator drug. They also note that the modest plaque reduction noted in this study "may not be the best measure of the treatment's effect on hard cardiovascular end points", however, they do applaud the pioneering work using intravascular ultrasound to help understand the anatomy and pathophysiology of coronary atherosclerosis and the effect of medical therapy on atheroma (*JAMA*. 2006;295:1583-1584).

Alternative Therapy for Depression?

Patients who fail SSRI treatment for depression may respond to an alternative medication, or the addition of a second medication, according to 2 studies in the March 23 *New England Journal of Medicine*. In the first study, 727 adults with a nonpsychotic major depressive disorder who had no remission of symptoms or could not tolerate the SSRI citalopram (Celexa) were randomized to receive sustained release bupropion

This supplement was written by William T. Elliott, MD, FACP, Chair, Formulary Committee, Kaiser Permanente, California Division; Assistant Clinical Professor of Medicine, University of California-San Francisco. In order to reveal any potential bias in this publication, we disclose that Dr. Elliott reports no consultant, stockholder, speaker's bureau, research, or other financial relationships with companies having ties to this field of study. Questions and comments, call: (404) 262-5416. E-mail: leslie.hamlin@thomson.com.

(Wellbutrin) in a maximal daily dose of 400 mg, sertraline (Zoloft) at a maximum daily dose of 200 mg, or extended release venlafaxine (Effexor-XR) at a maximal daily dose of 375 mg for up to 14 weeks. The primary outcome was remission of symptoms based on the Hamilton Rating Scale of Depression (HRSD-17). Secondary outcomes included scores on the Quick Inventory of Depressive Symptomatology (Self-Report) (QIDS-SR-16). Remission rates, as assessed by the 2 scales, respectively, were bupropion - 21.3% and 25.5%, sertraline - 17.6% and 26.6%, venlafaxine - 24.8% and 25.0%. Response rates based on the QIDS-SR-16 were bupropion 26.1%, sertraline 26.7%, and venlafaxine 28.2%. There was no significant difference with respect to outcomes, tolerability, or adverse effects among the 3 drugs.

The authors conclude that after unsuccessful treatment with an SSRI, 1 in 4 patients have a remission after switching to another antidepressant, and all 3 drugs in the trial were reasonable choices (*N Engl J Med*. 2006;354:1231-1242). Another option for treating patients who failed treatment with citalopram was explored in the second study in the same issue. In the study, 565 adults who had a nonpsychotic major depressive disorder without remission after 12 weeks of citalopram therapy were randomized to receive add-on therapy with sustained release bupropion up to 400 mg per day, and 286 were randomized to receive buspirone (Buspar) at a dose of up to 60 mg per day. The same depression rating scales were used in this study as in the previous study. For bupropion and buspiron, respectively, HRSD-17 remission rate was 29.7% vs 30.1%, QIDS-SR-16 remission rate was 30.9% vs 32.9%, and QIDS-SR-16 response rate was 31.8% vs 26.9%. Bupropion was associated with a greater change in QIDS-SR-16 score, as well as the overall lower QIDS-SR-16 score at the end of the study and a lower dropout rate to due to intolerance (12.5% vs 20.6%, $P < 0.009$).

The authors conclude that the addition of bupropion or buspirone to citalopram is useful; however, the addition of bupropion may have some advantages, including a greater reduction in the severity of symptoms in fewer side effects (*N Engl J Med*. 2006;354:1243-1252).

FDA Actions

The FDA has approved the first generic HIV/AIDS drug for use in the United States. Zidovudine, manufactured under the trade name Retrovir by GlaxoSmithKline, was initially approved in 1987, and the company has had exclusive manufacturing rights until the drug's patent expired in September 2005. The generic is made by Aurobindo Pharma LTD of India. This is the same company that recently received approval from the FDA to co-package 3 antiretroviral drugs for the treatment of HIV/AIDS outside the United States. The regimen consists of lamivudine/zidovudine combination tablet along with efavirenz tablets. The co-packaging of these products has met the clinical safety, efficacy, and manufacturing quality standards required by the FDA. The approval is part of the Presidents Emergency Plan for offering full HIV treatment regimens for targeted areas of the world that are at risk to prevent HIV transmission and to treat AIDS and associated conditions. Patents and exclusivity prevent marketing of this combination in United States.

The FDA has approved a transdermal patch for the treatment of children with attention-deficit hyperactivity disorder. The patch delivers methylphenidate, the same ingredient found in Ritalin, in a daily patch that is applied early in the morning and removed 9 hours later. Methylphenidate patch is manufactured by Shire Pharmaceuticals and Noven Pharmaceuticals under the trade name Daytrana.

Salix pharmaceuticals has received approval to market a new tablet bowel prep for colon cleansing prior to colonoscopy. The virtually tasteless sodium phosphate tablets are an alternative to traditional liquid PEG bowel preps. The recommended dose is 32 tablets taken orally with a total of 2 quarts of clear liquids, administered as 4 tablets with 8 ounces of liquid every 15 minutes. Twenty tablets are given on the night prior to the procedure, with the remaining 12 tablets administered 3 to 5 hours prior to colonoscopy. Sodium phosphate tablets will be manufactured under the trade name OsmoPrep. ■