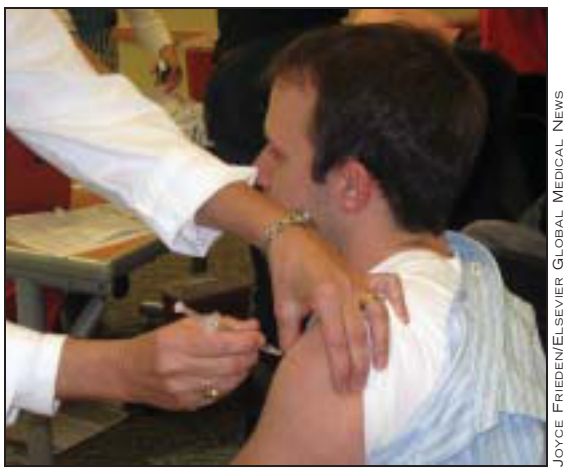
Concomitant Vaccine Dosing Safe, Effective

BY MITCHEL L. ZOLER

PHILADELPHIA — Administering two or more vaccines simultaneously was safe and immunogenic in results from two separate studies reported at the annual meeting of the Infectious Diseases Society of America.

One study assessed the immune response when healthy girls received concomitant vaccination with a human papillomavirus (HPV) vaccine along with a vaccine for tetanus, diphtheria, and pertussis (Tdap), and a third vaccine with a quadrivalent, conjugated meningococcal formulation (MCV4). The second study tested coadministration of the 2007-2008 seasonal influenza vaccine with an investigational, 13-valent, conjugated pneumococcal vaccine in adults aged 50-59 years.



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Simultaneous administration of more than one vaccine did not impair immunogenicity.

The first study enrolled 1,283 healthy girls aged 11-18 years at 48 U.S. centers. The researchers randomized the participants to one of six different treatment schemes: HPV vaccine only at months 0, 1, and 6; HPV with Tdap at month 0 followed by HPV only at months 1 and 6; HPV with the meningococcal vaccine at month 0 followed by HPV only at months 1 and 6; all three vaccines at month 0 followed by HPV only at months 1 and 6; Tdap only at month 0 followed by HPV only at months 1, 2, and 7; and MCV4 only at month 0 and then HPV only at months 1, 2, and 7, said Cosette M. Wheeler, Ph.D., professor of pathology and obstetrics and gynecology at the University of New Mexico in Albuquerque.

Her study used the Cervarix formulation of HPV vaccine, the Boostrix formulation of Tdap, and the Menactra formulation of meningococcal vaccine. The Cervarix and Boostrix vaccines are marketed by GlaxoSmithKline, which funded the study. Menactra is marketed by Sanofi Pasteur.

The results showed that 1 month after the subjects received any of the concomitant doses, their immune responses all fell within the prespecified criteria for noninferiority, compared with the responses when the vaccines were administered individually. Also, the immune responses to the HPV vaccine 6 months after the final dose, when one dose was given in combination with one or two of the other vaccines, were noninferior to the responses to the HPV vaccine given by itself. The recipients of two or more simultaneous vaccines also had similar incidence rates for adverse events.

The second study examined concomitant administration of an investigational, 13-valent, conjugated pneumococcal vaccine and the trivalent, seasonal influenza vaccine of 2007-2008 in 1,106 healthy adults aged 50-59 years who had no history of previously receiving a pneumococcal vaccine, said Dr. Robert W. Frenck Jr., professor of pediatrics at Cincinnati Children's Hospital Medical Center.

He and his associates randomized subjects to receive either the pneumococcal and flu vaccines together at month 0 followed by placebo at month 1, or the flu vaccine and placebo at month 0 followed by the pneumococcal vaccine at month 1.

One month after vaccination, the immune responses to both vaccines in people who received them simultaneously fell within the prespecified noninferiority limit, compared with the responses in people who received the two vaccines 1 month apart, Dr. Frenck reported. Simultaneous administration also resulted in similar rates of local and systemic reactions compared with giving the vaccines 1 month apart. ■

Disclosures: *Dr. Wheeler has received research support from GlaxoSmithKline, Merck (which markets the HPV vaccine Gardasil), and Roche Molecular Systems. Dr. Frenck's study was funded by Wyeth, which developed the pneumococcal vaccine; he had no other disclosures.*

THE EFFECTIVE PHYSICIAN

Intravascular Catheter-Related Infections

BY WILLIAM E. GOLDEN, M.D., AND ROBERT H. HOPKINS, M.D.

Background

Hospitals and clinics purchase more than 150 million intravenous devices in the United States annually; these are associated with approximately 80,000 catheter-related infections in ICUs, as well as uncounted infections in other settings. The Infectious Diseases Society of America published a revised guideline addressing this common issue in mid-2009.

Conclusions

The risk of bloodstream infection varies according to the type of catheter, insertion site, experience and skill of the person inserting the catheter, frequency with which the catheter is accessed, duration the catheter is in use, staff adherence to methods shown to reduce catheter infection, and patient-related factors.

Most catheter-related infections originate at the insertion site, catheter hub, or both.

The most common microbes causing infections in percutaneously inserted uncuffed catheters are, in order of prevalence, coagulase-negative staphylococci, *Staphylococcus aureus,* Candida species, and enteric gram-negative bacilli. In contrast, surgically implanted catheters are most commonly infected with coagulase-negative staphylococci, enteric gram-negative rods, *S. aureus,* and *Pseudomonas aeruginosa*.

Clinical signs and symptoms have poor sensitivity and specificity for the diagnosis of catheter-related infection. Fever is the most sensitive sign, but it has very poor specificity. Paired cultures (from catheter blood or tip culture and a peripheral blood culture, or from two separate catheter lumens) must grow the same organism to make a definitive diagnosis of a catheter-related bloodstream infection.

Implementation

Screening catheter cultures should not be obtained, but cultures should be obtained when a catheter is removed for suspected infection.

Paired blood cultures should be obtained from the catheter and a peripheral vein prior to starting antimicrobial therapy for suspected catheter-associated infection. If peripheral blood samples are not available, samples from two or more catheter lumens should be sent for culture. The catheter tip should be submitted for culture if the catheter is removed.

If available, culture samples should be obtained by a phlebotomy team using site and catheter prep in accord with recommendations to minimize the risk of skin contamination.

Empiric vancomycin is recommended for suspected catheter-associated bloodstream infection in health care settings with elevated prevalence of methicillin-resistant *S. aureus*; in those institutions in which the vancomycin minimum inhibitory concentration (MIC) exceeds 2 mcg/mL, alternative agents such as daptomycin should be substituted.

Linezolid should not be used empirically for suspected catheter-associated bloodstream infection.

The choice of empiric gram-negative coverage should be based on the local institution's antimicrobial susceptibility data and the severity of the patient's illness.

Empiric combination antimicrobial treatment, including drugs effective for multidrug-resistant gram-negative organisms, is recommended when catheter-associated infection is suspected in patients who are neutropenic, have sepsis, and who have been colonized with these bacteria. The antimicrobial agents may be reduced once culture and sensitivity data are available.

Treatment for suspected catheter-associated bloodstream infection in critically ill patients with femoral catheters should include antimicrobials that cover for gram-positive and gram-negative bacteria and for Candida species.

Catheter-associated Candida infection should be suspected in septic patients on total parenteral nutrition, those who have recent exposure to broad-spectrum antibiotics, those with hematologic malignancies, those with recent organ or bone marrow transplants, and those colonized with Candida at multiple sites.

An echinocandin antifungal should be used for empiric treatment of suspected catheter-related candidemia. Fluconazole is a reasonable alternative in selected patients in settings where the risk of *Candida glabrata* and *C. krusei* are low and who have not been treated with azole antifungals in the past 3 months.

Short-term catheters (those in place less than 14 days) should be removed from patients with catheter-related bloodstream infections due to *S. aureus,* enterococci, mycobacteria, fungi, or gram-negative bacilli.

Long-term catheters should be removed from patients who have catheter-related infections associated with severe sepsis, endocarditis, suppurative thrombophlebitis, persistent bacteremia 72 hours after the initiation of antimicrobial therapy to which the bacteria are reportedly susceptible, and infections due to *S. aureus, P. aeruginosa,* mycobacteria, or fungi.

Antibiotic-lock therapy with antibiotic infusion should be administered for catheter salvage. When catheter salvage is attempted, blood cultures should be repeated 72 hours after effective antimicrobials are begun, and the catheter should be removed if these cultures remain positive.

References

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