Providing Evidence-based Clinical Information for 25 Years

INFECTIOUS DISEASE ALERT®

A monthly update of developments in infectious disease, hospital epidemiology, microbiology, infection control, emporiatrics, and HIV treatment

AHC Media LLC Home Page—www.ahcmedia.com

CME for Physicians—www.cmeweb.com

AHC Media LLC

INSIDE

Financial Disclosure:

Infectious Disease Alert's Physician Editor, Stan Deresinski, MD, FACP, serves on the speaker's bureau of Merck, Pharmacia, GlaxoSmithKline, Pfizer, Bayer, and Wyeth, and does research for Merck. Peer reviewer Connie Price, MD, reports no consultant, stockholder, speaker's bureau, research, or other financial relationship with any company related to this field of study. Updates author Carol A. Kemper, MD, FACP, reports no financial relationship relevant to this field of study.

Shaking Things Up: The New Guidelines for Antibiotic Prophylaxis of Endocarditis

ABSTRACT & COMMENTARY

By Stan Deresinski, MD, FACP

Source: Wilson W, et al. Prevention of infective endocarditis. Guidelines from the American Heart Association. A guideline from the American Heart Association Rheumatic Fever, Endocarditis, and Kawasaki Disease Committee, Council on Cardiovascular Disease in the Young, and the Council on Clinical Cardiology, Council on Cardiovascular Surgery and Anesthesia, and the Quality of Care and Outcomes Research Interdisciplinary Working Group. *Circulation* 2007 Apr 19 [Epub ahead of print].

Synopsis: *The new guidelines recommend antibiotic prophylaxis of infective endocarditis in a much more restricted group of patients than did previous guidelines.*

THE AMERICAN HEART ASSOCIATION LAST PUBLISHED GUIDELINES on the use of antibiotic prophylaxis for the prevention of infective endocarditis in 1997.[1] Those guidelines were quite complex, characterizing patients as having high, moderate and low risk of infection, and including recommendations for all but the low risk group undergoing a variety of dental, respiratory, genitourinary, and gastrointestinal procedures. These guidelines have remained in place since that time and are included in the latest (2007) Sanford guide.[2] They cast a very wide net. leading to very frequent use of antibiotic prophylaxis in a large number of patients. In addition, it has been my experience that, in practice, the use of antibiotic prophylaxis has become the default position, so that it is administered to many patients despite their not meeting the broad criteria of the 1997 guidelines. Despite the guidelines and the even more expansive practice, skepticism has been expressed regarding the benefit of antibiotic prophylaxis in many circumstances. In this regard, included along with the 2007 Sanford guide recommendations is a caveat that at least one study "brings into serious question

VOLUME 26 • NUMBER 9 • JUNE 2007 • PAGES 97-106

NOW AVAILABLE ONLINE
www.ahcmedia.com

whether dental procedures predispose to endocarditis and whether antibiotic prophylaxis is of any value."

This skepticism is based on a number of factors, including the lack of any randomized clinical trial demonstrating efficacy of prophylaxis of endocarditis - the large number of individuals required for such a study make it likely that no sufficiently powered trial to definitively answer the question will ever be performed. Furthermore, as outlined by Wilson and colleagues in the 2007 guideline, which has been endorsed by the Infectious Disease Society of America, "infectious endocarditis is much more likely to result from frequent exposure to random bacteremias associated with daily activities than from bacteremia caused by a dental, GI tract, or GU tract procedure". For instance, it has been estimated that twice daily tooth brushing for one year entails a risk of bacteremia that is 154,000 times greater than the risk of exposure resulting from a single tooth extraction. As a consequence, if antibiotics given in relation to these procedures are capable of preventing infective endocarditis, the number of such cases prevented is likely to be "exceedingly small" and, taking into account the potential adverse effects of antibiotic use on the individual and the general bacterial ecology, such use should be limited. It is estimated that, while the risk of endocarditis associated with a dental procedure is, eg, 1.1 per million procedures in a patient with mitral valve prolapse, the incidence of fatal anaphylaxis after penicillin administration is 15 - 25 per million. Finally, the effective maintenance of good oral hygiene, by reducing the frequency and intensity of bacteremia associated with daily activities, is the most effective means of endocarditis risk reduction.

Taking these factors into account, the new guidelines do not recommend antibiotic prophylaxis for endocarditis prevention for almost exclusively individuals undergoing procedures other than certain high risk dental procedures. Thus, antibiotic prophylaxis is recommended for individuals undergoing dental procedures that involve manipulation of gingival tissue or the periapical region of teeth or perforation of the oral mucosa, as well as for individuals undergoing surgical procedures on infected skin, skin structure or muscle, or incision of respiratory tract mucosa and who have one of the following cardiac conditions :

- Presence of a prosthetic cardiac valve
- History of previous infective endocarditis
- Congenital heart disease with one of the following:
  - — Cyanotic congenital heart disease that has not been repaired (including individuals with incomplete repair with palliative shunts and conduits)
  - — Completely repaired congenital heart defect with prosthetic material or device within the first 6 months after the procedure
  - — Repaired congenital heart disease with residual defects at the site or adjacent to a prosthetic patch or device
- Cardiac transplant recipients with valvulopathy

Among the dental procedures for which antibiotic prophylaxis is *not* indicated include "routine anesthetic injections through noninfected tissue, taking dental radiographs, placement of removable prosthodontic or orthodontic appliances, adjustment of orthodontic appliances, placement of orthodontic brackets, shedding of deciduous teeth, and bleeding from trauma to the lips or oral mucosa". Prophylaxis is not indicated for individuals undergoing genitourinary or gastrointestinal procedures, including endoscopy. Actual site infections should, of course, be appropriately treated.

The recommended orally administered regimen for most adults for whom dental prophylaxis is indicated is a single 2 gram dose of amoxicillin 30 to 60 minutes before the procedure. In patients with a history of allergy to penicillins, a single 600 mg dose of clindamycin may be given. Alternatively, if the allergic manifestation was other than anaphylaxis, angioedema, or urticaria, a single 2 gram dose of cephalexin may be administered. If oral administration is not possible, parenterally administered alternatives include ampicillin (2 grams IV or IM), cefazolin (1

Infectious Disease Alert, ISSN 0739-7348, is published monthly by AHC Media LLC, 3525 Piedmont Rd., NE, Bldg. 6, Suite 400, Atlanta, GA 30305.

SENIOR VICE PRESIDENT/GROUP PUBLISHER: Brenda Mooney.

ASSOCIATE PUBLISHER: Lee Landenberger.

MARKETING PRODUCT MANAGER: Shawn DeMario.

ASSOCIATE MANAGING EDITOR: Jennifer Corbett

GST Registration Number: R128870672.
Periodicals postage paid at Atlanta, GA.
POSTMASTER: Send address changes to ***Infectious Disease Alert***, P.O. Box 740059, Atlanta, GA 30374.

Back issues: $21.
Missing issues will be fulfilled by customer service free of charge when contacted within one month of the missing issue's date.

Subscriber Information

Customer Service: 1-800-688-2421
Customer Service E-Mail Address:
customerservice@ahcmedia.com
E-Mail Address: jennifer.corbett@ahcmedia.com
World-Wide Web: www.ahcmedia.com

Subscription Prices

United States
1 year *with* free AMA Category 1 credits: $289
Add $9.95 for shipping & handling.
(Student/Resident rate: $125).

Multiple Copies
Discounts are available for group subscriptions. For pricing information, please call Tria Kreutzer at (404) 262-5482.

Canada
Add 7% GST and $30 shipping.

Elsewhere
Add $30 shipping.

Accreditation

AHC Media LLC is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians.

AHC Media LLC designates this educational activity for a maximum of *36 AMA PRA Category 1 Credits™*. Physicians should only claim credit commensurate with the extent of their participation in the activity.

This CME activity is intended for the infectious disease specialist. It is in effect for 36 months from the date of the publication.

AHC Media LLC

Questions & Comments

Jennifer Corbett,
Associate Managing Editor, at (404) 262-5431, or e-mail to jennifer.corbett@ahcmedia.com between 8:30 a.m. and 4:30 p.m. ET, Monday-Friday.

gram IV or IM), ceftriaxone (1 gram IV or IM),or clindamycin 600 mg IV or IM). Recommended pediatric regimens are also provided.

"The Committee…recognizes that these new recommendations may cause concern among patients who have previously received antibiotic prophylaxis to prevent infective endocarditis before dental or other procedures and are now advised that such prophylaxis is unnecessary." It is likely that many health care providers will also be made anxious. ■

References:

1. Dajani AS, et al. Prevention of bacterial endocarditis. Recommendations by the American Heart Association. *JAMA* 1997; 277:1794-1801.
2. The Sanford Guide to Antimicrobial Therapy, 2007. pg 162.

Acute Hepatitis in the U.S. — A Success Story, But the Game Isn't Over

ABSTRACT & COMMENTARY

By Stan Deresinski, MD, FACP

Source: Centers for Disease Control and Prevention. Surveillance for acute hepatitis - United States, 2005. Surveillance Summaries. *MMWR* 2007; 56(No. SS-3):1-24. www.cdc.gov/mmwr/preview/mmwrhtml/ ss5603a1.htm

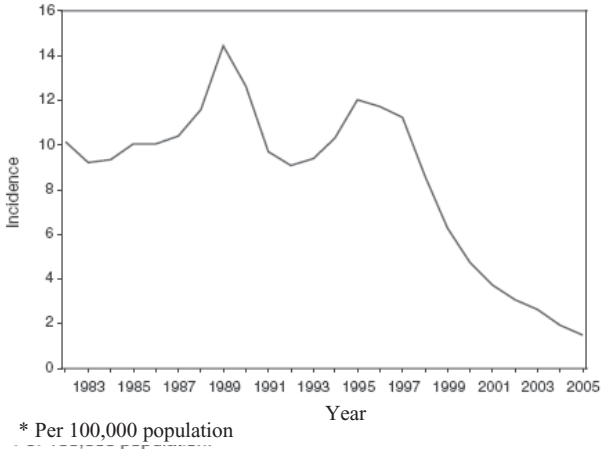
Synopsis: *There have been dramatic decreases in the reported cases of acute hepatitis due to hepatitis viruses A, B and C in the U.S.*

THE INCIDENCE OF ACUTE HEPATITIS A, WHICH HAS previously cycled at 10 to 15 year intervals, has steadily decreased since its last peak in 1995, reaching a nadir in 2005 when 4488 cases were reported. The incidence in 2005, 1.5 per 100,000 population, was the lowest ever reported and, in fact, was more than 80% lower than that observed at the previously recorded cycle nadir. The most frequently identified risk factor was international travel, accounting for 15% of cases, with most associated with travel in Mexico, Central and South America. Sexual and household contact with another individual acutely infected with hepatitis A virus accounted or 12% of cases.

The onset of the decrease in incidence of acute hepatitis A (Figure 1) infections coincides with the introduction of hepatitis A vaccines in 1995 and the issuance of public health recommendations for their use in the following year. More dramatic decreases occurred after implementation of childhood vaccination recommendations made in 1999. Not all states implemented vaccination programs and, in 2005, approximately two-thirds of cases arose in states without childhood vaccination recommendations. At the end of 2005, recommendations were made that all children aged 12 to 23 months be vaccinated.

Acute Hepatitis A (Figure 1).

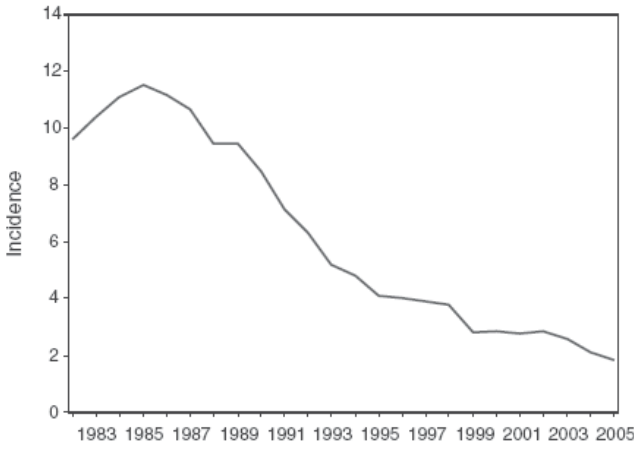
Incidence* of acute hepatitis A, by year — United States1982-2005



* Per 100,000 population

Acute Hepatitis B (Figure 2).

Incidence* of acute hepatitis B , by year – United States, 1982-2005



* Per 100,000 population

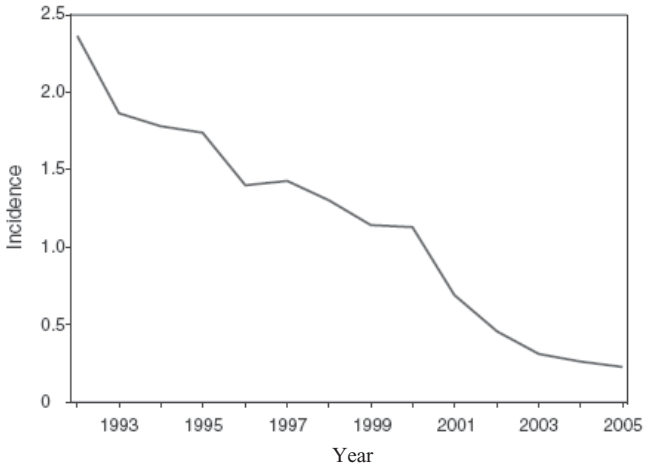
The incidence of acute hepatitis B infection in 2005, 1.8 cases per 100,000 population, was the lowest ever reported. This represented a total of 5494 reported cases, but taking into account the asymptomatic nature of many infections and underreporting, it was estimated 51,000 cases had occurred in 2005. Approximately one-third reported a sexual risk factor; 9.3% reported undergoing surgery 6 weeks to 6

months before the onset of illness.

The decrease in incidence of acute hepatitis B infection (Figure 2) began during the middle of the 1980s and coincided with the implementation, in steps, of a comprehensive national prevention strategy. This consisted of universal infant vaccination, routine screening of pregnant women and administration of immunoprophylaxis of at-risk infants, routine

Acute Hepatitis C (Figure 3).

Incidence* of acute hepatitis B, by year – United States, 1982-2005.



* Per 100,000 population

†Acute hepatitis Cwas reported as acute hepatitis non-A, non-B until 1995.

vaccination of children and adolescents not previously vaccinated, and vaccination of at-risk adults. The last include healthcare workers, dialysis patients, household and sexual contacts, individuals with multiple sexual partners or a sexually transmitted disease, men who have sex with men, injection drug users, and recipients of certain blood products.

Only 671 cases of acute hepatitis C infection were reported in 2005, for an incidence of 0.2 per 100,000 population. Taking into account missed diagnoses of asymptomatic cases and underreporting, it was estimated, however, that 20,000 new infections had occurred. Injection drug use accounted for 50% of cases; 14% reported having had surgery, 23% had had multiple sex partners, and 8% reported occupational exposure to blood.

The incidence of reported acute hepatitis C infections peaked in the late 1980s and has declined since. (Figure 3) While in 2005, the most commonly identified risk factor remained injection drug use, the overall decrease in incidence was due in large part to a decrease in cases among that group. The second most frequently reported risk factor was having multiple sexual partners. Transfusion was rarely identified as a risk factor.

Overall, these results illustrate the results of a remarkably successful public health program in the prevention of viral hepatitis in the U.S. - but there is still a long way to go. ■

Varicella-Zoster Virus Vaccine (Zostavax)

SPECIAL REPORT

By Jessica C. Song, MA., PharmD, and Paul Hsiao, Pharm D

Jessica C. Song, MA, PharmD, is Pharmacy Residency Coordinator, Santa Clara Valley Medical Center. Paul Hsiao, Pharm D, is a Pharmacist Specialist at Santa Clara Valley Medical Center.

Jessica C. Song and Paul Hsiao report no financial relationships relevant to this field of study.

HERPES ZOSTER RESULTS FROM REACTIVATION OF latent varicella-zoster virus (VZV) residing in the sensory ganglia of the cranial and spinal dorsal root ganglia. It is estimated that up to one million adults in the United States experience this debilitating illness yearly, and the number of cases will likely increase in the future, because of the aging population. Furthermore, affected individuals may experience serious adverse consequences, including postherpetic neuralgia, paresis, myelopathy, and vasculopathy. Postherpetic neuralgia has been shown to persist for longer than one year in 36% and in 47%, respectively, in those older than 60 years and 70 years.[1]

Concerns about the burden of illness associated with herpes zoster (HZ) episodes have stimulated the development of a novel method of prophylaxis against HZ in the elderly patient population. In December 2005, the Food and Drug Administration (FDA) approved the live attenuated VZV vaccine (Zostavax) for use in the prevention of HZ in adults, 60 years and older. Moreover, the Advisory Committee on Immunization Practices (ACIP) has recommended that this vaccine should be administered to all individuals age 60 and older.[2] This article will: (1) review the pharmacology and FDA indications of VZV vaccine, (2) review the safety and efficacy of VZV vaccine, and (3) review the dosage and cost of this new vaccine.

VZV vaccine is marketed as a lyophilized preparation of the Oka/Merck strain of live, attenuated VZV derived from children with varicella. The next step in the production of this vaccine involved the introduction of virus into human embryonic lung cell cultures and propaga-

tion in human embryonic lung cell cultures. Finally, propagation occurred in human diploid cell cultures.[3]

The commercially available VZV vaccine is marketed as a single-dose vial of lyophilized vaccine, that should be stored frozen at -200C° or colder. Reconstitution of the vaccine involves the use of the manufacturer-supplied, preservative-free diluent. In order to minimize potency decay of VZV vaccine, the reconstituted vaccine must be administered immediately. If the reconstituted product is not used within 30 minutes, it should be discarded.[3]

The FDA-approved dose of VZV is a single dose of 0.65 ml of the vaccine (minimum potency, 19,400 plaque-forming units) administered subcutaneously to adults age 60 and older. Individuals who have a history of anaphylactic/anaphylactoid reaction to gelatin or neomycin, who are immunocompromised (AIDS; leukemia; any type of lymphoma; receiving immunosuppressive therapy), who have active/untreated tuberculosis, or are pregnant, should not receive VZV.

Table 1 summarizes the key pharmacologic properties of VZV vaccine.[1-5] *See pages 102-103.*

CLINICAL EFFICACY OF VZV VACCINE

VZV vaccine is marketed as a lyophilized preparation of the Oka/Merck strain of live, attenuated VZV derived from children with varicella. The next step in the production of this vaccine involved the introduction of virus into human embryonic lung cell cultures and propagation in human embryonic lung cell cultures. Finally, propagation occurred in human diploid cell cultures.[3]

The commercially available VZV vaccine is marketed as a single-dose vial of lyophilized vaccine, which should be stored frozen at -200C or colder. Reconstitution of the vaccine involves the use of the manufacturer-supplied, preservative-free diluent. In order to minimize potency decay of VZV vaccine, the reconstituted vaccine must be administered immediately. If the reconstituted product is not used within 30 minutes, it should be discarded.[3]

The FDA-approved dose of VZV is a single dose of 0.65 ml of the vaccine (minimum potency, 19,400 plaque-forming units) administered subcutaneously to adults age 60 and older. Individuals who have a history of anaphylactic/anaphylactoid reaction to gelatin or neomycin, who are immunocompromised (AIDS; leukemia; any type of lymphoma; receiving immunosuppressive therapy), who have active/untreated tuberculosis, or are pregnant, should not receive VZV.

VZV vaccine has been studied for its efficacy in preventing HZ and postherpetic neuralgia in a total of 7 trials.[5] Data from the "Shingles Prevention Study" provided sufficient evidence in support of the vaccine's efficacy against development of HZ and postherpetic neuralgia in adults older than 60 years.[1,5]

In brief, this study included 38,546 subjects from multiple Veterans Affairs Medical Centers throughout the United States (not including Hawaii), of whom 95% were Caucasians residing in the U.S. for a minimum of 30 years.[1,5] The primary efficacy measures used in this pivotal study were incidence of postherpetic neuralgia and the HZ burden of illness score (BOI), a composite of the incidence, severity, and duration of pain/discomfort caused by HZ. Secondary efficacy measures included the incidence of HZ, duration of clinically significant HZ pain, and severity of HZ.

Because the focus of this study involved the use of a live vaccine, numerous exclusion criteria were set in place by the investigators. Immunodeficiency, inability to adhere to the study protocol, history of anaphylactic reaction to gelatin, allergic sensitivity to neomycin, prior HZ, prior receipt of varicella vaccine, premenopausal status, receipt of inactivated vaccine within the past 2 weeks, and receipt of antiviral therapy at the time of study enrollment precluded subjects from participating in the Shingles Prevention Study.[5]

Administration of a single dose of VZV (0.5 mL) resulted in a lower incidence (cases per 1000 patient years) of postherpetic neuralgia compared with placebo (0.46 vs. 1.38; relative risk, 0.665; 95% CI, 0.475 to 0.792, $P < 0.001$). In addition to superiority in prevention of postherpetic neuralgia, receipt of VZV resulted in significantly lower BOI scores compared with those observed in placebo-treated patients (2.21 vs. 5.68; relative risk, 0.611; 95% CI, 0.511 to 0.691, $P < 0.001$). The secondary endpoint of HZ incidence (cases per 1000 patient years) was noted to be significantly lower in VZV-treated subjects compared with placebo-treated patients (5.42 vs. 11.12; relative risk, 0.513; 95% CI, 0.442 to 0.576, $P < 0.001$). Of note, a post-hoc analysis revealed a much lower efficacy of VZV in preventing HZ in older patients (≥ 75 years), as vaccine efficacies were only 37% in participants 75 to 79 years of age, and 18% in participants over age 80 years. However, the proportion of subjects over age 80 years (~ 7%) and the number of HZ events were low in this study.[1,5]

Table 2 summarizes the key points of the Shingles Prevention Study. *See page 103.*

CONCLUSION

To date, VZV represents the only commercially available agent shown to prevent HZ and postherpetic neuralgia in older (especially 60-69 years), adult patients. Questions that remain to be answered include the effica-

Table 1. Pharmacologic Properties of Zostavax ® (Live Zoster Vaccine)

Brand/Generic[3]	Zostavax® (Live Zoster Vaccine)
Classification[3]	Vaccine
Mechanism of Action[3]	This vaccine is a lyophilized preparation of the Oka/Merck strain of live, attenuated varicella-zoster virus (VZV), initially obtained from a child with varicella. The virus was then introduced into human embryonic lung cell cultures and underwent propagation in embryonic guinea pig cell cultures, followed by propagation in human diploid cell cultures. This vaccine is thought to protect humans against developing herpes zoster (HZ) via development of VZV antibodies.
AHFS number[4]:	80:12:00.
FDA-Labeled Indications[3]	Zostavax® (Live Zoster Vaccine) is indicated for: Prevention of herpes zoster in people ≥ 60 years
Immunogenicity[3]	A subset of patients (N = 1395) from the Shingles Prevention Study was the focus of an immune response analysis, which revealed that 6 weeks post-vaccination, VZV antibody levels (measured by glycoprotein enzyme-linked immunosorbent assay) were increased 1.7-fold (95% CI, 1.6 to 1.8) compared with placebo.
How Supplied[3]	Injection: Single-dose vial of lyophilized vaccine (either as one single-dose vial, or as set of 10 single-dose vials); diluents are available as a separate set of 10 single-dose vials
Dose[3]	Vaccine is administered as a single dose to adult patients 60 years and older via the subcutaneous route (refer to Storage/Administration below for more details).
Dosage Adjustment[3]	**Renal Impairment:** -No dosage adjustments were listed in the prescribing information for this product. **Hepatic Impairment:** -No dosage adjustments were listed in the prescribing information for this product.
Storage/Administration[3]	**Storage/Reconstitution:** -Store the lyophilized vaccine in a freezer (any, including frost-free) that has a separate sealed freezer door and has an average maintained temperature of -200C or lower. -The diluent can either be stored at room temperature (200-250C, 680-770F) or in the refrigerator (20 to 80C, 360-460F) -Reconstitution: Remove the entire contents of the diluent vial into a syringe and inject the total volume into the vial of lyophilized vaccine. Mix by gently agitating the contents of the vial. -If the reconstituted vaccine is not used within 30 minutes, discard, since potency may be diminished. **Administration:** -Inject the total volume of the reconstituted solution subcutaneously in the upper arm of the patient. -Note: the vaccine should be administered immediately following reconstitution.
Monitoring Requirements[3]	-Monitor for rash (especially in immunosuppressed individuals) -Contact the Vaccine Adverse Event Reporting System (VAERS) at 1-800-822-7967 or at www.vaers.hhs.gov if a patient has experienced a suspected adverse event following administration of Zostavax vaccine.
Contraindications[3]	-History of anaphylactic/anaphylactoid reaction to neomycin, gelatin, or any other vaccine component -History of primary or acquired immunodeficiency states including AIDS (or other infections associated with human immunodeficiency viruses), leukemia, any type of lymphoma, or other malignant neoplasms affecting the lymphatic system or bone marrow -Receiving immunosuppressive therapy, including high-dose corticosteroids - Pregnancy - Current, active, untreated tuberculosis
Warnings/Precautions[3]	-Consider delaying vaccine administration if the patient has a fever > 38.50C (> 101.30F) -Avoid pregnancy for three months after vaccination -Duration of protection after Zostavax administration not established, but protection up to 4 years has been demonstrated in a pivotal clinical trial -There is a theoretical risk of transmitting vaccine virus from Zostavax recipients to individuals who may be susceptible to varicella (chicken-pox naïve pregnant females)
Adverse Effects[3]	Most commonly observed adverse effects: Injection site reactions, including erythema (33.7%), pain/tenderness (33.4%), swelling (24.9%), and pruritis (6.6%). Serious adverse effects: Asthma exacerbation, polymyalgia rheumatica (2 patients experienced this in the Shingles Prevention Study)
Drug/Food Interactions[3]	Concurrent administration of Zostavax with other vaccines has not been studied.
IV solution Compatibility[1]	Not applicable, since a diluent is provided with the lyophilized vaccine.
Pregnancy Category[3]	**C**
Lactation[3]	Excretion in human milk unknown, use caution.

Chart continues on next page

(Continued from previous page)

Table 1. Pharmacologic Properties of Zostavax ® (Live Zoster Vaccine)

Overdose/Toxicity[3]	Not applicable, since a health-care provider administers a single-dose of vaccine to the individual.
Sounds Like …	Zostavax ® may be confused with: Zovirax.
Formulary Considerations[1-5]	"As of October 26, 2006, the Advisory Committee on Immunization Practices (ACIP) has recommended that Zostavax should be given to all individuals age 60 and older. The Shingles Prevention Study showed a 50% decrease in the occurrence of shingles following Zostavax administration. A recent cost-effectiveness study showed that vaccination may be more cost-effective in adults 60-64 y vs. adults ≥ 80 y. — Estimated cost of a single dose of Zostavax at Santa Clara Valley Medical Center: $145.35 - $152.50.

Table 2. Clinical Trial of Zostavax for the Prevention of Herpes Zoster and Postherpetic Neuralgia

Investigators	Study Design	Primary Endpoint/Patients	Primary Findings
Oxman MN et al. (2005)[1,5]	Multicenter, randomized, placebo-controlled, double-blind clinical trial conducted in the United States (N = 38,546) **Intervention:** "Subjects were given one subcutaneous injection of Zostavax (0.5 ml) or placebo **Follow-up:** "Interactive, automated telephone-response system was used to ensure active follow-up and identification of herpes zoster cases.	**Primary endpoints:** Burden of illness secondary to herpes zoster, and pain severity/discomfort associated with herpes zoster; incidence of post-herpetic neuralgia. **Secondary endpoints:** Incidence of herpes zoster; duration of clinically significant herpes zoster pain; severity of herpes zoster **Patients:** • ***Included if*** they had a history of varicella or resided in the U.S. for a minimum of 30 years. • ***Excluded if*** -Immunocompromised (except intermittent or inhaled, < 800 mcg/d beclomethasone dipropionate or equivalent) -Unable to adhere to study protocol -History of anaphylactic reaction to gelatin -Allergic sensitivity to neomycin -Active neoplastic disease (except local skin cancer or other malignancies that are stable in the absence of immunosuppressive therapy (e.g., prostate cancer)) -Prior herpes zoster or receipt of varicella vaccine -Anticipated death within next 5 years -Premenopausal females -Received antiviral therapy at time of enrollment -Received any other vaccines within 1 month prior to study vaccination (2 weeks for inactivated vaccines) • ***Patient characteristics*** -Median age: 69 years; 95% Caucasian -**Nearly 7% of patients were ≥ 80 y** -Mean duration of herpes zoster surveillance, 3.13 years (range, 1 day to 4.9 years) -Less than 1% of patients withdrew from study, or lost to follow-up	-Total number of confirmed cases of herpes zoster: 957 (vaccine recipients, 315, placebo-recipients, 642) -The overall incidence of herpes zoster was reduced by 51.3% with the use Zostavax ($P < 0.001$) • The efficacy of the vaccine with respect to the incidence of herpes zoster was lower in subjects 70 years vs. younger sub jects (37.6% vs. 63.9%, $P < 0.001$) -The overall incidence of postherpetic neuralgia was reduced by 66.5% ($P < 0.001$) -Post-hoc analysis (**not pre-specified endpoint**) **HZ incidence/1000 yrs** Age / Zostavax / Placebo / Vaccine Efficacy 70-74 / 6.435 / 11.438 / 0.44 75-79 / 7.182 / 11.312 / 0.37 80-84 / 9.773 / 12.230 / 0.20 85-59 / 10.040 / 11.570 / 0.13 90+ / 19.608 / 14.286 / -.037 Vaccine Efficacy = incidence of herpes zoster (PBO-ZVx)/PBO -Burden of illness score: Zostavax reduced it by 61.1% vs. placebo (95% CI, 51.1-69.1, $P < 0.001$) -Duration of clinically significant pain: Zostavax group, 20 days; placebo group, 22 days ($P < 0.001$) -Severity of illness scores were 39 points lower in the Zostavax-treated patients, compared with placebo ($P = 0.008$)

cy of VZV in the oldest adult population (≥70 years), the duration of immune response (data available up to 4 years post-administration), and the safety/efficacy of VZV in non-Caucasian individuals. ■

References:

1. Oxman MN, et al. A vaccine to prevent herpes zoster and postherpetic neuralgia in older adults. *N Engl J Med* 2005;352:2271-2284.
2. CDC Press Release. CDC's Advisory Committee Recommends "Shingles" Vaccination. Accessed on May 1, 2007. www.cdc.gov/od/oc/media/pressrel/r061026.htm
3. Live Zoster Vaccine (Zostavax) prescribing information. Whitehouse Station, NJ: Merck & Co., Inc.: February 2007.
4. Hornberger J, Robertus K. Cost-effectiveness of a vaccine to prevent herpes zoster and postherpetic neuralgia in older adults. *Ann Intern Med* 2006;145:317-325.
5. VHA Pharmacy Benefits Management Strategic Healthcare Group and the Medical Advisory Panel. National PBM Drug Monograph: Varicella Virus Vaccine Live (Zostavax). November 2006. Accessed on May 11, 2007. www.pbm.va.gov

The California Encephalitis Project — 1998-2005

ABSTRACT & COMMENTARY

By Carol A. Kemper, MD, FACP

Dr. Kemper reports no financial relationships relevant to this field of study.

Synopsis: *Despite the use of a large number of diagnostic tests, the etiology of the majority of cases remains obscure.*

Source: CA. Glaser et al. Beyond viruses: Clinical profiles and etiologies associated with encephalitis. *Clin Infect Dis* 2006; 43: 1565-1577.

Since 1998, researchers at the Viral and Rickettsial Disease Laboratory in Richmond, CA (near Berkeley) have conducted a large-scale epidemiologic project to identify causes of encephalitis in California. Requirements for participation included hospitalization with symptoms of encephalitis for ≥ 24 hours, along with at least one other criteria (fever, seizures, focal neurologic deficits, CSF pleocytosis, or abnormal neuroimaging studies or eeg). Patients were "referred" by their treating physician, who collected a detailed history, and forwarded acute and convalescent sera, and CSF and respiratory specimens. A core battery of tests was performed for each patient, including CSF PCR for HSV-1, HSV-2, VZV, enterovirus, and *Mycoplasma pneumoniae*; CSF viral culture; and serologic tests for SLE, WEE, WNV, M. pneumoniae, measles, HSV, VZV, Adenovirus, Chlamydia, Influenza A and B, and Bartonella spp. In addition, PCR testing and viral culture was performed on respiratory specimens. Other selective tests were performed depending on the clinical history (eg, rabies, Borrelia, Colorado Tick Fever, etc.).

A total of 2494 patients were referred from 195 institutions throughout California from 1998-2005, of which 1570 met the criteria for analysis. Of these 98% provided adequate CSF and acute sera, and 44% provided adequate convalescent samples. The median age was 23 years (0-92 years); 56% were male; 58% required admission to ICU; 42% had seizures, and 18% were comatose. Two-thirds of the patients presented with fever, one-third had respiratory symptoms, one-third had gastrointestinal symptoms, and 13% had rash. The median CSF cell count was 23 (0-13,000), the median protein level was 57 (7-11,723), and the median glucose was 64 (6-533). Slightly more than half had abnormal neuroimaging studies. Eleven percent died.

A viral etiology was identified for 170 cases (10.8%), and was most frequently due to infection with either enteroviruses (25%) or HSV-1 (24%). Not surprisingly, the mean age of patients with HSV-1 (54 years), VZV (44 years), and WNV (66 years) was considerably older than those with enterovirus (12 years), measles (12 years), or EBV (11 years). Three-fourths of patients with a viral etiology presented with fever, which was more common than those with a non-viral etiology, and seizures occurred in 38% (most commonly, in those with measles, HSV-1 and human herpesvirus-6 infection). Arboviruses were only infrequently detected in this study, and there were no cases of WEE or SLE.

Non-viral infectious causes of encephalitis were identified in 78 persons (5%), and included a broad range of bacterial, mycobacterial, parasitic and, rarely, fungal etiologies. For example, bacterial etiologies included pyogenic bacteria in 14 cases; *M. tuberculous*, presenting as an acute encephalitis, occurred in 19; Bartonella spp. (n = 13), M. pneumonia (n = 2), and Tropheryma whippelii (n = 1). Parasitic infections were identified in 7 cases, including the raccoon tapeworm, *Baylisascaris procyonis* (n = 4). Fungal infections were identified in 3 cases, including coccidioidomycosis (n =2) and cryptococosis (n = 1).

An additional 204 patients (13%) were identified with

possible etiologies. This generally involved a positive culture or PCR from a non-CSF site, but the organism could not be detected in CSF. The most common diagnosis in this category was *M. pneumoniae* in 94 cases (6%), but also included cases of enterovirus, influenza, HSV, chlamydia, human metapneumovirus, VZV, HHV-6, RSV, brucella, rotavirus, parainfluenza virus, bartonella, EBV, and CJD.

A non-infectious etiology was identified in 8% of patients, typically an autoimmune disorder or vasculitis, neoplasm, or metabolic disorder.

COMMENTARY

Many of us in the local community participated in the project for years, and have been eager to see the results, which were surprising in their frequent inability to identify a causative agent in the majority of cases. I guess most of us believed that the newer molecular tools and the broad panel of assays available to the researchers (many of which were considered "experimental" and otherwise not available to clinicians) would provide a diagnostic advantage. However, despite the comprehensive nature of the laboratory investigation, a confirmed or probable infectious cause was identified in 248 (16%) of patients, and a non-infectious etiology was identified in 122 (8%). No etiology was found in 68% of cases. Roughly one-third of patients presenting with encephalitis had a definite, probable or possible infectious etiology, about two-thirds of which was viral and one-third was non-viral. Although 13% of the total cases had non-CSF evidence of an infectious etiology (most commonly, a respiratory illness) without confirmation of a CNS infection, a causal relationship was considered likely. Thus, thorough testing of respiratory specimens for potential causes of encephalitis, including testing for enterovirus, influenza, adenovirus, *M. pneumoniae*, RSV, and human metapneumovirus, may be helpful.

Some broad generalizations can be drawn from this data. Temporal lobe seizures or MRI findings were common (9%), and were most frequently associated with HSV-1 infection, although were also seen in patients with VZV, EBV, and HHV-6. Seizures were common in bartonellosis (85%), measles (83%), EBV (63%), as well as HSV-1 (59%) but were less common in enterovirus (28%), VZV (13%) and WNV (12%). Movement and extra-pyramidal disorders, sometimes with evidence of basal ganglia involvement on neuroimaging studies, tended to occur in young patients, with no predominant etiology identified, but the survival rate was not much better than that of the group as a whole (91%). Both seizures and extrapyramidal and movement disorders tended to result in long hospital stays (>1 month). Cerebellar disorders also tended to occur in young people, and were associated with a better survival outcome (98%).

Diffuse cerebral edema, occurring within the first 7 days of presentation, was associated with worse outcome (72% died). Although this presentation was most consistent with a Reyes-like condition, VZV infection could not be confirmed. A non-viral etiology was found in one-half of cases presenting with hydrocephalous, including mycobacterial, fungal, and parasitic causes, and was also associated with a worse prognosis.

The authors suggest that the inability to identify a causative agent in the majority of cases in the state-wide survey may be the result of a selection bias towards diagnostically challenging cases. As a physician-participant in this project, I beg to differ. One of the frustrations of caring for these patients is the wait time between presentation and the results of any "real-time" PCR or serologic testing, which for most community-based hospitals requires referral to a reference laboratory for many of the tests required. It is not uncommon to wait up to 2 weeks before the initial test results are available. And, by definition, the results of convalescent serologies, take even longer. Thus, in my experience, most patients with encephalitis present a "diagnostic challenge". This extensive survey demonstrates that a thoughtful and thorough approach to patients with encephalitis can provide an infectious etiology in 16% to 29% of patients,

and occasionally yields some unusual diagnoses. It may be helpful to the families of these patients to understand that even with the most sophisticated and current techniques, the diagnosis in two-thirds of cases remains elusive. ■

CME Questions

33. Which of the following is correct with regard to the new recommendations for antibiotic prophylaxis of infectious endocarditis?

A. It is recommended that patients with mitral valve prolapse undergoing colonoscopy receive antibiotic prophylaxis.

B. It is recommended that patients with previous endocarditis undergoing dental cleaning alone receive antibiotic prophylaxis.

C. It is recommended that patients with mitral stenosis undergoing dental radiography receive antibiotic prophylaxis.

D. It is recommended that patients with a prosthetic cardiac valve undergoing manipulation of the periapical region of teeth receive antibiotic prophylaxis.

34. Which of the following is correct regarding the incidence of acute hepatitis in the U.S.?

A. The incidence of acute hepatitis A,B, and C have significantly decreased over recent years.

B. While the incidence of acute hepatitis A has been decreasing, that of hepatitis B and C is increasing.

C. While the incidence of acute hepatitis A and B have each been decreasing, that of hepatitis C is increasing.

D. While the incidence of acute hepatitis C has been decreasing, there has been no significant change in the incidences of either hepatitis A or B.

35. Which of the following is correct?

A. Zostavax is a killed viral vaccine for the prevention of herpes zoster.

B. Zostavax is identical in contents, including viral dose, to the childhood varicella vaccine, Varivax.

C. Zostavax has received FDA approval for use in individual 60 years of age and older.

D. Zostavax is approved for use in patients with severe immunocompromise.

Answers: 33.(d) 34.(a) 35.(c)

In Future Issues:

Another echinocandin: micafungin in candidemia.

UPDATES

By Carol A. Kemper, MD, FACP

H5N1 Influenza Vaccine Approved

Source: FDA News, April 18, 2007; www.fda.gov

In April, the United States Food and Drug Administration announced the approval of the first human vaccine against H5N1 Avian Influenza virus. The inactivated vaccine is derived from a/Vietnam/1203/2004 influenza virus, is administered as a 2-part vaccine one month apart, and contains thimerosal (similar to other multidose vials of influenza vaccine). It is manufactured by sanofi pasteur Inc at their Swiftwater, PA, facility.

Clinical investigation of the vaccine in healthy adults found that 103 persons receiving two 90 microgram doses of vaccine 28 days apart had an adequate antibody response (what is thought to be sufficient levels of antibody to prevent infection). In addition, 300 adults receiving lower doses of vaccine developed a lesser antibody response that may nonetheless be sufficient to reduce the severity of disease if infected. The vaccine was generally well tolerated, and additional safety data is being examined.

The vaccine is not commercially available but has been purchased by the federal government for the U.S. Strategic National Stockpile. The idea is to make vaccine available to the public as needed within 12 hours. ■

Leprosy revealed with HIV treatment

Source: A ProMED-mail post, October 25, 2006; promed@promedmail.org

HIV/AIDS specialists in Britain and the U.S. caring for HIV+ persons from developing countries are reporting a new phenomenon - exacerbations of previously unrecognized leprosy in HIV+ persons receiving highly active antiretroviral therapy (HAART). As patients initiate HAART, and with improvement in their immune systems, their leprosy appears to "wake up." Patients have developed painful nodules around the nerves of the neck and face, with numb fingers and toes. The diagnosis of leprosy may not be immediately obvious, and the granulomatous response seen in nodules may be misleading. The clinical and histopathological presentation appears similar to a Type 1 reversal reaction, where activated CD4 cells migrate into infected lesions and produce cytokines. As such, it seems analogous to other HIV-related infections, with paradoxical worsening with immune reconstitution.

There are an estimated 300,000 new cases of leprosy diagnosed annually around the world, mostly in Brazil, India, Africa, and the Caribbean, although I have cases in my clinic from Central America, China and the Philippines. Initial concerns that HIV infection may lead to thousands of new cases of leprosy in the developing world have not been born out. Some assume this may be a function of patients dying of their HIV before developing clinically apparent leprosy, which typically incubates for up to 8 to 13 years. It is estimated that perhaps 2% of leprosy patients in places like Brazil may be co-infected with HIV. Interestingly, even in HIV+ patients with leprosy, the histology on biopsy maybe similar to that seen in non-HIV-infected persons. Even patients with advanced HIV disease appear able to mount a granulomatous response to M. leprae, in contrast to those infected with M. tuberculosis. Type 1 reversal reactions, associated with T cell activation to M. leprae have been described in 2 HIV+ patients who did not receive ART.

Clinicians caring for HIV+ patients from developing countries should be alert to the possibility of asymptomatic leprosy being unmasked by antiretroviral therapy. ■

Vaccine-strain smallpox masquerades as genital herpes

Source: *MMWR Weekly*, May 3, 2007, 556(17), 417-419.

A woman presented to a public health clinic in Alaska in October 2006 with painful herpetic-like genital lesions. She reported having a new male sex partner for 10 days, ending about 10 days earlier. Condoms were used, although on the final day of their liaison, the condom broke. Examination showed 2 shallow painful 3 to 5 mm. ulcers, one the on labia majora and one on the labia minora. She had no fever, itching, dysuria or inguinal adenopathy. A viral culture was obtained, and tests for GC and chlamydia were negative. Over the next 2 days the lesions became increasingly painful and red, and she was treated with cephalexin for possible cellulitis. The ulcers healed within 10 days.

Although the presumptive diagnosis was genital herpes, the viral culture yielded an identified viral pathogen that repeatedly tested negative for HSV. At the Alaska State Viral Laboratory, the virus was successfully passed through 2 cell lines, but consistently stained negative for HSV and CMV. An outside reference lab was also unable to make an identification. The isolate was forwarded to the CDC January 9, 2007, where pan-herpes virus PCR and a DNase-single-primer amplification restriction enzyme

digestion (DNase-SISPA) tests were performed. The latter yielded distinct DNA fragments that, when amplified, matched vaccinia virus sequences. Additional PCR testing demonstrated consistency with vaccine-strain vaccinia virus. The results were relayed back to the ASVL on January 30th.

So, what is the logical explanation for this woman's genital infection? One clue: her partner was in the military, stationed at a local military base. He had just been vaccinated for vaccinia 1 day prior to beginning his 10-day liaison with the woman. He had no skin conditions or contraindications to vaccination. The woman recalled no bandages or lesions on his arms. The report indicates that manual genital contact occurred, or maybe virus was transmitted when applying the condom. She had never been vaccinated against smallpox.

Transmission of vaccine strain virus to another site on the vaccinee's body or to non-vaccinated persons was not uncommon back when people were vaccinated against smallpox. Frequent sites of secondary infection included the face, nose, eyes, lips, genitals, and anus. In the past few years, 6 cases of secondary transmission associated with military personnel to non-military persons have been reported, including 2 with genital involvement.

The accompanying editorial stressed the importance of newer molecular tools in the identification of the unknown pathogen, especially in the absence of clinical history to guide the evaluation. However, a more careful history may have prompted the correct diagnosis, especially as there was a nearby military base. And no matter how "powerful" the tools employed, it took the various laboratories involved nearly 4 months to identify the virus. Fortunately, there was no evidence of transmission to other persons, including medical personnel.

Clinicians should be aware the military personnel are still being vaccinated for smallpox with the potential for causing secondary infections in others. ■

Condoms prevent HPV in Sexually Naïve Women

Source: Winer RL, et al. Condom use and the risk of genital human papillomavirus infection in young women. *N Engl J Med* 2006,354,25;2635-2654.

The debate surrounding the relative merits of abstinence and fidelity vs. condom use (as if the two were mutually exclusive) remains a hotly contested issue, at least in the United States, where it has even spilled over into U.S. international family planning policy. In 2001, conservative groups successfully pressured Congress to pass a law requiring the FDA to define the medical accuracy of condom effectiveness in preventing STD's other than HIV. By then, condom use had clearly been shown to reduce the risk of HIV, and, at least in men, gonorrhea. But while most experts agree that condoms were likely to decrease the risk of transmission of other STDs, such as syphilis, HSV, and HPV, clear data was lacking. Indeed, controlled clinical trials to prove that condoms are effective in reducing transmission of such diseases, for example, as syphilis, are not possible, and probably unethical. However, given that sex can often be messy, it is not inherently obvious to what degree condom use may decrease the risk of HSV or HPV transmission.

Fortunately, 6 years later, the group in Seattle has weighed in with a positive result, that young women having sex for the first time whose partners use condoms 100% of the time have a 70% lower risk of HPV infection than a similar group of women whose partners infrequently used condoms.

A total of 210 female university students aged 18 to 22 years who were sexually naive or newly sexually active with a single partner were evaluated at baseline, and every 4 months for up to 2 years. Cervical and vulvovaginal specimens were tested for HPV DNA and routine Papanicolaou smears were performed, as well as testing for other STDs. The data for 82 young women who were sexually active less than 2 weeks prior to enrollment and who kept detailed daily computerized diaries of the sexual activities were analyzed. After first time intercourse with a first time partner, most HPV infections occurred within 8 months (before a second partner), and the shortest interval from the first sexual experience to an HPV event was 20 days. Thus, data for the time period of 20 days to 8 months was analyzed to best answer the FDA's question.

A total of 126 incident infections were identified in 40 women after their first intercourse, for an overall 12-month cumulative incidence of 37.2% (confidence interval, 27 to 49%). The 24-month cumulative incidence of squamous intraepithelial lesions was 15% (confidence interval 8.3 to 26.2%), including one high grade lesion and 14 low grade lesions. Three women were found to have HPV infection at baseline, before any reported sexual intercourse.

Comparing young women who partners used condoms 100% of the time vs those with <5% use, the incidence of genital HPV infection was 38 vs 89 per 100-person years, respectively (adjusted hazard ratio, 0.3). No cervical squamous intraepithelial lesions were detected in women whose partners used condoms 100% of the time, compared with 14 lesions in those whose partners used condoms less consistently. Thus regular consistent condom use resulted in a significant reduction in the transmission of HPV in young women who were sexually active for the first time. Because sex so often may involve genital contact before the application of a condom, it is not surprising that some women who reported consistent condom use nonetheless developed HPV infection, or that a small number had evidence of HPV infection even before experiencing intercourse.

It is important to note that the results may not be generalizable to older women, or women who have already been sexually active for some time, or women of lower socioeconomic class. Nonetheless, the FDA can now prominently and decisively display the benefits of condom use in the reduction of HPV transmission. ■

PHARMACOLOGY WATCH

Supplement to Clinical Cardiology Alert, Clinical Oncology Alert, Critical Care Alert, Infectious Disease Alert, Internal Medicine Alert, Neurology Alert, OB/GYN Clinical Alert, Primary Care Reports, Travel Medicine Advisor.

Risk With Preventative Antibiotics Outweighs Benefit for Most

Sweeping new changes have been made to the guidelines for prevention of endocarditis in patients undergoing dental procedures. The new recommendations dramatically reduce the indications for dental prophylaxis and reduce the number of patients who need preprocedure antibiotics. The guideline was issued by the American Heart Association in conjunction with the American Dental Association, Infectious Diseases Society of America, and the Pediatric Infectious Diseases Society and was published online April 19, 2007, in *Circulation*. The guidelines reflect evidence that the risk of taking preventative antibiotics outweighs the benefit for most patients. It is also been found that infectious endocarditis (IE) is more likely to result from frequent exposure to random bacteremias from activity such as flossing and brushing than from dental work. Specifically, the guidelines say that prophylactic antibiotics are no longer required for patients with mitral valve prolapse, rheumatic heart disease, bicuspid valve disease, calcified aortic stenosis, or congenital heart conditions such as ventricular septal defect, atrial septal defect, and hypertrophic cardiomyopathy. There are still patients who are at extremely high risk of IE who should continue to receive prophylactic antibiotics: patients with artificial heart valves, a history of infective endocarditis, congenital heart disease including unrepaired or incompletely repaired cyanotic congenital heart disease, including those with palliative shunts and conduits, those with a completely repaired congenital heart defect with prosthetic material during the first 6 months after the procedure, repaired congenital heart defect with residual defect at the site or adjacent to the site of a prosthetic patch or prosthetic device, or a cardiac transplant patient with a cardiac valvulopathy. Antibiotic prophylaxis is no longer recommended for any other form of congenital heart disease. Dosing regimens are essentially the same as previous recommendations and include oral amoxicillin 2 gm 30 to 60 minutes prior to procedure. Oral alternatives include cephalexin, clindamycin, azithromycin or clarithromycin. Parenteral regimens include ampicillin, cefazolin, ceftriaxone, and clindamycin. The guideline also no longer recommends antibiotics to prevent IE in patients undergoing genitourinary or gastrointestinal tract procedures (*Circulation* 2007, doi:10.1161/CIRCULATIONAHA.106.183095). The full guideline is available at http://www.ada.org/prof/resources/ topics/infective_endocarditis_guidelines.pdf. ■

Gonococcal Infections, CDC's Updated Treatment

The CDC has issued updated treatment recommendations for gonococcal infections and associated conditions due to the high level of resistance of gonorrhea to fluoroquinolones. The agencies Gonococcal Isolate Surveillance Project demonstrates that fluoroquinolone-resistant gonorrhea is continuing to spread and is now widespread

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) 262-5431. E-mail: jennifer.corbett@ahcmedia.com.

throughout United States. Therefore, fluoroquinolones such as ciprofloxacin, ofloxacin, or levofloxacin are no longer recommended. Current recommended regimens for gonococcal infections of the cervix, urethra, and rectum are ceftriaxone 125 mg IM and a single dose or cefixime 400 mg orally in a single dose plus treatment for chlamydia if chlamydial infection is not ruled out. Uncomplicated gonococcal infections of the pharynx should be treated with ceftriaxone 125 mg IM plus treatment for chlamydia, if chlamydial infection is not ruled out. Disseminated gonococcal infection should be treated with ceftriaxone 1 g IM or IV every 24 hours. Pelvic inflammatory disease may be treated with parenteral and oral therapy. Parenteral therapy regimens include cefotetan or cefoxitin plus doxycycline or clindamycin plus gentamicin. An alternative regimen is ampicillin/sulbactam plus oral doxycycline. Oral therapy can be considered in women with mild to moderate disease. With the loss of fluoroquinolones, cephalosporins are the mainstay of most regimens. For patients who are highly allergic to cephalosporins, spectinomycin may be considered although it is not generally available in this country. Another option is azithromycin, however, prescribing should be done in consultation with an infectious disease specialist due to concerns over emerging antimicrobial resistance to macrolides. The CDC's full recommendations are available online at www.cdc.gov/std/treatment/2006/updated-regimens.htm. ■

Head Lice — Malathion First-Line Treatment

Malathion should be first-line treatment for children who have lice according to a new review in the journal *Pediatrics*. Head lice have become resistant to nearly all first-line treatments in United States including permethrin, which has been considered first-line treatment for years. Malathion, in the formulation containing isopropyl alcohol and terpineol, is safe and effective for lice and all existing points within the life cycle, and generally requires a single treatment, reducing the duration of infestation, and lost time from school and work. Concern about flammability seems to be over emphasized, as there have been no reported cases of bodily injury related to burns (*Pediatrics* 2007. 119:965-974).

Statins, May Cut the Risk of Cataracts

Statins, the cholesterol wonder drugs, have been associated with a number of other benefits including reduction of inflammation within the arteries, improved bone density, reduction in the risk of colon cancer, renoprotective effects, and reduction in the risk of Alzheimer's disease and other dementias. Now, a new study suggests that the drugs may also cut the risk of cataracts by 50%. Researchers from Australia reviewed the rate of cataract development in 3,654 elderly patients. After 10 years, after controlling for age, gender and others factors, the hazard ratio for any type of cataract in statin users was 0.52. In subgroups, there was a decreased risk of nuclear cataracts (HR = 0.66) and cortical cataracts (HR =0.76), but neither of these reached statistical significance. The authors conclude that there may be a protective influence of statins on cataracts and this needs to be further explored (*Am J Ophthalmol* 2007; 143:687-689). ■

FDA Actions

Sanofi Aventis has been approved to produce a vaccine to prevent bird flu in humans. The vaccine against the H5N1 virus will not be produced commercially, but will instead be stockpiled by the U.S. government for distribution in case of the outbreak. The FDA admits that the vaccine is not optimal, requiring a higher dose than normal flu vaccine, and 2 shots which must be given 28 days apart. But until other vaccines are developed, this vaccine will be used as the "interim measure."

The FDA is recommending updating black box warning regarding suicidality in young adults (under age 24) starting on antidepressants, calling for appropriate monitoring and close observation. The new recommendation should also include the statement that there was no increase in suicidality in adults over the age of 24, and a decrease in the risk in adults over the age of 64.

The FDA has approved generic versions of 2 of the most popular drugs of the last decade, Ambien (zolpidem) and Zoloft (sertraline). Zolpidem will be available in 5 mg and 10 mg immediate-release tablets. Thirteen manufactures have received approval to market the product. Sertraline is approved in the 25 mg, 50 mg and 100 mg strengths, and will be produced by Ranbaxy Laboratories.

The FDA has issued a warning about the health risks of dietary supplements touted as sexual enhancement products and treatments for erectile dysfunction that have been distributed under the trade names True Man and Energy Max. Both drugs have been sold throughout United States. Energy Max was found to contain an analogue of sildenafil, the active ingredient in Viagra, while True Man was found to contain an analogue of sildenafil and vardenafil, the active ingredient in Levitra. Both drugs can have serious interactions with nitrates. ■