



# FAMILY PRACTICE ALERT™

The essential monthly guide to developments in family medicine

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## Update on Otitis Media Treatment

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**A B S T R A C T & C O M M E N T A R Y**

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**Synopsis:** An expert group convened by the Centers for Disease Control and Prevention addressed key questions related to treatment of otitis media in the current circumstances of increasing drug-resistant *Streptococcus pneumoniae*.

**Source:** Dowell SF, et al. *Pediatr Infect Dis J* 1999;18:1-9.

**P**ublished and unpublished data summarized from the scientific literature and from the experience of more than 30 experts provided consensus opinion on the following questions: 1) Which is the best initial agent for treatment of acute otitis media (AOM)? Amoxicillin should remain the first-line antimicrobial agent for treating AOM, at doses of 80-90 mg/kg/d; 2) What are suitable alternatives if amoxicillin fails? For patients with clinically defined treatment failure after three days of therapy, alternative agents include oral amoxicillin-clavulanate, cefuroxime axetil, and intramuscular ceftriaxone; 3) Should empirical treatment of AOM vary by geographic region? Local surveillance data of pneumococcal resistance that are relevant for the clinical management of AOM are not available from most areas in the United States.

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**■ COMMENT BY HAL B. JENSON, MD, FAAP**

The management of otitis media has entered a new era with the increasing prevalence of drug-resistant *Streptococcus pneumoniae*. This organism causes 40-50% of all cases of AOM, with reduced susceptibility to penicillin in 8-35% (2-4% highly resistant) of isolates and reduced susceptibility to third-generation cephalosporins in 10% of isolates (about 4% highly resistant); the reduced antibiotic susceptibilities occur independently. The recommendations of this group provide a framework for appropriate management of AOM in 1999.

There is no single oral antimicrobial that eradicates all AOM pathogens. Amoxicillin at higher doses of 80-90 mg/kg/d, which achieves the higher middle ear fluid concentrations necessary to treat resistant *S. pneumoniae*, is effective as a first choice. There are surprisingly (at least to me) few adverse events even at these higher doses, and amoxicillin is inexpensive compared to many of the alternatives.

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There are compelling data for cefuroxime axetil (Ceftin) and amoxicillin-clavulanate (Augmentin) orally, and ceftriaxone (Rocephin) intramuscularly, as second-line drugs for treatment failure, which is defined as ear pain, fever, or bulging tympanic membrane or otorrhea after three days of therapy. (Persisting middle ear fluid is found in 70% of children at 10 days and, in the absence of specific evidence of ongoing infection, does not represent treatment failure.) However, many of the 13 other drugs approved by the Food and Drug Administration lack good evidence for efficacy against drug-resistant *S. pneumoniae*. There are promising but insufficient data at this time to recommend cefpodoxime (Vantin) and cefprozil (Cefzil), but many of the traditional second-line drugs should now be considered ineffective for AOM. These include trimethoprim-sulfamethoxazole and erythromycin-sulfisoxazole, which have traditionally been used for AOM, and the newer macrolides, clarithromycin and azithromycin, which initially showed promise. Some of these other drugs may be useful for selected cases based on susceptibility testing of middle ear fluid isolates obtained by tympanocentesis.

The increasing frequency of drug-resistant pneumococci further increases the urgency of the release of a conjugated pneumococcal vaccine that may be effective in preventing the 40% of infantile otitis media that are now caused by *S. pneumoniae*, especially drug-resistant strains. (*Dr. Jenson is Chief, Pediatric Infectious*

Diseases, University of Texas Health Science Center, San Antonio, Tex.) ♦

## Isoflavones from Red Clover Improve Systemic Arterial Compliance but not Plasma Lipids in Menopausal Women

### A B S T R A C T & C O M M E N T A R Y

**Synopsis:** Arterial compliance improved in menopausal women who ingested isoflavones derived from red clover. The effect size was comparable to that seen in hormone replacement therapy.

**Source:** Nestel PJ, et al. *J Clin Endocrinol Metab* 1999;84:895-898.

Isoflavones (phytoestrogens) are found in many legumes, including soy. They have been credited with conferring cardioprotection. For example, epidemiological studies suggested the reason Japanese women living in Japan had less cardiovascular disease than Japanese women living in the United States was due to consumption of a diet high in legumes and, therefore, isoflavones. Nestel and associates have performed several studies looking at modification of arterial compliance in postmenopausal women by weight loss, diet, hormone replacement therapy, and soy-derived isoflavones. The present study extended their previous work by examining isoflavones derived from red clover. Specifically, red clover contains genistein, diadzein, and their methylated precursors biochanin A and formononetin. (Soy contains genistein and diadzein.) Twenty-six women began the trial and 13 completed all aspects of the active intervention. Most of the drop-outs were menopausal women who quit their hormone replacement regimen to enroll and then could not tolerate the ensuing hot flashes. Subjects were postmenopausal women younger than 70 years of age who were not currently taking hormones or who had discontinued hormones at least four weeks before the study began. The study involved a three-week observation and dietary training interval followed serially by five weeks of placebo, five weeks of 80 mg of red clover-derived isoflavones, and five weeks of a 160 mg daily dose of isoflavones. Arterial compliance was measured by ultrasound at the end of each treatment window. Decreased arterial compliance is an important risk

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VICE PRESIDENT/ GROUP PUBLISHER:

Donald R. Johnston.

EXECUTIVE EDITOR: Glen Harris.

MARKETING PRODUCT MANAGER:

Schandale Kornegay.

ASSISTANT MANAGING EDITOR: Robin Mason.

COPY EDITORS: Holland Johnson,

Neill Lammre, Michelle Moran.

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Customer Service E-Mail Address: customerservice@ahcpub.com

Editorial E-Mail Address: holland.johnson@medec.com

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factor for cardiovascular disease because it leads to systolic hypertension and increased left ventricular work. Compliance was unchanged after placebo and increased after five weeks of either dose of isoflavones. Blood pressure and lipids did not change throughout the study.

#### ■ COMMENT BY SARAH L. BERGA, MD

This study is a good example of what needs to be done to determine the effects of various food supplements now being “hawked” to the American public. In this study, isoflavones derived from red clover had a similar effect upon arterial compliance as did isoflavones derived from soy or flax. Notably, estrogen replacement therapy also had a similar effect upon arterial compliance as did isoflavones. Nestel et al interpret the relatively short response time as evidence for endothelial-related arterial relaxation.

A logical question that one might ask after reading this report is whether isoflavones might be recommended as a substitute for hormone replacement therapy. One needs to keep in mind that the present study only looked at a few cardiovascular end points, so it would not allow one to adequately determine if isoflavones were a substitute for hormones for cardioprotection. Further, based on this report, nothing can be said about the effects of isoflavones upon other tissues and age-related disorders. Thus, it is premature to recommend isoflavones as substitutes for hormones.

This brings me to the next point. Nestel et al should study the effects of isoflavones and estrogens together to see if there is synergism. The rationale for such a study includes the observation that many women were unable to complete the study because of vasomotor symptoms. Clearly, isoflavones will not be a panacea for the spectrum of symptoms linked temporally to menopause. Although isoflavones are referred to as phytoestrogens, they are primarily antioxidants and they do not have the same range of effects upon the brain as do estrogens, which are also antioxidants. The two together might be far better than either one alone. Synergism of this type is the rule rather than the exception. I raise this point because the choice facing patients regarding the use of dietary supplements is often framed as an either/or scenario. The either/or approach is likely to be short-sighted and I recommend abandoning such a simplistic line of reasoning. It reminds me of the old question about whether calcium and exercise could substitute for estrogen use for protection against osteoporosis. We now know that there is synergism between exercise, calcium and vitamin D intake, and estrogen use in bone maintenance. Performing all of these interventions is far better than any one of them alone. I predict we will find similar synergism between estrogens and isoflavones in car-

diovascular protection and possibly in protection from dementia. (Dr. Berga is Associate Professor, Departments of Obstetrics, Gynecology, Reproductive Sciences, and Psychiatry, University of Pittsburgh.) ♦♦

## Antibiotic Resistance in Uncomplicated UTIs

#### A B S T R A C T & C O M M E N T A R Y

**Synopsis:** *The days may be numbered when trimethoprim/sulfamethoxazole should be used for empiric therapy for uncomplicated UTI.*

**Source:** Gupta K, et al. *JAMA* 1999;281:736-738.

Prevalence and trends in antimicrobial resistance among the narrow spectrum of organisms responsible for acute uncomplicated cystitis were examined in this study from Washington state. Included were those patients with a positive urine culture ( $\geq 10^3$  CFUs/mL) from a population of women, ages 18-50, in a health maintenance organization, who sought treatment at an outpatient clinic or ED. The study spanned five years, controlled for seasonal variation, and included 4342 urine isolates. Selected chart review confirmed that more than 95% of the study population included visits for uncomplicated cystitis.

The distribution of causative uropathogens was not surprising: *Escherichia coli*, 86%; *Staphylococcus saprophyticus*, 4%; *Proteus* species, 3%; *Klebsiella* species, 3%; *Enterobacter* species, 1.4%; *Citrobacter* species, 0.8%; *Enterococcus*, species 0.5%; and others, 1.3%. More than 20% of *E. coli* isolates were resistant to ampicillin, cephalothin, and sulfamethoxazole. Alarmingly, resistance among *E. coli* to trimethoprim/sulfamethoxazole doubled over the course of the study, rising from 9% to 18%. A significant increasing linear trend in resistance was found for all isolates to ampicillin, cephalothin, trimethoprim, and trimethoprim/sulfamethoxazole. Ciprofloxacin, nitrofurantoin, and gentamicin fared the best with regard to limited resistance. Recognizing that in vitro resistance may not directly translate to altered patient outcome, Gupta and colleagues conclude that the days may be numbered when trimethoprim/sulfamethoxazole should be used for empiric therapy for uncomplicated UTI.

#### ■ COMMENT BY RICHARD A. HARRIGAN, MD

And so, more evidence of emerging antimicrobial resistance is published; important news, but is it time to

stop using trimethoprim/sulfamethoxazole as the first-line antibiotic for uncomplicated UTI? Not yet. As Gupta et al caution, this is not a clinical outcomes study, but rather a report of a microbiological trend. Moreover, trimethoprim/sulfamethoxazole is concentrated in the urine, achieving higher concentrations than in the blood;<sup>1</sup> thus, the pathogen might still be eradicated. Finally, a treatment failure in cases of uncomplicated UTI generally does not result in life-threatening illness, but, rather, persistence of symptoms. Thus, treatment failures should make us think not only of an alternative diagnosis, but also of the antimicrobial resistance issue. (*Dr. Harrigan is Associate Professor of Medicine, Temple University School of Medicine, Associate Research Director, Division of Emergency Medicine, Temple University Hospital, Philadelphia, Pa.*) ♦

## Reference

1. *Physicians' Desk Reference*. 53<sup>rd</sup> ed. Montvale NJ: Medical Economics Company; 1999:2655.

About one-half of the nurses and physicians and 84% of the remaining personnel reported at least one percutaneous needlestick injury within the previous five years. However, 46% failed to report all of their injuries, including 80% of the physicians and 45% of registered nurses. Reasons for nonreporting included the perception that the stick was sterile or clean (39%), or represented no risk (26%), too busy (9%), and dissatisfaction with follow-up (8%).

## ■ COMMENT BY CAROL A. KEMPER, MD

While educational interventions regarding actual risk may enhance reporting behaviors, establishing user-friendly mechanisms by which needlestick injuries can be dealt with quickly and appropriately, as well as adequate follow-up, is essential. The use of the ER for after-hours injuries is, in my experience, inadequate in that patients are often required to wait longer than that recommended for the administration of post-exposure prophylaxis (< 1 hour), and the management is often inconsistent and occasionally incorrect. This is despite the availability of approved hospital protocols. A designated 24-hour hotline, such as the one established at the San Francisco General Hospital, (which, after-hours, usually rings a knowledgeable fellow or faculty member) appears to more consistently meet the needs of their hospital personnel. The hotline number is prominently posted in blazing colors throughout the hospital to encourage reporting. (*Dr. Kemper is Associate Director, AIDS Program, Division of Infectious Diseases, Santa Clara Valley Medical Center.*) ♦

## Encouraging Needlestic Reporting

### ABSTRACT & COMMENTARY

**Editor's Note:** Please see the Rapid Reference Card, "Determining the Need for HIV Postexposure Prophylaxis (PEP) After an Occupational Exposure," enclosed with this issue of Family Practice Alert.

**Synopsis:** About one-half of the nurses and physicians and 84% of the remaining personnel reported at least one percutaneous needlestick injury within the previous five years. However, 46% failed to report all of their injuries, including 80% of the physicians and 45% of registered nurses.

**Source:** Haiduven DJ, et al. *Hosp Infect* 1999;41:151-154.

**F**ailure to report needlestick injuries is remarkably common, especially among physicians and medical students (Osborn EH, et al. *Ann Intern Med* 1999;130:45-51). Haiduven and colleagues distributed confidential surveys to healthcare personnel at a public teaching hospital in San Jose between 1992 and 1995. A total of 549 individuals responded to the survey, 83% of whom were nurses and 7% of whom were physicians. The remaining subjects included operating room technicians, dentists, and other hospital personnel.

## Spinal Surgical Alternative: Exercise?

### ABSTRACT & COMMENTARY

**Synopsis:** Committed motivated patients who wish to avoid back or neck surgery may be able to do just that.

**Source:** Nelson BW, et al. *Arch Phys Med Rehabil* 1999; 80:20-25.

**T**o determine if patients recommended for spinal surgery can avoid it through an aggressive strengthening program, a privately owned medical clinic treated consecutive referred patients. Study entry criteria included a physician's recommendation for lumbar or cervical surgery, no medical condition preventing exercise, and willingness to participate in an outpatient 10-week program.

Intensive, progressive resistance exercise of the iso-

lated lumbar or cervical spine was practiced and continued to failure, and patients were encouraged to work through their pain. Forty-six of 60 participants completed the program; 38 were available for follow-up (average 16 months, range 12-30 months after discharge); three required surgery after completing the program.

#### ■ COMMENT BY JOHN LA PUMA, MD, FACP

Back pain hurts. It is the leading cause of disability in the United States, and a pile of frustration among practitioners and patients alike. It is also expensive—early 1990s data from the Worker's Compensation Back Pain Claim Study show that “the average cost per industrial back injury in the U.S. is now more than \$24,000.” Here, the authors present surgical cost data of \$60,000 for a cervical laminectomy and more than \$168,000 for a lumbar fusion.

Of 651 patients referred for rehab, 62 with chronic pain (mean 28 months) met the inclusion criteria. Sixty began the outpatient program; 14 dropped out. Twenty-eight men and 18 women, mean age 42, completed the 10 weeks in an average of 21 visits, most to physical therapists. Nearly all patients—90%—had already tried and failed some type of exercise program.

The program emphasized progressive resistance, and used lumbar and cervical extension devices to isolate and strengthen lumbar extensors, cervical extensors and rotators, and thoracic rotators. A self-monitored maintenance program was also taught to maintain strength, vigor, self-care, and newly improved body mechanics.

Statistically significant gains in strength for lumbar and cervical extensor and rotator muscles in men and women were reported, and only three patients underwent surgery.

These Minneapolis area authors acknowledge their methodologic limitations—unblinded, no control group, no randomization, selection bias, variable follow-up, only regrets offered for the nearly one-quarter drop-out. Yet they observe that even patients recommended for spinal surgery can tolerate intensive, specific exercise. By specific they mean isolated musculature; by intensive they mean muscular exercise against dynamic resistance to volitional failure, through a full range of motion.

These bold investigators take a hands-on approach to patients famed for fragility, who “develop a keen sense of fear when it comes to spinal motion ... few understood that literally millions of people develop the same radiologic diagnoses with few or no symptoms.” Provided there is no physical deterioration, emphasizing activity tolerance as a means to symptom relief is sensible, empowering, and precise.

Committed motivated patients who wish to avoid back or neck surgery may be able to do just that. This innovative program deserves better evaluation. (*Dr. La Puma is*

*Adjunct Professor of Nutrition, Kendall College, Director, C.H.E.F. Clinic, C.H.E.F. Skills Research, Alexian Brothers Medical Center, Elk Grove, Ill.*) ♦

## Pharmacology Update

### Cilostazol Tablets (Pletal-Otsuka)

By William T. Elliott, MD, FACP,  
and James Chan, PharmD, PhD

In January, the FDA approved the first new drug for intermittent claudication in more than 15 years. Cilostazol (Pletal-Otsuka) will be co-marketed by Otsuka and Pharmacia Upjohn. While the mechanism of action of cilostazol in improving intermittent claudication is not precisely known, it is reported to have antiplatelet and vasodilation actions and also demonstrates greater dilation of the femoral arteries than other arteries.<sup>1</sup> The drug was approved among some controversy since it is a phosphodiesterase inhibitor, a class known to be dangerous to patients with congestive heart failure.

#### Indications

Cilostazol is indicated for the reduction of symptoms of intermittent claudication, as indicated by an increase in walking distance.

#### Dosage

The recommended dose of cilostazol is 100 mg twice daily taken one-half hour before meals or two hours after meals. Patients taking inhibitors of cytochrome P450 3A4, such as ketoconazole, itraconazole, erythromycin, or diltiazem, should undergo initial therapy with 50 mg twice of cilostazol. Grapefruit juice should be avoided as it can also inhibit 3A4.<sup>1</sup>

Cilostazol is supplied as 50 mg and 100 mg tablets.

#### Potential Advantages

In addition to its antiplatelet and vasodilation effect, cilostazol has been reported to have beneficial effects on lipoproteins.<sup>2</sup> After 12 weeks of therapy (100 mg bid), plasma triglycerides decreased by 15%, high-density lipoprotein cholesterol increased by 10%, with the HDL-2 subfraction showing the greatest increase. Subjects with a baseline triglyceride of more than 140 mg/dL showed the greatest increase in HDL-C and decrease in TG.

## Potential Disadvantages

Cilostazol is contraindicated in patients with congestive heart failure. The drug is a phosphodiesterase III inhibitor and drugs of this class have been shown to decrease survival in patients with class III-IV heart failure.<sup>1</sup>

Most common side effects associated with cilostazol compared to placebo are headache (34% vs 14%), diarrhea (19% vs 7%), palpitations (10% vs 1%), and tachycardia (4% vs 1%).<sup>1</sup> Sixteen percent of patients dropped out of clinical trials, with 73% of those taking the recommended dose of 100 mg twice daily, citing side effects as the reason.<sup>5</sup>

## Comments

Claudication is a common symptom of atherosclerotic occlusive disease of the lower extremities.

Intermittent claudication is generally characterized as severe pain or cramping in the legs that occurs with walking and is relieved by rest. This tends to progress as the patient is able to walk shorter and shorter distances before experiencing pain. Results from several clinical trials involving about 2000 patients showed that cilostazol improved maximal walking distance compared to placebo in patients with stable intermittent claudication.<sup>1,3,4</sup> In general, patients on cilostazol were able to walk about 1.3 city blocks further than those on placebo. This represents a mean improvement of about 40%.<sup>1,3</sup> Benefits may be experienced in 2-4 weeks but may take up to 12 weeks. Cilostazol has not been studied in patients with rapidly progressing claudication or other more serious conditions such as leg pain at rest.<sup>1</sup>

Cilostazol costs about \$2.45 per day for either 50 mg or 100 mg twice daily. This compares to about \$1.70 per day for generic pentoxifylline (400 mg three times a day).

## Clinical Implications

Approximately 10% of elderly patients older than the age of 70 have symptoms of atherosclerotic occlusive disease of the lower extremities. Generally, this population has cardiovascular risk factors such as hypertension, diabetes mellitus, hypercholesterolemia, and cigarette smoking.<sup>7</sup> Intermittant claudication is one of the most difficult clinical entities to treat. Treatment involves an exercise program, management of risk factors, and drug treatment. Cilostazol offers only moderate relief for patients with moderately severe disease.

About 50% of patients indicate that the drug improves their ability to work as assessed by the patients themselves or by physicians compared to 19-22% for patients on placebo.<sup>3</sup>

Pentoxifylline is the only other drug approved for treating intermittent claudication, and few comparisons of the

two drugs are available. Two unpublished trials have been conducted to compare cilostazol and pentoxifylline with inconclusive results. One study indicated that cilostazol improved walking distance at week 24 by a mean of 113 meters compared to 68 meters for pentoxifylline. The other study showed no significant difference.<sup>5</sup> Some of the difficulties in claudication studies in general are large placebo effects and inherent variability of this test method.<sup>3</sup> A meta-analysis of pentoxifylline trials indicate an improvement of 48.4 m over placebo while cilostazol studies suggest a numerically better improvement of 65 m.<sup>4,6</sup>

Cilostazol offers an alternative to pentoxifylline and may prove superior in some patients, but it carries the risk of use in patients with heart failure, a condition that commonly accompanies peripheral vascular disease. ♦

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## CME Questions

### 22. Initial antibiotic treatment of otitis media:

- should use amoxicillin, 40 mg/kg/d.
- should be changed if fever and pain are still present after three days.
- should be guided by local surveillance data.
- should be changed if middle ear fluid is still present after 10 days in an otherwise well child.

### 23. Which of the following statements is false?

- Phytoestrogens derived from soy, flax, and red clover have comparable effects upon arterial compliance when administered to menopausal women.
- The degree to which phytoestrogen use benefits a given menopausal woman can be monitored by longitudinally following lipoprotein profiles.
- Phytoestrogen use has not been shown to be a substitute for hormone replacement therapy in menopausal women.
- Two common phytoestrogens are genistein and diadzein.
- The phytoestrogens that are isoflavones are best thought of as antioxidants.

### 24. With regard to *Escherichia coli* as a uropathogen, which of the following antibiotics has been linked to increasing resistance in uncomplicated UTI?

- Trimethoprim/sulfamethoxazole
- Ciprofloxacin
- Nitrofurantoin
- Gentamicin

By Louis Kuritzky, MD

## Weight Control in Obese Subjects Treated with Orlistat

Traditional nonpharmacological methods for weight reduction based upon diet and exercise show poor long-term performance. Since unchecked obesity contributes to consequences of diabetes, cardiovascular disease, and overall mortality, the need for more efficacious tools is substantial.

Orlistat (Xenical) is an agent that blocks activity of pancreatic and gastric lipases, resulting in about a one-third reduction in absorption of ingested fat. This randomized, double-blind, placebo-controlled study ( $n = 892$ ) prospectively evaluated patients receiving orlistat, 120 mg three times daily for one year; a second year of the study randomized subjects to 60 mg or 120 mg orlistat three times daily. A controlled-energy diet was used for all study subjects.

At the end of the first year, subjects receiving orlistat had lost an average of 8.76 kg, compared to 5.81 kg in the placebo group; during the second year of the trial, persons who continued either dose of orlistat regained less weight than those on placebo, but the higher dose had a significantly better maintenance effect. Blood pressure, lipids, glucose, and insulin were favorably affected in the active treatment group when compared with placebo. Adverse events, the most common of which were gastrointestinal, were similar in placebo and treatment groups. The withdrawal from treatment rate was actually higher in the placebo group than in the active treatment group in the first year, but both groups had equal withdrawal rates in the second year.

Orlistat can produce sustained weight loss, as well as improvements in lipids and insulin, and is well tolerated by most patients. ♦

Davidson MH, et al. *JAMA* 1999;281: 235-242.

## Safety of Revaccination with Pneumococcal Polysaccharide Vaccine

Since post-vaccination antibody levels as well as protective efficacy of pneumococcal vaccine decline over time, revaccination after five years or more is recommended for immunocompromised persons and people older than 65 who were vaccinated before the age of 65. Implementation of these recommendations has been suboptimal, to some degree perhaps because of concern about adverse reactions to revaccination. This report details results from a large prospective trial that enrolled more than 1400 individuals aged 50-74 comparing the adverse event rate for persons revaccinated vs. first-time recipients.

Fever, fatigue, myalgia, headache, arthralgia, and rash in the first two weeks post-vaccination were no more frequent in the revaccination group than the new vaccination group. For local adverse reactions, revaccinees had a larger area of redness or swelling, more tenderness and arm soreness, and more limitation of arm movement than new vaccinees in the first six days, but this difference disappeared during days 7-13. Fifteen percent of healthy immunocompetent adults ( $RR = 4.9$  compared to new vaccinee) had a sizable local reaction, defined as more than 4 inches of local redness or swelling. Fortunately, even these reactions are self-limited, resolving in a median of three days. There were no serious adverse reactions in any patient from either vaccination group. Revaccination is associated with a greater frequency of local adverse reactions, including sizeable local reac-

tions, but the self-limited nature and brief duration of such adversities should not preclude implementation of current revaccination recommendations. ♦

Jackson LA, et al. *JAMA* 1999;281: 243-248.

## Is There Gulf War Syndrome?

Military veterans from the United Kingdom who were stationed in the Persian Gulf during the Gulf War from Sept. 1, 1990, until June 30, 1991 ( $n = 53$ ; 462) have reported impaired physical functioning, psychological morbidity, and perception of poor physical health more frequently than individuals not deployed to this area. A similar picture has been reported for U.S. servicepersons. Using a population-based cross-sectional design, Ismail and colleagues sent a standardized survey about 50 physical symptoms to 12,592 men who had served in either the Gulf War or Bosnia, or servicemen who had not been deployed overseas.

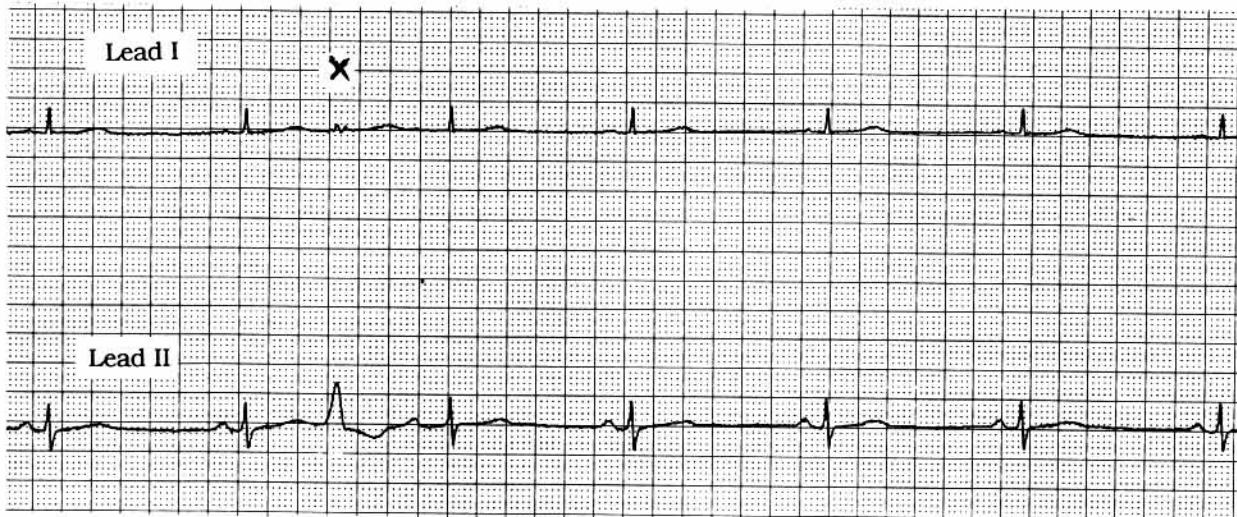
The most commonly reported symptoms were headaches, irritability, sleeping difficulties, feeling jumpy, feeling unrefreshed after sleep, fatigue, feeling cut off from others, forgetfulness, loss of concentration, avoidance behaviors, distressing dreams, difficulty breathing deeply, tachypnea, dyspnea, wheezing, and numbness or tingling in extremities. The structure of correlations between symptoms was similar among Gulf War veterans to Bosnia veterans, or servicemen not deployed abroad.

Ismail et al conclude that, although results from complex modeling procedures must be interpreted with caution, the data do not support a unique Gulf War syndrome. ♦

Ismail K, et al. *Lancet* 1999;353: 179-182.

**What is Beat X?**

By Ken Grauer, MD

**Figure.** Simultaneous rhythm strip recording of leads I and II. What is beat X?

**Clinical Scenario:** The Figure shows a rhythm strip with simultaneously recorded leads I and II. What is beat X? What is unusual about this beat? Why is the PR interval of the following beat prolonged?

**Interpretation:** The underlying rhythm is sinus bradycardia and arrhythmia. Beat X is a premature ventricular contraction (PVC). Although the amplitude of this beat is greatly reduced (and easy to overlook) in lead I, confirmation of its true etiology is readily apparent from inspection of simultaneously recorded lead II, where this beat is obviously wide and very different in appearance from normal sinus complexes. QRS amplitude in a given lead may be null (or almost so, as in this case) when the mean vector of a beat is oriented perpendicular to the lead being monitored.

The second unusual aspect of beat X is that there is

no compensatory pause following this beat, as usually occurs because the premature ventricular complex renders the AV node refractory to conduction of the next sinus impulse. Instead, the R-R interval containing the PVC in this tracing is barely longer than the R-R interval of the underlying sinus rhythm. Such PVCs are said to be "interpolated." The final finding of interest is the presence of *concealed* conduction, which produces PR interval prolongation in the beat following the PVC (seen best in lead II). The term concealed conduction is used when an ECG finding is seen that is not explained by the surface ECG. Instead, one has to postulate that the reason the PR interval of the third sinus beat is prolonged reflects the greater amount of time needed for the atrial impulse to penetrate an AV node rendered partially refractory from the preceding ventricular beat. ♦

**In Future Issues:****HGH Therapy in Normal but Short Children**