

# INTERNAL MEDICINE ALERT<sup>®</sup>

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FACP, FAAA, FACA**  
Clinical Professor, Department  
of Medicine, UCLA School of  
Medicine, Los Angeles

## Review of Alcoholic Drinks: Important Triggers for Asthma

ABSTRACT & COMMENTARY

**Synopsis:** *There is a need for increased awareness among asthmatic subjects (and their physicians) that alcoholic drinks can trigger asthma in a large number of patients.*

**Source:** Vally H, et al. *J Allergy Clin Immunol* 2000;105:462-467.

Alcoholic drinks are known to trigger symptoms in asthmatic individuals. However, the prevalence, components responsible, and characteristics of those who are sensitive have not been well studied. Using a validated food allergy questionnaire, 366 Australian adults who had experienced attacks with alcoholic drinks on at least two occasions were assessed. A total of 33% responded positively. Wine (red or white) was the worst culprit, with symptoms appearing within less than one hour. The following associations proved statistically significant: symptoms were more often in women, in those taking oral steroids, in those reporting their first attack at a younger age, and by those who had previously visited an alternative health practitioner for asthma. There was a significant association between wine-induced asthma and asthma triggered by foods containing sulfite as well as those triggered by aspirin and nonsteroidal anti-inflammatory medications.

### ■ COMMENT BY SHELDON L. SPECTOR, MD

Questionnaires of large numbers of asthmatic subjects as used in this study can yield interesting data such as the high prevalence of alcohol- (especially wine) associated asthma. One of the values of such investigations is to suggest future studies based on the correlations seen. Perhaps Vally and colleagues could have expanded their knowledge further with more subgroup analyses. For example: 1) Were those subjects with aspirin-induced asthma almost invariably those with nasal polyps? Published studies would support this association.<sup>1,2</sup> 2) Do those individuals with facial swelling or hives have different characteristics (e.g., predominantly react to other alcoholic drinks than wine, vs those with the asthma-induced syndrome)? Again, the mechanisms of these syndromes appear to be different.<sup>3</sup> 3) Would Asian non-

## INSIDE

*Snoring, snorting, and blood pressure—What's the story?*  
**page 90**

*Mortality and institutionalization following hip fracture*  
**page 91**

*Impressive performance of a self-rating scale for depression*  
**page 93**

*Linezolid (Zyvox): A new antibiotic for resistant gram-positive organisms*  
**page 93**

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whites behave differently than other nonwhites? Perhaps not enough patients fit into the Asian group but Japanese investigators suggest that alcohol induces high blood concentration of acetaldehyde leading to release of histamine from basophils and mast cells<sup>4</sup> and an effect on bronchial hyperresponsiveness.<sup>5</sup>

The biggest criticism of this study is the severity classification and Vally et al's conclusions without considering the medications used. A patient requiring both oral steroids and steroid aerosols may have no asthma attacks or doctor visits because of these medications, yet have much more severe asthma than someone taking no asthma medications who is symptomatic. Additionally, medications such as azelastine may specifically block alcohol-induced asthma<sup>6</sup> so patients on such medications may not mention symptoms with alcohol due to the blocking effect.

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VICE PRESIDENT/GROUP PUBLISHER:

Donald R. Johnston.

EDITORIAL GROUP HEAD: Glen Harris.

MARKETING PRODUCT MANAGER:

Schandale Komegay.

ASSOCIATE MANAGING EDITOR: Robin Mason.

ASSISTANT MANAGING EDITOR: Neill Lamore.

GST Registration Number: R128870672.

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Please call **Robin Mason**, Associate Managing Editor, at (404) 262-5517 (e-mail: robin.mason@ahcpub.com) or **Neill Lamore**, Assistant Managing Editor, at (404) 262-5480 (e-mail: neill.lamore@ahcpub.com) between 8:30 a.m. and 4:30 p.m. ET, Monday-Friday.

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Customer Service: 1-800-688-2421.

Customer Service E-Mail: customerservice@ahcpub.com

Editorial E-Mail: neill.lamore@ahcpub.com

World-Wide Web: http://www.ahcpub.com

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Despite these and other limitations of the study, I agree with Vally et al that there is a need for increased awareness among asthmatic subjects (and their physicians) that alcoholic drinks can trigger asthma in a large number of patients. ❖

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# Snoring, Snorting, and Blood Pressure—What's the Story?

ABSTRACT & COMMENTARY

**Synopsis:** This study found a "dose-response" curve between measures of sleep disordered breathing and degree of hypertension.

**Source:** Nieto FJ, et al. *JAMA* 2000;283:1829-1836.

The sleep heart health study (shhs) is a multicenter study of the consequences of obstructive sleep apnea. It is an ongoing prospective cohort study of subjects who are already participating in ongoing studies of cardiovascular or respiratory disease. The objectives of this report were to investigate the relationship of sleep-disordered breathing (SDB) and hypertension in a large population, controlling for confounding variables—particularly obesity. The study population included more than 6000 individuals aged 40 years or older. Nieto and colleagues used well-defined and reproducible criteria for SDB and sleep data, and collected data on relevant behavior and physical findings by questionnaire and physical examination. This study found that mean systolic and diastolic blood pressure and the prevalence of hypertension increased significantly with increasing SDB indices. After controlling for body mass index (BMI),

neck circumference, alcohol use, and cigarette smoking, the odds ratio (OR) for hypertension was significantly increased for those with an Apnea/Hypopnea Index (AHI) of 30 or more events per hour of sleep and for those with oxygen desaturation of 12% or greater.

■ **COMMENT BY BARBARA A. PHILLIPS, MD, MSPH**

This study is important because it controlled for the significant confounders that have undermined confidence in previous studies showing an association between SDB and hypertension. Previous work showing an association between SDB and hypertension has been criticized because obesity is a common predisposing factor for both conditions and has been difficult to control for. This study found a “dose-response” curve between measures of SDB and degree of hypertension. Another strength of this study is that the measures and definitions of apnea and hypopnea used in the SHHS are clearly spelled out and are rapidly becoming the consensus.

The report of Nieto et al confirmed and strengthened findings from two other large cohort studies. Grote and colleagues showed an independent linear association between Respiratory Disturbance Index ([RDI], a term essentially synonymous with AHI), blood pressure, and heart rate.<sup>1</sup> The OR in this study was 4.15 for those with an RDI of more than 40 compared with those with an RDI of more than 5. Grote et al also controlled for BMI, age, alcohol and nicotine use, cholesterol level, and daytime arterial blood gases.

Lavie and associates also found a dose-response relationship between levels of SDB and hypertension, again controlling for important confounders.<sup>2</sup>

These reports really don't surprise those of us who take care of sleep apnea patients, but they are vindicating. We have come a long way from the scathing analysis of the data on the “Health effects of obstructive sleep apnoea (sic) and the effectiveness of continuous positive airways pressure: A systematic review of the research evidence,” in which Wright and colleagues concluded that, “The relevance of sleep apnoea to public health has been exaggerated.”<sup>3</sup>

What remains to be done now is to show that treatment of sleep apnea improves blood pressure, and to try to elucidate the mechanisms by which SDB affects blood pressure. Work is already underway in these areas. Dimsdale et al compared titrated Continuous Positive Airway Pressure (CPAP) with placebo (about 2 cm H<sub>2</sub>O) CPAP in 39 sleep apnea patients.<sup>4</sup> Daytime blood pressure decreased significantly in both CPAP and placebo groups, but the mean nighttime blood pressure drop

increased significantly more in the therapeutic CPAP group. Another study showed that three days of CPAP therapy converted 15 of 22 sleep apneic patients who had lost their early morning blood pressure dip (10 mm Hg systolic and 5 mm Hg diastolic) to dippers.<sup>5</sup>

Should these findings change your practice? Both sleep apnea and hypertension are common conditions, and not every hypertensive patient needs a sleep study. I think it is reasonable to screen for sleep apnea in patients who have hypertension, particularly difficult to control hypertension. A history of witnessed apneas or sleepiness that interferes with daily function ought to raise a red flag, as should the physical findings of a BMI greater than 30 or neck circumference greater than 17 inches in a man or 16 inches in a woman.<sup>6</sup> ♦

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## Mortality and Institutionalization Following Hip Fracture

ABSTRACT & COMMENTARY

**Synopsis:** *Impaired mental status on admission was found to increase the chance of both mortality and institutionalization in older hip fracture patients, and each additional 10 years of age increased institutionalization risk 2.5 times in this large, one-year, population-based study of Canadian residents in Edmonton older than 64 years of age. Male gender also increased mortality risk fourfold, while socioeconomic factors did not influence the outcomes.*

**Source:** Cree M, et al. *J Am Geriatr Soc* 2000;48:283-288.

Previous studies of hip fracture outcomes in community-living elderly have shown surprisingly high rates of mortality and institutionalization, leading to further research on which variables might be modifiable to improve our current treatments. A 1993 British study following 1000 consecutive acute proximal femoral fractures found 33% mortality overall at one year; six-month mortality was similar at 28% for all

fractures (the overall rates included 8 patients < 65). For older patients, the mortality was higher: 38% for extracapsular fractures with a mean age of 80 years on admission. This figure rose to more than 50% mortality for those older than the age of 90. Intracapsular fractures gave a slightly lower overall mortality of 29% at one year. Institutionalization at one year was 30% for extracapsular fractures and 10% for intracapsular. More than 15% of patients died before leaving the hospital.<sup>1</sup>

In the United States, the New Haven Established Population for Epidemiologic Studies of the Elderly (EPESE) project followed 2812 residents 65 years of age and older for six years and tracked 120 persons suffering acute hip fractures with 18% mortality and 29% institutionalization at six months. They also found that fracture site (worse for subtrochanteric and femoral neck fractures compared to intertrochanteric) predicted worse outcomes, and additionally identified that poor mental status, male gender, comorbid conditions, and complications were statistically associated with more deaths. Patients who had four or more errors on the 10-item Short Portable Mental Status Questionnaire died at a rate of 36% compared to 12% for those with three or fewer errors.<sup>2</sup>

Now this Canadian study from Edmonton, Alberta, has extended the previous research by tracking more variables including demographics, social support, and health perception in a prospective inception cohort study in 1996-1997 that assessed new fractures both in the hospital and at three-month follow-up. The three-month period was chosen based on existing literature that shows little change in the mortality curve between three and 12 months. Fractures from pathological conditions such as Paget's disease or bone cancer were excluded, as well as recurrent fractures on the same hip within five years.

Starting with an elderly population in Edmonton of approximately 67,500, over the year 610 acute fractures were admitted to one of two available facilities, and 470 were interviewed for the study with an average age of 81 years. Three-quarters were female, 60% of all were widowed. Early deaths of 36 prevented inclusion in the study. By three months, the total mortality was 44 (or 8% of the group) of 558 analyzed. Of the group that died, one-half were male and 39% had previously resided in long-term care institutions.

Mental status was measured using the Mini-Mental State Exam (MMSE) scored between 0-30 (low to high mental functioning) as part of an in-person baseline interview in the hospital within the first week following the acute fracture. Follow-up was by telephone interview. Sixty-five percent of participants were able to be interviewed personally, and information was obtained

for the remainder from caregivers. When patients of the same age were paired by MMSE results, the lower scores ( $\leq 20$ ) were eight times as likely to be institutionalized as higher scores. For patients of different ages with identical MMSE scores, each additional 10 years of age tripled the risks of institutionalization.

Additional variables were evaluated that might be thought to influence better outcomes: social support, health perception and physical function both prefracture and three months postfracture were assessed by interview using the widely accepted Barthel Index, SF-12, and OARS scales. Years of education and preretirement occupation were used to calculate an "occupational prestige score." None of these appeared to contribute to institutionalization risk except postfracture physical function (prefracture status was not significant), including no effect from comorbidities obtained from the medical record. Even prefracture residence in a long-term care facility was not significant. The only variables in this study significantly related to the 17% risk of institutionalization were low cognitive function, increasing age, and postfracture physical function.

Mortality for hip fracture patients was only related to low cognitive function and male gender. Other studies have also confirmed gender as a higher risk and have speculated that males may have more serious falls, more comorbidities, or less social support to explain the difference. In this study, however, male gender was still associated with higher mortality even after controlling for social support and comorbidities.

#### ■ COMMENT BY MARY ELINA FERRIS, MD

Given the high frequency of hip fractures in the elderly (> 200,000 annually in the United States), and the devastating consequences and costs that they incur, research such as this article that contribute to our understanding of patient outcomes is most welcome. Although the different studies noted above are not completely comparable in populations used or variables analyzed (such as whether fracture patients were previously residing in the community or what type of mental status testing was used), they all reveal startling high mortality rates after acute fractures and high rates of subsequent institutionalization. Cree and colleagues did not comment on the lower mortality rates they found compared to previous studies, but perhaps advancing medical knowledge is having an effect here.

Since operative treatment of hip fractures was introduced in the 1950s, surgical experience provides a variety of options depending on the type of fracture and the degree of the patient's prefracture mobility, from simple percutaneous pinning to total hip replacement. A recent

article suggests that surgery is not advisable for bedridden or moribund patients, or those with osteoporotic bones and extensively comminuted fractures.<sup>3</sup> An extensive evidence-based review comparing conservative vs. operative treatment for extracapsular hip fractures revealed surprisingly limited evidence for improved outcomes from surgical management. No differences in medical complications or mortality were found, although surgery did result in shorter hospital stays and possibly a higher return to the patient's original residence. Conservative treatments produced less surgical complications but longer rehabilitation.<sup>4</sup>

There seems little doubt that poor mental function is associated with worse outcomes, leading to speculation that specialized rehabilitative services for this group might be beneficial. Or should we dare to suggest that an entirely different treatment approach, such as nonsurgical conservative comfort measures for low functioning fracture patients, might actually be the better choice? The lack of statistical association most variables contribute to better outcomes in this study stimulates creative thinking on what should be the treatment and rehabilitation of hip fractures. New approaches with appropriate outcome research are needed to provide more guidance for clinicians, patients, and their families facing difficult decisions on the most humane and beneficial treatments for the common condition of acute hip fracture. ❖

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## Impressive Performance of a Self-Rating Scale for Depression

ABSTRACT & COMMENTARY

**Synopsis:** *The Beck Depression Inventory (BDI) is an adequately sensitive and specific self-rated instrument to detect patients with major depression.*

**Source:** Lasa L, et al. *J Affect Disord* 2000;57:261-265.

This concise study from Spain examined the sensitivity and specificity of the Beck Depression

Inventory (BDI) in detecting the presence of major depression in the general population. Lasa and associates studied 1250 subjects between 18 and 64 years old, identified through census data. All individuals completed the short, self-rated BDI. Fifty-two cases had elevated BDI scores (a priori defined as greater than 12), as defined in previous published literature. Forty-four of these 52 subjects agreed to be interviewed. Thirty-two of the 44 subjects with BDI scores greater than 12 met criteria for major depression in a structured interview with a research psychiatrist. A random sample of 5% of the cohort who scored less than 13 on the BDI were also interviewed. None of these subjects with low BDI scores met criteria for major depression.

The statistical analysis of Lasa et al's findings revealed an extremely high sensitivity and specificity for their cutoff value for the BDI. A low BDI (< 13) was 100% predictive of not being depressed.

#### ■ COMMENT BY ANDREW L. STOLL, MD

In summary, this study examined the predictive value of the BDI for independently diagnosed major depression in the general population. The strong results suggest that the BDI is an adequately sensitive and specific self-rated instrument to detect patients with major depression. Because it is self-rated and requires little or no work from the clinician, the BDI may be a useful screening tool in a primary care practice, where detecting major depression has traditionally been a time-consuming and less than satisfactory process. (Dr. Stoll is Director, Psychopharmacology Research Laboratory, McLean Hospital, Belmont, MA.) ❖

## Pharmacology Update

### Linezolid (Zyvox): A New Antibiotic for Resistant Gram-Positive Organisms

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

The oxazolidinones are a new class of antimicrobial agents with a wide range of activity against many important human pathogens including many gram-positive bacteria. The FDA recently approved linezolid (Zyvox—Pharmacia & Upjohn), the first agent in this class. Linezolid is bioavailable both parenterally and orally and is active against

methicillin-resistant *Staphylococcus aureus* and vancomycin-resistant enterococci, among others.

### Indications

Linezolid is indicated for the treatment of infections in adults caused by designated susceptible microorganisms:

- Vancomycin-resistant *Enterococcus faecium* including concurrent bacteremia.
- Nosocomial pneumonia caused by *S. aureus* (methicillin-susceptible and -resistant strains), or *Streptococcus pneumoniae* (penicillin-susceptible strains only).
- Complicated skin and skin structure infections caused by *S. aureus* (methicillin-susceptible and -resistant strains), *Streptococcus pyogenes*, or *Streptococcus agalactiae*.
- Uncomplicated skin and skin structure infections caused by *S. aureus* (methicillin-susceptible strains only) or *S. pyogenes*.
- Community-acquired pneumonia caused by *S. aureus* (methicillin-susceptible strains only), or *S. pneumoniae* (penicillin-susceptible strains only).

Combination therapy may be clinically indicated if gram-negative organisms are documented or suspected.

### Dosage

For vancomycin-resistant *E. faecium* infections, including concurrent bacteremia, the recommended dose is 600 mg IV or orally every 12 hours for 14-28 consecutive days. For nosocomial pneumonia, community-acquired pneumonia (including concurrent bacteremia), or complicated skin and skin structure infections the dose is 600 mg IV or orally every 12 hours for 10-14 consecutive days. For uncomplicated skin and skin structure infections, the dose is 400 mg orally for 10-14 consecutive days.<sup>1</sup> Linezolid may be taken without regard to meals, but high-fat food should be avoided. No dosage adjustment is needed for geriatric patients or those with moderate renal impairment. Two metabolites of linezolid may accumulate in patients with renal impairment and the accumulation increases with the severity of impairment.<sup>1</sup>

Linezolid is available as injections (2 mg/mL, 100 mL, 200 mL, 300 mg), 400 mg and 600 mg tablets, and powder for oral suspension (100 mg/5 mL, 150 mL).

### Potential Advantages

Linezolid is well absorbed after oral administration with bioavailability close to 100%. It may be administered intravenously or orally without dose adjustment.<sup>1</sup> This allows for step-down therapy and outpatient treatment. Linezolid is not an inducer of cytochrome P450 isoenzymes and is not detectably metabolized by this

system; thus, drug interactions involving P450 system are unlikely.<sup>1</sup> In vitro data suggest that linezolid may be more active than either vancomycin or quinupristin/dalfopristin against *Enterococcus faecalis*.<sup>2</sup>

### Potential Disadvantages

Linezolid is a reversible nonselective inhibitor of monoamine oxidase. Mean maximum increases in systolic blood pressure of 32-38 mg Hg have been reported in normotensive subjects coadministered with pseudoephedrine (60 mg) or phenylpropanolamine (25 mg) given as two doses four hours apart.<sup>1</sup> These changes were seen 2-3 hours after the second dose of pseudoephedrine or phenylpropanolamine and returned to baseline 2-3 hours after peak. Large quantities of foods or beverages with high tyramine content should be avoided.<sup>1</sup> The most common side effects are diarrhea (2.8-11%), headache (0.5-11.3%), and nausea (3.4-9.6%).<sup>1</sup> Thrombocytopenia has been reported in subjects who were treated with 600 mg every 12 hours for up to 28 days.<sup>1</sup> Patients at risk for bleeding, those with pre-existing thrombocytopenia, those concurrently taking medication that may decrease platelets, or those who may require therapy of two weeks or longer should be monitored. The estimated rates of thrombocytopenia were 5% for subjects receiving more than 1 g per day and 3% for those receiving less than 1 g per day.<sup>6</sup> Resistant *E. faecium* has been seen in clinical trials.<sup>1</sup> The availability of linezolid as an oral formulation may increase the potential for inappropriate use and lead to resistant strains.

### Comments

Linezolid is the first approved member of a new class of antimicrobial agents, the oxazolidinones. These drugs inhibit protein synthesis by binding to bacterial 23 S ribosomal RNA of the 50s subunit. Linezolid is bacteriostatic against enterococci and staphylococci, and bactericidal for the majority of streptococci strains.<sup>1,3</sup> It is active against multidrug-resistant enterococci and multi-resistant gram-positive bacteria.<sup>2,5</sup> It is active against penicillin-sensitive, intermediate, and resistant *S. pneumoniae* as well as strains resistant to erythromycin, ceftriaxone, clindamycin, and tetracycline.<sup>3</sup> The cure rate based on an intent-to-treat analysis in subjects with documented vancomycin-resistant enterococcal infections with or without bacteremia was 67% (39/58) for the high dose (600 mg every 12 hours) and 52% (24/46) for the low dose (200 mg every 12 hours) when treated for 7-28 days.<sup>1</sup> Subjects could receive aztreonam or aminoglycoside if clinically indicated. This study was conducted without a comparator and the FDA's Anti-infective Drug Advisory Committee has recommended a comparative

trial with quinupristin/dalfopristin.<sup>4</sup> The cure rate for nosocomial pneumonia based on a modified intent-to-treat analysis was 57% (n = 94) for linezolid and 46% (n = 83) for vancomycin. The cure rate for complicated skin and skin structure infections was 86% (n = 316) for linezolid and 82% (n = 313) for oxacillin.<sup>1</sup>

### Clinical Implications

Linezolid is the second antimicrobial to be recently approved for treatment of vancomycin-resistant *E. faecium* after quinupristin/dalfopristin (Synercid). There are currently no head-to-head trials between linezolid and quinupristin/dalfopristin. In addition, linezolid is approved for the treatment of methicillin-resistant *S. aureus* in nosocomial and complicated skin and skin structure infections. The major advantage of linezolid is its oral bioavailability. Linezolid may be a useful alternative to vancomycin and streptogramin (quinupristin/dalfopristin) as cross-resistance has not been observed among these classes. Pharmacia & Upjohn is expected to submit additional efficacy data for the treatment of infections due to penicillin-resistant *S. pneumoniae* in hopes of gaining FDA approval for these indications. The average wholesale cost of linezolid (600 mg twice daily) is about \$100 per day for the tablets and about \$140 for the injectable. ❖

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**37. Which of the following triggered the quickest asthmatic response in the Vally et al study?**

- a. Beer
- b. Liquor
- c. Wine
- d. All of the above
- e. None of the above

**38. Which of the following is the most important determinant of both institutionalization and mortality following acute hip fractures in the elderly?**

- a. Socioeconomic and caregiver support
- b. Cognitive function (mental status) on admission
- c. Physical function prior to fracture
- d. Type of surgical treatment

**39. A 52-year-old man with hypertension reports daytime fatigue and heavy snoring at night. His weight is 240 lbs, height 5 feet, 9 inches. Blood pressure is 162/88 on three antihypertensives. Appropriate investigations at this point include:**

- a. referral for cardiac catheterization.
- b. urinary catecholamines.
- c. discussion with his bedpartner about snoring at night.
- d. taking a family history of the presence of hypertension.
- e. hospitalization for blood pressure management.

**40. Which of the following is true about the relationship between blood pressure and sleep apnea?**

- a. Sleep apnea is associated with hypertension in a “dose-dependent” way, and treatment of sleep apnea improves blood pressure.
- b. Sleep apnea is associated with hypertension in a “non-dose-dependent” way, and treatment of sleep apnea improves blood pressure.
- c. Sleep apnea is not associated with hypertension, and treatment of sleep apnea does not improve blood pressure.
- d. Sleep apnea is not associated with hypertension, but treatment of sleep apnea improves blood pressure.
- e. Sleep apnea is associated with hypertension in a “dose-dependent” way, but treatment of sleep apnea does not improve blood pressure.

**41. The self-rated Beck Depression Inventory may be used in clinical practice to screen for the absence of depression.**

- a. True
- b. False

**42. Which one of the following statements about linezolid (Zyvox) is not correct?**

- a. Linezolid is the first approved member of a new class of antimicrobial agents, the oxazolidinones.
- b. Linezolid is well absorbed after oral administration with, bioavailability close to 100%.
- c. The availability of linezolid as an oral formulation may increase the potential for inappropriate use and lead to resistant strains.
- d. The major disadvantage of linezolid is its oral bioavailability.

By Louis Kuritzky, MD

## Differences Between Men and Women in the Rate of Use of HNA

Gender discrimination has been suggested to have played a role in the use of a variety of medical and surgical procedures, including coronary revascularization and renal transplantation, but the data are inconclusive since gender differences for disease prevalence, contraindications to surgery, and personal preference are scanty and may have an important effect.

Hip and knee arthroplasty (HNA) improve symptoms and reduce disability in persons with advanced arthritic disease. Although more women than men undergo HNA, these data are confounded by the fact that women demonstrate a higher incidence of hip and knee arthritis, as well as osteoporotic hip fracture. The intention of this report was to evaluate whether gender differences exist as far as need for, or willingness to undergo, arthroplasty are concerned.

Women were slightly more likely than men to report chronic hip or knee problems (OR = 1.16). Despite the greater self-reported osteoporosis and arthritis among women, they were less likely than men to have undergone HNA (OR = 0.78). Women reported having discussed HNA with their physician less often than men (32% vs 42%), and this gender disparity persisted when adjusted for age and disease severity.

In Hawker and colleagues' final analyses, they conclude that though HNA is underused by both genders, underuse is more substantial for men than women. The fact that women appear to initiate discussion about their arthritis or seek a surgical solution less often than men, may be part of the explanation for

the observed disparities. ❖

Hawker GA, et al. *N Engl J Med* 2000; 342:1016-1022.

## Cost Effectiveness of RBV/IFN Alfa-2b After Interferon Relapse in Chronic Hepatitis C

Although interferon (ifn) can transiently eliminate virus from the serum in almost half of hepatitis C infected individuals, most relapse, with or without sustained treatment. Fortunately, combining ribavirin (RBV) with interferon (RBV/IFN) is able to produce undetectable virus levels in almost half of patients who relapse after IFN monotherapy. Unfortunately, RBV/IFN costs almost three times as much as IFN alone, calling into question the cost effectiveness of this regimen.

Using short-term clinical trial data to predict short-term events, and a long-term model based upon the natural history of chronic hepatitis C, Wong and colleagues evaluated the cost effectiveness of RBV/IFN vs. IFN alone, including patients who relapse after IFN monotherapy. Estimates below reflect model projections.

RBV/IFN would decrease lifetime major hepatic consequences (e.g., cirrhosis, CA, hepatic failure/death) by up to 20%, thereby reducing lifetime medical costs by almost \$5000, and increasing life expectancy by 4.2 quality-adjusted life years. Patients with moderate hepatitis (as compared with mild) would be anticipated to enjoy greater cost efficacy, since they are inherently more likely to suffer progression of disease.

Wong et al conclude that their analysis supports a six-month course of RBV/IFN for patients who have relapsed

after IFN monotherapy, both on a cost and mortality reduction basis. ❖

Wong JB, et al. *Am J Med* 2000;108: 366-373.

## Vitamin and Mineral Supplement Use in the United States

Vitamin and mineral supplements (V&M) represent the third largest over-the-counter (OTC) drug category used in America, yet there are scant data to define the frequency, type, and diversity of use of this class of product. A dietary supplement is defined as "a product other than tobacco intended to supplement the diet that bears or contains one or more of the following dietary ingredients: a vitamin, a mineral, an herb or other botanical, an amino acid, or a dietary substance for use by man to supplement the diet" (adapted from the Dietary Supplement Health and Education Act of 1994). Household questionnaires were administered to almost 34,000 persons with inquiry about V&M administration.

Approximately 40% of respondents reported V&M use over the past month. In this group of products, vitamin C was the most commonly used ingredient, followed by vitamin B<sub>12</sub>, B<sub>6</sub>, niacin, thiamin, B<sub>2</sub>, vitamin E, vitamin A, vitamin D, and folic acid. Persons with higher levels of education were more likely to take V&M, as did persons with higher income and those living in the western regions of the United States.

The dramatically high frequency of V&M use by patients suggests that clinicians might routinely inquire about habits of their patients in this sphere, lest potential toxicity go undetected. ❖

Balluz LS, et al. *Arch Fam Med* 2000; 9:258-262.

In Future Issues:

Beneficial Effects of High Dietary Fiber