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Wine, Women, and . . . Improved Glucose Tolerance?

ABSTRACT & COMMENTARY

Synopsis: *Two drinks per day (30 g) of alcohol improved insulin and triglyceride concentrations and insulin sensitivity in healthy postmenopausal women.*

Source: Davies MJ, et al. *JAMA.* 2002;287:2559-2562.

THIS WAS A WELL-CONTROLLED, PROSPECTIVE STUDY OF 63 healthy postmenopausal women. Participants consumed 0, 15, or 30 g/dL of alcohol (ethanol dissolved in orange juice) for 8 weeks in a randomized, blinded, crossover design. Diet and fluid intake were rather rigorously controlled. Measurements included glucose, insulin concentrations, triglyceride concentrations, and corrected insulin sensitivity. Davies and colleagues controlled for body mass index (BMI), caloric intake, and overall nutritional intake. The diet prescribed was 54% carbohydrates (and alcohol, if applicable), 32% fat, and 14% protein. Weight remained stable throughout the testing period.

Data were reported for 51 women. The "high-dose" alcohol condition (30 g/dL or 2 drinks/d) resulted in significant improvement in fasting insulin (reduced by 19.2%; $P = 0.004$), insulin sensitivity (increased by 7.2%; $P = 0.002$), and triglyceride levels (reduced by 10.3%; $P = 0.001$) compared with 8 weeks of no alcohol consumption. The changes in these measures with "low-dose" alcohol (15 g/dL) were not significant except for triglyceride levels, which were reduced by 7.8% ($P = 0.03$). Serum glucose did not change significantly compared with no alcohol intake for either alcohol consumption condition. Findings were consistent for all BMI strata (eg, were independent of BMI).

COMMENT BY BARBARA A. PHILLIPS, MD, MSPH

Previous studies have documented that moderate alcohol intake is associated with reduced risk of type 2 diabetes, reduced serum insulin concentration, and improved insulin sensitivity,[1-3] but this is the first study to demonstrate reduced fasting insulin concentrations in postmenopausal women.

INSIDE

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So, what do you say to your menopausal or postmenopausal patient about alcohol consumption, diabetes, and diet? This study suggests that her lipid profile and insulin sensitivity may fare better if she drinks at least 30 g/dL alcohol a day. Further, moderate alcohol intake has a cardioprotective effect.[4,5]

In their discussion, however, Davies et al point out that data from this same cohort have previously demonstrated that 1-2 drinks a day result in increased serum levels of dehydroepiandrosterone sulfate and estrone sulfate compared with placebo.[6] These steroid hormones may increase the risk of breast cancer.[7] Many women have an unreasoning fear of breast cancer, which is misguided, since heart disease (and lung cancer, for that matter) kill far greater percentages of women. A discussion about the risks and benefits of moderate alcohol intake might include some reality testing about relative likelihood (and modifiability of risk factors) for heart disease, lung cancer, and breast cancer. ■

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Is Viagra Safe?

ABSTRACT & COMMENTARY

Synopsis: *Cardiovascular effects of sildenafil are of relatively minimal degree even in patients with known CAD.*

Source: Arruda-Olson AM, et al. *JAMA.* 2002;287:719-725.

ERECTILE DYSFUNCTION (ED) AFFECTS 30 MILLION men in the United States and, since it usually occurs with increasing age, significant coronary artery disease (CAD) frequently coexists with this condition.[1] Millions of prescriptions have been written for sildenafil citrate (ie, Viagra) over the past 3 years for patients with and without CAD despite the fact that adverse cardiac events including acute myocardial infarctions, ventricular tachycardia, hypotension, and even death have been associated with its use.[2-7] Although multiple questions have been raised regarding the accuracy of these reports and the potential for reporting bias, the important central issue has always been whether the adverse cardiovascular events associated with sildenafil's use reflect a risk from the drug itself or if these events occurred simply because of the inherent risk of physical activity in patients with CAD.

Arruda-Olson and colleagues recently reported in *JAMA* the results of a randomized, double-blind, placebo-controlled, crossover trial conducted on 105 men with an average age of 66 years who were afflicted with ED and known or highly suspected CAD. These patients were carefully studied with respect to their resting heart rate, diastolic blood pressure, wall motion score index (ie, a measure of the extent and severity of wall motion abnormalities), and exercise capacity. Arruda-Olson et al

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concluded that in men with stable CAD, sildenafil had no effect on symptoms, exercise duration, or presence or extent of exercise-induced ischemia as assessed by exercise echocardiography.

COMMENT BY HAROLD L. KARPMAN, MD, FACC, FACP

The study by Arruda-Olson et al suggests that the cardiovascular effects of sildenafil are of relatively minimal degree even in patients with known CAD in that the presence and degree of ischemia and the heart rate at which ischemia occurred were no different in the control group or the group of patients who took sildenafil. These findings confirm previously reported noninvasive and invasive studies that have demonstrated how sildenafil influences coronary flow reserve but apparently does not significantly influence ischemia per se in a clinically important way. The available evidence also suggests that even though sildenafil does not provoke myocardial ischemia and is not associated with measurable adverse hemodynamic abnormalities, its use may be associated with dramatic decreases in blood pressure if nitrates are used within 24 hours of taking sildenafil and, therefore, the combination of these 2 agents is contraindicated.[8]

Since sildenafil itself does not appear to potentiate myocardial ischemia in patients with known CAD who are not taking nitrates, the important clinical issue appears to be how to assess risk when patients with established CAD request treatment for ED. Recognizing that the workloads of sexual activity are generally analogous to walking a mile in 20 minutes or climbing 2 flights of stairs in 10 seconds, the patient's description of his functional capacity and/or limitations will be helpful in assessing whether sexual activity is likely to precipitate clinically important ischemia with secondary symptoms. Also, a provocative stress test (ie, treadmill, stress echocardiogram, Cardiolite nuclear study, etc) should be considered if the patient has significant functional abnormalities or symptom production or if he/she is at high risk for CAD because of associated diabetes, hypertension, is a cigarette smoker, etc. If any of the functional tests are significantly abnormal, limitation of sexual activities may be advised in these patients simply because of the severity of their CAD and not because of alleged untoward hemodynamic effects of sildenafil.

In summary, it seems more likely that the cardiac events reported with sildenafil in patients with known CAD are related more to the physical demands of sexual activity in a patient with CAD than to the drug itself. Although the relative risk of myocardial infarction may be increased 2-2½ times in the 2 hours after sexual activity in men with or without angina, the absolute risk remains small.[9] However, in all patients with known CAD, a thorough discussion should be conducted with them about the risk of sexual activities if sildenafil is being prescribed and, if functional capacity is limited or significant symptoms are part of the picture, a provocative stress test is indicated. Sildenafil use should not be denied in patients solely because they possess the diagnosis of CAD. ■

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Treating Onychomycosis: A Head-to-Head Comparison of Terbinafine and Itraconazole

ABSTRACT & COMMENTARY

Synopsis: *Terbinafine had higher cure rates and lower relapse rates than itraconazole at 5 years.*

Source: Sigurgeirsson B, et al. *Arch Dermatol.* 2002;138: 353-357.

This study follows up the Lamisil vs. Itraconazole in Onychomycosis (LION) study whose results were published in 1999. Briefly, the LION study demonstrated that continuous terbinafine (Lamisil®) had higher mycological and clinical cure rates than itraconazole (Sporanox®). The original cohort of patients was multinational. The trial was prospective, randomized, double-blind, and double-dummy and analysis was intention-to-treat. The doses given were terbinafine 250 mg/d for 12 or 16 weeks and itraconazole 400 mg/d for 1 week every 4 for 12 or 16 weeks. The patients were followed for 18 months.

The current study (the LION Icelandic Extension Study) examined the 144 patients enrolled in the 3 Icelandic centers. The study had 2 parts. The first part sought to determine what happened to the patients over a course of 5 years. The second part took patients who had relapsed under either treatment and treated them with terbinafine for additional 12-week courses, whenever they had clinical signs of infection or when fungal cultures became positive after initial clearing.

Sigurgeirsson and colleagues had 3 definitions of "cure." First, there was mycological cure, which was the primary end point. It was defined as negative culture and no dermatophytes seen on microscopy. Second, there was clinical cure: 100% normal-looking toenail. Finally, there was complete cure, a combination of mycological and clinical. Relapses could also be mycological or clinical and were defined as you might expect, except that mycological was determined at 12 months and clinical at 18 months. The difference allowed toenails that were mycologically cured, but clinically abnormal, to grow out.

The patients were followed for an average of 54 months with visits every 6 months. Both groups were similar. They averaged 48 years old and were two-thirds male. The offending organism in 97% of cases was *Trichophyton rubrum*. The patients had onychomycosis for little better than 12 years with an average of 5.5 toenails infected.

After 18 months, 46% of terbinafine patients and 13% of itraconazole patients had a mycological cure without need of a second intervention. The clinical cure rates were 42% and 18%, respectively. Complete cure rates were 35% and 14%, respectively.

At the 18-month check, 5 of 57 (9%) terbinafine patients who were mycologically cured at 12 months had relapsed. The corresponding relapse rate among itraconazole patients was 7 of 32 (22%). At the end of the study, 13 of 57 (23%) terbinafine and 17 of 32 (53%) itraconazole patients had a mycological relapse. The clinical relapse rates were similar, 21% and 48%, respectively.

Seventy-two patients, who at 18 months had clinical signs of onychomycosis, accepted an offer of continued treatment with terbinafine. There were 25 patients from the terbinafine group and 47 patients who had taken itraconazole. At the end of the study, 23 (92%) of the terbinafine group and 40 (85%) of the itraconazole group were mycologically cured. Clinical cure rates were 76% and 77%, respectively.

■ COMMENT BY ALLAN J. WILKE, MD

In this head-to-head study, terbinafine had better clinical and mycological cure rates when compared to itraconazole. Additionally, most patients, who had failed initial treatment with either drug, responded to repeat courses of terbinafine. This may be explained by the fact that terbinafine is *fungicidal* and itraconazole is *fungistatic*. This study did not evaluate itraconazole performance after treatment failure.

Apparently, there is money to be made in foot fungus. No doubt, you have seen the direct-to-consumer advertisements that Janssen and Novartis run, emphasizing the cosmetic improvements achievable with their drugs. Indeed, both companies host web sites (http://www.sporanox.com/ and http://www.lamisil.com/fsite/html/ symptomatic.htm) that offer information about the disease, the medications, and coupons for the first prescription. This is not to play down the serious nature of onychomycosis, which can lead to more severe disease and affect quality of life, but to highlight the competition for our patients' attention and dollars.

One of the criticisms leveled at LION, which the LION Extension Study aimed to answer, was length of follow-up. Since toenails typically take 12-18 months to grow out, there was concern that the 18-month follow-up was too short. Five years seems long enough.

The cost of therapy was not addressed. A 12-week course of itraconazole 400 mg/d for a week (84 100-mg capsules) would retail around $500. Terbinafine 250 mg/d for the same length of time (also 84 tablets) is about $550. This does not include the cost of physician visits or liver function testing for terbinafine. Because itraconazole has many drug interactions (cyclosporine, digoxin, quinidine, and phenytoin, for instance), there may be additional expense if you monitor those drugs. The dose of itraconazole is not the one that appears in the product information insert. Janssen recommends 200 mg/d for 12 weeks (168 capsules!). Not for the faint hearted or light of wallet!

There are other therapies for onychomycosis. Griseofulvin is cheaper, but less effective. Ciclopirox (Penlac®, which also has a web site http://www.dermik.com/prod/ penlac/penlac.html) is available as a lacquer that is applied once daily for 48 weeks. It costs $180, but its complete cure rate is less than 10% and after 12 weeks of stopping therapy, 40% of patients had relapsed.[1]

My one caveat is that Novartis funded this study. I will allow the reader to discover which drug Novartis manufactures. ■

Reference

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cagA+ *H pylori* Strains are Disappearing

ABSTRACT & COMMENTARY

Synopsis: *Pathogenic cagA+ strains of H pylori seem to be vanishing, changing our expectations regarding H pylori and human disease.*

Source: Perez-Perez GI, et al. *Gut.* 2002;50:295-298.

Gastric colonization by *Helicobacter pylori* is probably as old as mankind. Most adults in developing countries are positive for this organism, and prevalence is far lower in developed countries. In all settings, *H pylori* is more common in the elderly. The cagA+ strains of *H pylori* are associated with such unfavorable outcomes as peptic ulcers and gastric cancer, but they may also be correlated with decreased risk of esophageal diseases (eg, GERD). This study is from large numbers of Finnish subjects between 1973 and 1994. Both cagA+ and cagA- prevalence fell. However, prevalence of cagA+ strains fell more dramatically in subjects < 45 years of age (34% to 8%) vs. cagA- strains (falling from 12% to 6%). It was concluded that there is declining acquisition of cagA+ *H pylori* in younger subjects and that *H pylori* acquisition occurs primarily during childhood although low rates of adult acquisition do occur as well.

COMMENT BY MALCOLM ROBINSON MD, FACP, FACG

As mentioned a number of times in *Internal Medicine Alert*, there seem to be many misconceptions about the significance and management of *H pylori* infections in our patients. Although there has been a statistical correlation between this organism and some nasty diseases, most people with gastric colonization by *H pylori* are asymptomatic and totally unaffected. This work suggests that pathogenic *H pylori* are destined to become even less frequent than is currently the case. A recent article confirmed that most newly acquired *H pylori* infections happen before age 10,[1] suggesting that treatment and prevention strategies should be directed at that age group. One should assess adult patients for *H pylori* only in the presence of peptic ulcer, and the likelihood of any association between *H pylori* and disease will only get smaller as the years pass by. ■

Reference

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Acute Lung Injury and ARDS

ABSTRACT & COMMENTARY

Synopsis: *Although the survival rate among patients 70 or older was high, these patients were twice as likely to die of acute lung injury compared with their younger counterparts, even after adjustment for covariates.*

Source: Ely EW, et al. *Ann Intern Med.* 2002;136:25-36.

More than half of all days spent in an intensive care unit (ICU) are incurred by patients older than 65, and the number of days per year spent in the ICU is 7-fold higher for persons older than 75. The population of older persons and their respective proportion of health care expenditures are expected to double by 2030. However, previous reports of older patients with respiratory failure from various causes have indicated that recovery and overall prognosis in this age group do not justify using age alone to determine treatment decisions.

The incidence of acute respiratory failure requiring mechanical ventilation increases 10-fold from the ages of 55-85, therefore, health professionals need to understand the effect of age on outcomes of acute lung injury and the acute respiratory distress syndrome (ARDS) to guide their treatment decisions and prognostic discussions.

Ely and associates studied 902 mechanically ventilated patients who participated in the National Heart, Lung, and Blood Institute multicenter trials of the ARDS Network between 18 March 1996 and 28 May 1999. Patients were enrolled from 24 hospitals associated with 10 US medical centers. Patients were eligible if they required mechanical ventilation for acute lung injury, had a PO_2/FIO_2 ratio of 300 or less, bilateral pulmonary infiltrates consistent with pulmonary edema, and no clinical evidence of left atrial hypertension. If measured, the pulmonary capillary wedge pressure was required to be 18 mm Hg or less.

To determine the rate of recovery of older compared with younger patients, the earliest time at which patients had successfully passed 4 clearly defined recovery landmarks was recorded: 1) the daily weaning screen, 2) the 2-hour spontaneous breathing trial, 3) the date on which the patient began a period of unassisted breathing that lasted 48 hours or more, and 4) discharge from the ICU alive with no mechanical ventilation.

Baseline severity of illness was recorded at enrollment by using the Acute Physiology, Age, and Chronic Health Evaluation III (APACHE III) score. During analysis, a modified APACHE III score that excluded age was used so that age would remain an independent

factor of outcome. Outcomes included duration of mechanical ventilation, total length of stay in the ICU, and survival at day 28 and 180.

Median duration of mechanical ventilation was 19 days (7-28 days) for patients 70 or older (n = 173) compared with 10 days (5-26 days) for patients younger than 70 (n = 729; $P < 0.001$). The duration of ICU stay was 21 days for the older group and 16 days for the younger group ($P = 0.004$). Survival rates decreased across increasing decades of age ($P < 0.001$): patients younger than 70 had a greater 28-day survival rate than patients 70 or older (74.6% vs 50.3%; $P < 0.001$). Older patients did not differ from younger patients with respect to achieving spontaneous breathing trials, but older patients required 1 more day than younger patients to achieve unassisted breathing and 3 more days to leave the ICU ($P = 0.005$). Of note, the reintubation rate for older patients was more than twice that for younger patients. In a multivariable Cox proportional hazards analysis, age of 70 or older was a strong predictor of in-hospital death ($P < 0.001$).

Ely et al concluded that patients 70 or older had 28-day and 180-day mortality rates that were nearly twice those of younger patients. Even after adjustment for covariates, age was a strong predictor of mortality. In fact, older persons had a hazard ratio of 2.5 for in-hospital death, and varying the age cut-off by using 65 or 80 years of age did not alter the significance of these results.

COMMENT BY DAVID OST, MD, & ALI MOJAVERIAN, MD

Survival has improved for patients with ARDS in recent years, and mortality is currently estimated at approximately 35-40%. One study of 918 patients with ARDS at a single institution between 1983 and 1993 found that the mortality from sepsis-related ARDS declined from 67% in 1990 to 40% in 1993; improvements in outcome were most pronounced for patients younger than 60.[1]

Studies of the natural history of ARDS and the efficacy of therapeutic interventions are complicated by the fact that respiratory failure is unusual as a direct cause of death. In one study of 47 patients, death during the first 3 days usually resulted from the underlying cause of ARDS, not respiratory failure itself.[2] Later, nosocomial infections and sepsis accounted for most deaths. The initial Murray Lung Score, designed to describe the severity of lung damage based on hypoxemia, compliance, radiographic appearance, and required positive end expiratory pressure, is a weak predictor of outcome, whereas failure to improve clinically over the first several days more accurately predicts a complicated course and mortality.[3]

This study emphasizes not only that older patients do worse, but also gives the details of what leads to their worse outcome. In particular, although they reach spontaneous breathing equally quickly compared to younger patients, they fail to come off the ventilator as quickly, require longer ICU stays, and are reintubated more often. This is consistent with prior observations that ARDS mortality is frequently not attributable to respiratory failure, but rather to its complications. Awareness of these complications may lead to earlier diagnosis and improved outcomes. ■

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Pharmacology Update

Alosetron Hydrochloride Tablets (Lotronex—GlaxoSmithKline) Reintroduction

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

THE FDA HAS APPROVED RESTRICTED MARKETING OF alosetron (Lotronex) for the treatment of women with diarrhea-predominant irritable bowel syndrome (IBS). The drug was originally approved in February 2000 and withdrawn in November 2000 due to serious and unpredictable gastrointestinal side effects. At least 7 deaths were associated with use of the drug. The approval includes a risk management program intended to ensure that both physicians and patients are fully informed about the risks and benefits of the drug.

Indications

Alosetron is only indicated for women with severe diarrhea-predominant IBS who have chronic IBS (> 6 months), failed to respond to conventional therapy, and severe diarrhea-predominant IBS with no anatomic or biochemical abnormalities. Severe diarrhea is defined as frequent and severe abdominal pain/discomfort, frequent bowel urgency or fecal incontinence, or disability or restriction of daily activity due to IBS.[1]

Dosage

The starting dose is 1 mg daily for 4 weeks. The dose

may be increased to 1 mg twice daily if symptoms are not controlled. Alosetron should be discontinued if adequate symptom control has not been achieved after 4 weeks with twice daily dosing.

Alosetron is available as 1 mg tablets.

Potential Advantages

Studies have indicated that alosetron was modestly effective compared to placebo in women with diarrhea-predominant IBS. In 2 reports with similar study design (n = 626,647) between 41-43% of patients treated with alosetron reported relief of IBS pain and discomfort compared to 26-29% for placebo ($P < 0.001$) for 3 months.[2,3] The primary end point was adequate relief of IBS pain and discomfort for at least 2 weeks per month. In another, (n = 801) using satisfactory control of bowel urgency as an end point, 73% of alosetron-treated patients had a satisfactory control of urgency compared to 57% for placebo ($P < 0.001$).[4] These studies were analyzed based on intent-to-treat and last observation carried forward.

Potential Disadvantages

Serious adverse events have been reported with alosetron. These include ischemic colitis and serious complications of constipation.[1] Since December 31, 2001, 352 hospitalizations have been associated with alosetron. There were 85 cases of ischemic colitis and 13 deaths. Seven of these were strongly associated with the drug.[5] Constipation occurred in 25-30% of patients compared to 3-5% for placebo.[2,3] The risks of serious problems resulting from constipation and ischemic colitis are about 0.1% and 0.3%, respectively.[1]

Comments

Alosetron is a 5HT3 receptor antagonist. These receptors are believed to regulate visceral pain, colonic transit, and gastrointestinal secretions. The manufacturer voluntarily withdrew the drug in November 2000 due to serious side effects. The FDA has now decided to approve a restricted marketing of alosetron. This approval was at least due to compelling testimony by patients who have benefited from the drug. The conditions of the marketing are that GSK will establish a prescribing program to enroll physicians who plan to prescribe the drug. These physicians will self-attest to his or her qualification and agree to educate patients on the risk and benefit of the drug. The physician will provide the patient with a copy of the FDA-approved Medication Guide and the patients will be asked to read and sign a Patient-Physician Agreement before receiving the initial prescription. The pharmacist will only be asked to fill prescriptions that display the prescribing program sticker affixed by an enrolled physician.[6] Patients will be started on a lower dose and titrated up to 1 mg twice daily as tolerated. GSK has committed to post-marketing studies and monitoring of the risk management program.

Clinical Implications

IBS is a common, non-life threatening disorder affecting about 20% of the population and twice as many women than men. It is a waxing and waning disorder with a high response rate to placebo. However, less than 5% is considered severe and only a fraction of the severe cases are diarrhea-predominant. It has been estimated that about 10% of severe patients would have a lasting effect with alosetron (about 0.5% or less).[7] This compares to the risk of ischemic colitis of 0.3% and the risk of serious problems resulting from constipation of 0.1%. ■

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CME Questions

37. In postmenopausal women, daily moderate alcohol intake is associated with:

a. increased BMI.
b. lower FSH levels.
c. fasting insulin concentrations.
d. increased blood pressure.
e. increased parathyroid hormone levels.

38. In the LION Icelandic Extension Study:

a. itraconazole had a higher clinical cure rate than terbinafine.
b. at 18 months, over half of the terbinafine patients were treatment failures.
c. patients who failed either drug did not respond to repeated courses of terbinafine
d. more patients had clinical cures than mycological cures.
e. *Trichophyton mentagrophytes* was the predominant organism.

39. *H pylori* is usually acquired:

a. by sexual contact.
b. in middle aged adults.
c. in adolescents.
d. in children younger than age 10.
e. by insect vectors (especially Anopheles mosquitoes).

By Louis Kuritzky, MD

The Effect of Creatine Supplementation on Anaerobic Performance: A Meta-Analysis

Male and female athletes of all ages sometimes use supplementation with various herbal and medicinal substances touted to enhance performance, appearance, or energy levels. Creatine monohydrate, more commonly known simply as creatine (CRT), has enjoyed a good deal of popularity among athletes interested in physical activities that require short bursts of high-intensity energy, such as sprinting or weight lifting. Despite the publication of more than 100 trials to date on CRT, consensus about the effect on speed, strength, or stamina remains elusive.

Misic and colleagues surveyed placebo-controlled studies (n = 29) addressing brief anaerobic activities in which CRT was the only known "performance aid" administered. Interested clinicians may be a bit stymied by the "fine print" which details the resulting data analysis, since they chose a somewhat unfamiliar measurement tool called an ES (reportedly similar to a 'z-score') to report their results; an ES of 0.2 is considered a small effect, 0.5 is moderate, and 0.8 is large.

The bottom line was that CRT did not show any significant favorable (or detrimental) effect on anaerobic performance. Though earlier trials have shown that CRT supplementation does enhance muscle levels of CRT, such augmentation does not appear to be reflected by enhanced performance. ■

Misic M, Kelley GA. Am J Sports Med. 2002;4:116-124.

Do Delayed Prescriptions Reduce the Use of Antibiotics for the Common Cold?

Despite well-established educational principles that decry the use of antibiotics for viral upper respiratory infections (URI), clinicians continue to prescribe them both here and abroad. Studies from the United States and United Kingdom have found that up to 60% of patients in some studies receive antibiotics for the common cold, with little encouraging news from distant neighbors like New Zealand, where as many as 78% of common cold sufferers are prescribed antibiotics.

One technique that holds promise for reducing the use of unnecessary antibiotics is that of delayed prescriptions (DRx), in which the clinician provides a prescription with the suggestion that it not be filled unless the patient remains symptomatic for a specific time period, usually 48-72 hours. Initial studies of DRx in the situation of pharyngitis have reported as much as a 66% reduction in subsequent prescription filling. This trial looked at the same technique in patients (n = 129) suffering the common cold.

Arroll and colleagues found that using the DRx technique resulted in a substantial reduction in use of antibiotics, from 89% in those patients who had been instructed to take antibiotics now, to 48% in those advised with DRx. Though optimally no patient with a common cold will use unnecessary antibiotics, the DRx method may be a valuable step toward achieving this goal. ■

Arroll B, et al. J Fam Pract. 2002;51: 324-328.

Immediate Repair Compared with Surveillance of Small Abdominal Aortic Aneurysms

Abdominal aortic aneurysms (AAA) are responsible for 9000 deaths annually in the United States. Surgical procedures for elective AAA repair are performed over 30,000 times annually, incurring up to 2800 deaths. Since risk of rupture is closely linked to AAA size, there is little disagreement about the appropriateness of surgical interventions for large (5-6 cm) lesions. Fewer consensus exists, however, about whether elective repair of "small" AAA (mean size, 4.7 cm) results in net gain for patients. This study randomized 1136 patients with small AAA to immediate repair vs. surveillance. Surveillance was performed with ultrasound, and patients were referred for surgical intervention if they became symptomatic, or if AAA enlargement rate suggested the need. Patients were followed for up to 4.9 years.

At the conclusion of follow-up, there was no demonstrable difference for all- cause mortality or death related to AAA between the group assigned to surveillance and the group receiving early surgical intervention. These findings are strengthened by the low operative mortality rate seen in the study group (2-2.4%). In concordance with the United Kingdom Small Aneurysm Trial, this trial demonstrated no benefit for early elective surgical repair of AAA less than 5.4 cm in diameter. ■

Lederle FA, et al. N Engl J Med. 2002; 346:1437-1444.

In Future Issues: Don't Be an Angry Young Man