Tips from Other Journals

Tips from Other Journals are written by the medical editors of *American Family Physician.*

The trade names of drugs listed in Tips from Other Journals are based on what is currently available and not necessarily the brand of drug that was used in the study being discussed.

Diagnosing Exercise-Induced Bronchoconstriction

Background: Airway obstruction following vigorous exercise, known as exercise-induced bronchoconstriction, is present in 60 to 90 percent of persons with asthma and 6 to 13 percent of persons without asthma or allergy. Symptoms of exercise-induced bronchoconstriction resemble those of an asthma exacerbation, including shortness of breath, chest tightness, and wheezing. Exercise-induced bronchoconstriction begins three to 15 minutes after the cessation of exercise and can last from 20 minutes to one hour. If a patient's clinical history suggests exercise-induced bronchoconstriction, the diagnosis can be confirmed by a standardized exercise challenge (e.g., controlled treadmill run followed by multiple spirometry measurements). Management includes education, improved physical fitness, and medications. Dryden and colleagues systematically reviewed evidence on the accuracy of several diagnostic tests for exercise-induced bronchoconstriction, and the effectiveness of nonpharmacologic and pharmacologic therapies.

The Study: Multiple electronic databases and proceedings from respiratory conferences were searched for publications through July 2009 that addressed one or more relevant topics. From 6,952 abstracts retrieved in initial searches, 137 articles met inclusion criteria for the review. Diagnostic tests for exercise-induced bronchoconstriction were compared with the standardized exercise challenge, whereas treatments were compared with no treatment or placebo. The authors assessed the quality of each of the retrieved studies using standard assessment instruments. The strength of evidence for each of the 12 key questions (six based on diagnosis, six based on treatment) was rated by two independent reviewers as high, moderate, low, or very low.

Results: In general, there was insufficient evidence to determine if a self-reported symptoms diary, methacholine challenge, sport- or venue-specific exercise challenge, eucapnic voluntary hyperpnea, free-running asthma screening test, and mannitol challenge were reliable diagnostic tools for exercise-induced bronchoconstriction compared with the standardized exercise challenge. Although the evidence for the methacholine and mannitol challenges was rated as moderate, estimates of sensitivity and specificity for these tests were imprecise or inconsistent across studies.

Pharmacologic therapies for exercise-induced bronchoconstriction included bronchodilators (e.g., short- and long-acting beta agonists, anticholinergics) and anti-inflammatory agents (e.g., leukotriene receptor antagonists, inhaled corticosteroids, mast cell stabilizers). There was consistent evidence that short- and long-acting beta agonists, leukotriene receptor antagonists, mast cell stabilizers, and anticholinergics were safe and effective for prophylaxis of exercise-induced bronchoconstriction in patients with asthma. The combination of a short-acting beta agonist and mast cell stabilizer was not more effective in preventing exercise-induced bronchoconstriction than a beta agonist alone. In comparisons by drug class, short-acting beta agonists were the most effective, followed by mast cell stabilizers, then anticholinergics. Leukotriene receptor antagonists were not directly compared with other therapies. Inhaled corticosteroids were found to be ineffective for prophylaxis. Despite a low strength of evidence, interval warm-up routines (e.g., short, intense sprints) and warm-up routines that combined interval and continuous components showed more promise for preventing exercise-induced bronchoconstriction than did continuous warm-up routines of up to 30 minutes.

Conclusion: The authors conclude that although several drug classes appear to be effective in preventing the onset of exercise-induced bronchoconstriction in patients with asthma, evidence on the accuracy of diagnostic tests is limited. They suggest that future research investigate the effects of treatments on patients who have exercise-induced bronchoconstriction alone without ▶

asthma, as well as subgroups defined by asthma severity, age, and baseline activity level.

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Source: Dryden DM, et al. Exercise-induced bronchoconstriction and asthma. Evidence Report/Technology Assessment No. 189. Rockville, Md.: Agency for Healthcare Research and Quality; 2010. AHRQ Publication No. 10-E001.

A Comparison of Screening Guidelines for Diabetes Mellitus

Background: According to 2005-2006 National Health and Nutrition Examination Survey data, the national prevalence of diabetes mellitus in ambulatory patients 20 years and older was an estimated 12.9 percent. Approximately 40 percent of these persons are unaware they have the disease, meaning 5.1 percent of U.S. adults 20 years and older have diabetes but do not know it. In recent years, type 2 diabetes has been confirmed to have the "legacy effect" associated with type 1 diabetes, which is defined as worsened cardiovascular morbidity and mortality after a period of untreated hyperglycemia, even if blood glucose levels are controlled at a later time. Sheehy and colleagues assessed the American Diabetes Association (ADA) and the U.S. Preventive Services Task Force (USPSTF) diabetes screening guidelines to determine their case-finding ability.

The Study: The authors analyzed electronic health records from a midwestern group practice from January 1, 2005, through December 31, 2007. The practice treated about 2 million patients in 48 million encounters since implementing electronic health records in 2003. Patients were included if they were 20 years and older on January 1, 2005; had seen their primary care physician for any reason at least twice in the previous 36 months, with one visit being within the previous 24 months; did not have a diagnosis of diabetes, prediabetes, or preexisting comorbidities in 2003 or 2004; did not have a visit for pregnancy between 2003 and 2007; and did not die during the study years. Among patients in the study who had one or more screening tests, 74.3 percent had random glucose testing; 9.1 percent, A1C measurement; 0.8 percent, fasting plasma glucose assessment; and 0.8 percent, glucose tolerance testing. ADA and USPSTF criteria for screening are shown in *the accompanying table*.

The authors used pre-2008 USPSTF guidelines during the study; additionally, they estimated how the newer 2008 USPSTF guidelines would compare in the same population by excluding hyperlipidemia as an inclusion criterion for patients who met the pre-2008 USPSTF criteria. The authors also studied how the number and type of high-risk factors affected the results, as well as if insurance status affected the rates of screening.

Table. Screening Criteria for Diabetes Mellitus

American Diabetes Association
Testing should be considered in all adults who are overweight (body mass index ≥ 25 kg per m^2) and have additional risk factors:
Physical inactivity
First-degree relative with diabetes
Members of high-risk ethnic populations
Women who delivered a newborn weighing > 9 lb (4.1 kg) or were diagnosed with gestational diabetes
Hypertension
High-density lipoprotein cholesterol < 35 mg per dL (0.91 mmol per L) or triglyceride level > 250 mg per dL (2.82 mmol per L)
Women with polycystic ovary syndrome
Impaired glucose tolerance or impaired fasting glucose on previous tests
Other clinical conditions associated with insulin resistance
History of cardiovascular disease
In the absence of the above criteria, testing for diabetes and prediabetes should begin at 45 years of age
If the results are normal, testing should be repeated at least at three-year intervals, with consideration of more frequent testing dependent on initial results and risk status
Pre-2008 U.S. Preventive Services Task Force
Screening for type 2 diabetes is recommended in adults with hypertension or hyperlipidemia
Evidence is insufficient to recommend for or against routinely screening asymptomatic adults for type 2 diabetes, impaired glucose tolerance, or impaired fasting glucose
2008 U.S. Preventive Services Task Force
Screening is recommended for asymptomatic adults with sustained blood pressure > 135/80 mm Hg
No recommendation for asymptomatic adults with blood pressure ≤ 135/80 mm Hg

Adapted with permission from American Diabetes Association. Standards of medical care in diabetes—2009. Diabetes Care. *2009;32 (suppl 1): S15, with additional information from U.S. Preventive Services Task Force. Guide to Clinical Preventive Services. 3rded. http://www.ncbi.nlm.nih.gov/bookshelf/br.fcgi?book=hscps3edrec&part=A26340. Accessed December 1, 2009, and Screening for type 2 diabetes mellitus in adults: U.S. Preventive Services Task Force recommendation statement [published correction appears in* Ann Intern Med. *2008; 149(2):147].* Ann Intern Med. *2008;148(11):846-854.*

Results: The study included 46,991 patients, of whom 59.4 percent were women and 99.5 percent were insured. A total of 33,823 patients met at least one of the three screening criteria (ADA criteria, 65.5 percent; pre-2008 USPSTF criteria, 58.0 percent; and 2008 USPSTF criteria, 25.6 percent). Of patients meeting the ADA criteria, 26,597 (86.4 percent) were screened, and 1,329 (5.0 percent) were diagnosed with diabetes. Among those meeting ▶

the pre-2008 USPSTF criteria, 24,221 (88.9 percent) were screened, and 1,293 (5.3 percent) were diagnosed with diabetes. Of those meeting the 2008 USPSTF criteria, 11,333 (94.0 percent) were screened, and 869 (7.7 percent) were diagnosed with diabetes. Of all patients who were eligible and tested by any criteria, 1,390 patients (4.8 percent) had newly diagnosed diabetes. Of those patients, the ADA screening criteria missed 4.4 percent, the pre-2008 USPSTF screening criteria missed 7.0 percent, and the 2008 USPSTF screening criteria missed 37.5 percent of patients who could have been diagnosed.

When individual high-risk factors were evaluated, prediabetes (15.8 percent), polycystic ovary syndrome (12.6 percent), and vascular disease (10.0 percent) indicated the highest rates of newly diagnosed diabetes. The authors' database did not include physical inactivity, family history of diabetes, or other conditions associated with insulin resistance, so they were unable to include patients with these possible risk factors in their analysis. The number of high-risk factors strongly correlated with a diagnosis of diabetes. Patients without insurance were less likely to be screened (54.9 versus 85.4 percent with insurance), but were more likely to be diagnosed with diabetes (14.0 versus 4.8 percent of the insured population).

Conclusion: The authors conclude that the ADA screening guidelines identify a significantly higher number of patients eligible for screening, and have an increased case-finding ability compared with the 2008 USPSTF guidelines. The number of risk factors and presence of certain high-risk factors can help determine prediabetes status. Patients without health insurance are screened significantly less often than those who are insured.

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Source: Sheehy AM, et al. Analysis of guidelines for screening diabetes mellitus in an ambulatory population. *Mayo Clin Proc.* January 2010;85(1):27-35.

EDITORS' NOTE: It is useful to note the rationale behind the 2008 USPSTF guidelines for screening adults for type 2 diabetes. The USPSTF concluded that there is no direct evidence suggesting that health outcomes for patients are altered when screening asymptomatic persons.[1] Additionally, the indirect evidence they reviewed did not show a benefit for screening general populations. The justification for eliminating hyperlipidemia from the 2008 screening guidelines includes a randomized controlled trial and a meta-analysis, both of which concluded that patients with hyperlipidemia benefit equally from lipid-lowering agents regardless of whether they have diabetes.[2,3] This is in contrast to patients with hypertension, because it has been demonstrated that they experience a greater benefit from more aggressive blood pressure control when they have a clinical diagnosis of diabetes.[3,4] Whereas intensive lifestyle modifications and some pharmacologic interventions have been shown to decrease the rate of progression from prediabetes to diabetes, the evidence of their impact on long-term health outcomes is lacking.[1] Despite their differing recommendations, the USPSTF and ADA guidelines should serve as tools to assist physicians in making a collaborative decision about diabetes screening with their patients.—C.H. and SUMI SEXTON, MD, Associate Medical Editor, *American Family Physician*

REFERENCES

1. Norris SL, Kansagara D, Bougatsos C, Fu R. Screening adults for type 2 diabetes: a review of the evidence for the U.S. Preventive Services Task Force. *Ann Intern Med.* 2008;148(11):855-868.
2. Collins R, Armitage J, Parish S, Sleight P, Peto R; Heart Protection Study Collaborative Group. MRC/BHF Heart Protection Study of cholesterol-lowering with simvastatin in 5963 people with diabetes: a randomised placebo-controlled trial. *Lancet.* 2003;361(9374):2005-2016.
3. Costa J, Borges M, David C, Vaz Carneiro A. Efficacy of lipid lowering drug treatment for diabetic and non-diabetic patients: meta-analysis of randomised controlled trials. *BMJ.* 2006;332(7550):1115-1124.
4. Hansson L, Zanchetti A, Carruthers SG, et al.; HOT Study Group. Effects of intensive blood-pressure lowering and low-dose aspirin in patients with hypertension: principal results of the Hypertension Optimal Treatment (HOT) randomised trial. *Lancet.* 1998;351(9118):1755-1762.

Is Lenient Rate Control Effective for Atrial Fibrillation?

Background: Rate control is the cornerstone of atrial fibrillation management, but the optimal target heart rate is unknown. Guidelines recommend strict rate control, but whether this approach actually improves patient outcomes has not been proven. Van Gelder and colleagues studied lenient rate control to determine if it is as effective as strict rate control in preventing cardiovascular morbidity and mortality in persons with atrial fibrillation.

The Study: The authors evaluated data from the Rate Control Efficacy in Permanent Atrial Fibrillation: a Comparison between Lenient versus Strict Rate Control II study, a prospective randomized trial examining whether lenient rate control (less than 110 beats per minute [bpm] at rest) was noninferior to strict rate control (less than 80 bpm at rest and less than 110 bpm with moderate exercise) in preventing cardiovascular events over two to three years. Eligible patients were younger than 80 years, had permanent atrial fibrillation for up to 12 months, were receiving anticoagulant therapy, and had a mean resting heart rate greater than 80 bpm. A total of 614 patients were given one or more rate-controlling drugs (i.e., beta blockers, nondihydropyridine calcium channel blockers, and digoxin) to achieve their target heart rate. The primary outcome was a composite of cardiovascular-associated outcomes, including death, embolism, sustained ventricular tachycardia, syncope, ▶

hospitalization for heart failure, and implantation of a cardioverter-defibrillator.

Results: Significantly more patients were able to achieve their target heart rates in the lenient rate-control group compared with the strict rate-control group (97.7 versus 75.2 percent, respectively), and significantly fewer follow-up visits were needed in the lenient rate-control group to achieve the target heart rate. No difference was noted between the groups regarding the primary outcome. There was also no difference between the groups with regard to all-cause mortality, heart failure stage, hospitalization rate, or adverse events, although the lenient rate-control group had a lower risk of stroke (hazard ratio = 0.35). There was no difference between the groups in the prevalence of atrial fibrillation symptoms, including palpitations, dyspnea, or fatigue.

Conclusion: The authors conclude that lenient rate control is easier to achieve than strict rate control in patients with permanent atrial fibrillation, with a similar rate of major clinical events.

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Source: Van Gelder IC, et al.; Race II Investigators. Lenient versus strict rate control in patients with atrial fibrillation. *N Engl J Med.* April 15, 2010;362(15):1363-1373.

Does Treating Periodontal Disease During Pregnancy Reduce Preterm Birth?

Background: Many studies have reviewed the relationship between clinical and subclinical infections and preterm birth. As a result, the inflammatory response to chronic subclinical infection has been used regularly in the etiology of preterm birth. Macones and colleagues conducted a randomized trial to assess the potential benefit of treating destructive periodontal disease in pregnant women to reduce the incidence of spontaneous preterm birth.

The Study: Pregnant women between six and 20 weeks of gestation were recruited from prenatal care clinics for the study. Gestational age and singleton pregnancy were verified by dates and ultrasound assessments. Women already receiving periodontal treatment and those who had used antibiotics or antimicrobial mouthwash were excluded from the study, as were women with mitral valve prolapse. The assessment for periodontal disease was based on an initial screening by nurses followed by a secondary screening of potential cases by dental hygienists. Women with attachment loss of at least 3 mm on three or more teeth were eligible for the study. Dental faculty members assessed 10 percent of participants at each site to monitor eligibility.

Study participants were randomly assigned to receive scaling and root planing (active treatment) or superficial cleaning (control). Routine prenatal care was provided to all participants. Obstetric physicians and staff were blinded to the study allocation of individual patients. The primary outcome was spontaneous preterm birth, defined as delivery before 35 weeks of gestation as a result of idiopathic preterm labor or preterm rupture of the amniotic membranes.

Results: One half of the more than 3,500 women screened met the criteria for periodontal disease. Of the 756 available participants, 376 were randomly assigned to scaling and root planing and 380 to superficial cleaning. The groups were comparable in gestational age, severity of periodontal disease, and history of preterm delivery. The average age of study participants was 24 years, 87 percent were black, and 85 percent were single. Twenty-nine percent of the active treatment group and 35 percent of the control group had some form of college education. Approximately one half of all participants had moderate to severe periodontal disease.

Spontaneous preterm delivery occurred in approximately 10 percent of women from each group, and the average gestational age at delivery (38 weeks) was also similar. No statistically significant differences were noted in other pregnancy outcomes, including mean birth weight, proportion of low– or very low–birth-weight infants, stillbirths, and measures of neonatal morbidity and mortality. A trend towards increased risk of preterm births indicated for maternal or fetal complications was noted in the active treatment group. Subgroup analysis showed an increased risk of preterm births in multiparous mothers assigned to active treatment, but no differences in nulliparous participants by study assignment. Increased risk of preterm birth was also noted in the active treatment group for women with a history of preterm birth and women with more severe periodontal disease.

Conclusion: The authors of this study found no evidence of improved pregnancy outcomes in mothers undergoing active periodontal treatment. The finding of a trend towards increased premature births in women receiving treatment for periodontal disease contrasts with reports of benefits from previous studies. Although differences in study populations and design may explain the differences in findings, the possibility that treatment of periodontal disease during pregnancy could increase the risk of premature birth is concerning.

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Source: Macones GA, et al. Treatment of localized periodontal disease in pregnancy does not reduce the occurrence of preterm birth: results from the Periodontal Infections and Prematurity Study (PIPS). *Am J Obstet Gynecol.* February 2010;202(2):147.e1-147.e8. ■