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Internal Medicine Alert's Editor, Stephen Brunton, MD, is a consultant for Sanofi-Aventis, Ortho-McNeil, McNeil, Abbott, Novo Nordisk, Eli Lilly, Endo, EXACT Sciences, and Astra-Zeneca, and serves on the speaker's bureau of McNeil, Sanofi-Aventis, and Ortho-McNeil. Peer reviewer Gerald Roberts, MD, reports no financial relationship to this field of study.

Motion and Mortality

ABSTRACT & COMMENTARY

By **Barbara A. Phillips, MD, MSPH**

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Dr. Phillips serves on the speaker's bureau of Cephalon, Boehringer Ingelheim, Merck, ResMed, and GlaxoSmithKline, and is a consultant for Boehringer Ingelheim, Wyeth-Ayerst, and ResMed.

Synopsis: Expending energy though any activity may reduce mortality in older adults.

Source: Manini TM, et al. Daily activity energy expenditure and mortality among older adults. *JAMA*. 2006;296:171-179.

THIS STUDY WAS A PROSPECTIVE, 6-YEAR FOLLOW-UP OF 302 people who were between 70 and 82 years of age at the beginning of the study. They were recruited from the ongoing Health, Aging, and Body Composition study cohort assembled through the Universities of Pittsburgh and Tennessee. Total energy expenditure was measured using the doubly labeled water technique¹ over a 2-week period. Resting metabolic rate was calculated using indirect calorimetry.² Free-living activity energy expenditure was calculated using the total energy expenditure and resting metabolic rate,³ using a standard formula. The participants also self-reported physical activity over a 7-day period. Height, weight and body fat were measured with precision, and detailed sociodemographic and medical history information was collected. Participants were followed for an average of 6.1 years; death was ascertained by phone contact every 6 months and verified by death certificates.

The average age of the assembled cohort was 74.8 years; 48.3% were black, 50.3% were women, and 46% were from Pittsburgh. Women had lower levels of energy expenditure than men (251 vs 769 kcals/day). Participants with the highest level of active energy expenditure were more likely to be from Pittsburgh and had a higher body mass index, but a lower percentage of body fat.

The cumulative mortality over 6 years of follow-up was 18.2% (43.2/1000 for men and 27.3/1000 for women). After adjusting for multiple confounders (including body mass index and baseline health status), there was an inverse linear relationship between activ-

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ity energy expenditure and mortality. The absolute risk for mortality in the highest, middle and lowest levels of activity were 12.1%, 17.6%, and 24.7%, respectively. Every 287 kcal/day energy expenditure lowered the 6-year mortality rate by about 30%, regardless of intensity of activity reported. Those who reported working for pay and climbing stairs were more likely to be in the higher energy expenditure category. There was good correlation between both duration and intensity of self-reported physical activity and free-living activity energy expenditure; intensity of activity or exercise did not predict or confer survival.

■ COMMENTARY

This study confirms many previous observational studies that have demonstrated reduced mortality in adults who exercise. What is new and important about

this work is that it demonstrates that physical activity which might not be “counted” as exercise confers survival benefit. Simply burning up calories by moving around (which was objectively measured in this study) can delay death. This appears to contradict the belief that exercise must be carried out at a specific intensity to reduce mortality.⁴ The authors estimated that performing 1¼ hours of a variety of activities, including housework, child care, walking at 2.5 miles/hour, will expend 287 kcals.

While it is possible that those who were sicker were less likely to be active, the investigators rigorously controlled for this possibility, and noted that both self-assessed and clinically determined health status was not significantly different across activity levels.

This paper confirms that longer life now joins a long list of benefits conferred by physical activity in older people, including reduced coronary heart disease,⁵ cancer,⁶ falls,⁷ and dementia.⁸

In the accompanying editorial, Blair and Haskell point out that fitness may be a stronger predictor of mortality than physical activity per se.⁹ They also clarify that a substantial difference in energy expenditure in those who were most active was accounted for by “nonexercise activity thermogenesis (NEAT),”^{10,11} which includes fidgeting, gum-chewing, maintenance of posture, and other physical activities of daily life. NEAT is a hot topic among obesity researchers, as it appears to account for some of the huge variability in human weight gain associated with overeating. The current paper suggests that NEAT has an important role in longevity as well. ■

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Sore Points on Treating Sore Throats

ABSTRACT & COMMENTARY

By Eileen C. West, MD

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Dr. West reports no financial relationship to this field of study.

Synopsis: *Clinicians seem not to follow any of several recommended guidelines when evaluating and treating pharyngitis and, as a result, there is widespread overtreatment with antibiotics.*

Source: Linder JA, et al. Evaluation and treatment of pharyngitis in primary care practice: the difference between guidelines is largely academic. *Arch Intern Med.* 2006;166: 1374-1379.

WHEN WAS THE LAST TIME YOU CAVED IN AND GAVE antibiotics, even though you weren't convinced the patient had strep throat? Apparently, you are not alone.

Every year, patients in the United States make about 11 million visits to a health care provider that result in a diagnosis of pharyngitis. Approximately 10% of adults with pharyngitis will have group A beta-hemolytic streptococci, the only common cause of sore throat for which antibiotics are indicated. However, 70% of American adults with pharyngitis are treated with antibiotics. Everyone seems to agree that the antibiotic prescribing rate is too high, but there is disagreement about the best way to evaluate and treat adults with pharyngitis.

The American College of Physicians (ACP), the American Academy of Family Practice and the Centers for Disease Control and Prevention together recommend the use of the 4-point Centor criteria in evaluating adults with pharyngitis. These criteria are: 1) subjective or objective fever > 100.4°F, 2) absence of cough, 3) tender anterior cervical lymphadenopathy, and 4) tonsillar exudate.¹

The ACP guideline then recommends two possible strategies.² The ACP EMPIRICAL STRATEGY suggests empirical treatment of patients who meet 3 or 4 Centor criteria. The ACP TEST STRATEGY suggests: 0 or 1 criteria met—no test or treat, 2 or 3 criteria—test using a rapid antigen detection test and prescribe antibiotics to patients with a positive test, 4 criteria—treat. The Infectious Diseases Society of America (IDSA) agrees with no testing or treating patients with 0 or 1 criteria, but recommends microbiologic confirmation for all adults with pharyngitis prior to antibiotic prescribing.³ The authors of the IDSA guideline have openly disagreed with the ACP guidelines stating that use of clinical criteria alone results in overprescribing antibiotics to patients unlikely to have streptococcal pharyngitis.

In their retrospective analysis of over 2000 visits to Boston area primary care sites for pharyngitis, Linder et al study adherence to established guidelines to evaluate patients for strep pharyngitis. The results show that not only is there disagreement about which guideline to follow, but in 66% of visits, no guidelines are followed at all. Most of the nonadherence (78%) is related to testing and treating patients with few clinical criteria for pharyngitis.

In these academic-affiliated practices, 80% of visits included a streptococcal test (rapid antigen detection [RADT] in 25%, throat culture in 39%, both in 16%). 33% of tests in the RADT only group were positive, 15% of the culture only group were positive, and in the group where both tests were performed, 12% RADT and 15% of cultures were positive.

In this study, clinicians prescribed antibiotics in 47% of visits overall. While lower than national rates, it still far exceeds the expected prevalence of strep throat. Those given antibiotics were younger, had symptoms for a shorter time, and had a higher mean temperature. Prescribing was more common for patients with Centor criteria. The lowest prescribing rate (24%) was found in the clinic with a 100% testing rate and the highest (77%) was found at the clinic with the lowest testing rate. Among patients who had a positive streptococcal test, 98% received antibiotics.

Among those with a negative test, 30% received antibiotics. Of all antibiotics given, 35% went to those with a positive test, 40% went to those with a negative test, and 24% went to those with no testing. Antibiotics were overprescribed in general, but in particular nonrecommended antibiotics were used 40% of the time. Penicillin remains the antibiotic treatment of choice.

■ COMMENTARY

There has been extensive debate about the best way to approach ambulatory patients with pharyngitis. Most of the debate focuses on how to test and manage patients with more severe pharyngitis who meet several well-defined clinical criteria.

As Centor himself points out in an editorial in the same issue,⁴ the management of adult pharyngitis rarely receives attention in residencies or CME programs. Yet is it one of the most common reasons for office visits. As the study shows, clinicians may be ordering tests but are not using the results to determine treatment. Adhering to any of the guidelines discussed above showed only modest differences in the antibiotic prescribing rate overall. By far the biggest issue was excessive testing and treating of patients with few or none of the established clinical criteria. It seems that in order to prevent unnecessary antibiotic use, which guideline to use is not as important as adhering consistently to one of the guidelines.

The bottom line is regardless of which guideline you choose, avoid testing and treating patients at low risk for streptococcal pharyngitis, particularly those with viral symptoms, such as cough, nasal congestion, or pharyngeal vesicles. Second, penicillin remains the antibiotic of choice because it is effective, well tolerated, and inexpensive and group A (beta)-hemolytic streptococci are universally susceptible. ■

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Finally an Optimal Strategy for Diagnosing Deep Vein Thrombosis

ABSTRACT & COMMENTARY

By Joseph E. Scherger, MD, MPH

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Dr. Scherger reports no financial relationship to this field of study.

Synopsis: A medical research unit in the United Kingdom analyzed 18 different strategies for managing patients with suspected deep vein thrombosis (DVT). Using systematic review, meta-analysis and cost effectiveness analysis, they settled on an algorithm based on clinical risk. The initial screen for all patients is a latex D-dimer test. If the D-dimer test is negative and the patient is low or intermediate risk (Wells rule), DVT is ruled out. If the clinical risk is high, and the D-dimer test is negative, an above-the-knee ultrasound is ordered and, if positive, the patient is treated. If the D-dimer test is positive, an ultrasound is ordered regardless of risk. If the ultrasound is negative and the patient is high risk, it is repeated before a treatment or discharge decision is made.

Source: Goodacre S, et al. How should we diagnose suspected deep-vein thrombosis? *QJM*. 2006;99:377-388.

DEEP VEIN THROMBOSIS OF THE PROXIMAL LOWER extremity is one of the most important and challenging diagnoses to make. The treatment requires inpatient care and is potentially life saving. Multiple evolving diagnosis and treatment algorithms are available which make clinical decision making difficult. Variations in the management of patients with suspected DVT are an important quality issue. Credit the United Kingdom and its National Health Service to commission a meticulous detailed analysis of multiple strategies to come up with an approach which is both highly accurate and cost effective.

After a systematic review and meta-analysis of 18 different strategies, a hypothetical group of 1000 patients were managed using each algorithm. A mean survival of 11.6 quality adjusted life years (QALYs) was used after a diagnosis of DVT at age 60. Clinical risk was assigned using the Wells Clinical Prediction Rule using 9 factors to score the risk of DVT. A recent analysis of the *Annals of Internal Medicine* questioned the reliability of the Wells rule in ruling out DVT.¹ However, in the British analysis, the Wells rule was mostly used to identify

patients at high risk of DVT for further analysis even if the D-dimer test is negative.

The latex D-dimer test is a major advance in screening for DVT and other hypercoagulation states. The D-dimer reflects fibrin degradation products which indicate thrombus formation, and is positive in a number of conditions besides DVT, such as in disseminated intravascular coagulation (DIC). The test is sensitive for DVT but not specific, and may rise in the elderly, with false positives in patients with rheumatoid arthritis, high triglycerides and elevated bilirubin. The test is not diagnostic for DVT and should be followed up by more specific testing such as venous ultrasound.

Using the algorithms in this study, the percentage of patients with proximal DVT who would be treated appropriately ranged from 90.1% to 99.5%, and the patients without DVT treated inappropriately ranged from 0.6% to 6.0%. The final recommendations for the most accurate and cost effective algorithm are quite simple. The initial screen for all patients is a latex D-dimer test. If the D-dimer test is negative and the patient is low or intermediate risk (Wells rule), DVT is ruled out. If the clinical risk is high, and the D-dimer test is negative, an above the knee ultrasound is ordered and if positive the patient is treated. If the D-dimer test is positive, an ultrasound is ordered regardless of risk. If the ultrasound is negative and the patient is high risk, it is repeated before a treatment or discharge decision is made.

■ COMMENTARY

Even though this study is based on hypothetical patients, the analysis is quite rigorous, and uses the best available evidence. No combination of tests is perfect and there is always a risk of a missed diagnosis. A main contribution of this analysis is that not all patients require ultrasound, which may be difficult to obtain acutely in the primary care setting. As the study in the *Annals of Internal Medicine* points out, some patients (2.9% in their analysis) will have a low Wells score and a negative D-dimer test and will be found on ultrasound to have DVT. Maybe clinical judgment here should also include the “thin slicing” of rapid clinical intuition described by Malcolm Gladwell in *Blink*. If our initial assessment makes us think of DVT, we should be quite certain it is not present before accepting that it is ruled out.

We now have coherence in the diagnosis of suspect DVT. The three-part assessment is easy to remember: D-dimer testing, the Wells rule, and venous ultrasound. Combined with the clinical judgment of an experienced clinician, we have sound and consistent strategies for the diagnosis of DVT. ■

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PPI or Testing for *Helicobacter pylori* as the First Step for Patients Presenting with Dyspepsia?

ABSTRACT & COMMENTARY

By Malcolm Robinson MD, FACP, FACG

Synopsis: Testing and treating *H. pylori* and empirical PPI treatment similarly relieved symptoms in dyspeptic patients, but the ‘test and treat’ strategy resulted in lower endoscopic workload and decreased cost.

Source: Jarbol DE, et al. Proton pump inhibitor or testing for *Helicobacter pylori* as the first step for patients presenting with dyspepsia? A cluster-randomized trial. *Am J Gastroenterol.* 2006;101:1200-1208.

MANAGEMENT OF DYSPEPSIA IN PRIMARY CARE COULD involve prompt endoscopic evaluation, ‘testing and treating’ *H. pylori*, or prescription of empirical anti-secretory therapy. Because discovery and eradication of *H. pylori* might obviate recurrent peptic ulcer disease (PUD) in populations where PUD is prevalent, many guidelines recommend testing for *H. pylori* followed by eradication of the organism when it is found. However, most practitioners do not follow such guidelines, and scientific support for this approach has been less than compelling. Most authorities agree that ‘test and treat’ provides comparable benefits vs. prompt endoscopy, but the comparative utility of initial PPI treatment is less well defined. The present government-funded study was done in 106 general practices in one Danish county (population 472,000) between 2001 and 2003. 250 patients were enrolled in each of 3 groups.

The three strategies employed were: a) esomeprazole 20 mg b.i.d. for one week; b) *H. pylori* testing followed by treatment for positive cases; c) esomeprazole 20 mg b.i.d. for one week followed by ‘test and treat’ approach if symptoms recurred. *H. pylori* testing involved the use of the well-validated 13-C urea breath test (in patients who had had no PPI treatment for at least one week). Eradication therapy was esomeprazole 20 mg, amoxicillin 500 mg, and clarithromycin 500 mg, all given twice daily for a

week. (This regimen is not approved in the United States). Diary cards querying GI symptoms and quality of life were mailed to all participants monthly for one year. 87% of patients completed all diaries. Symptom control and quality of life at 1 year didn't differ between treatment groups. More endoscopies were done in the PPI recipients than in either other group. The authors agreed that recruitment bias could have occurred between and among the various practice clusters. Many of these patients had reflux symptoms in addition to dyspepsia (epigastric discomfort), and the initial presence of GERD-type symptoms led to more PPI use during follow-up. This population had 24% of patients found to be *H. pylori*-positive. The authors admitted that their results could be affected if reflux were to worsen in patients whose *H. pylori* infection was eradicated or if such patients subsequently were shown to have antibiotic resistant infections.

■ COMMENTARY

This study has many peculiarities. It is hard to understand why the authors chose a single week of PPI therapy as one arm of the study since this is not the standard of care anywhere in the world. In most US populations, the prevalence of *H. pylori* would be lower than found in this Danish study. This would make the potential benefit from a 'test and treat' strategy. The real universal answer is not yet 'in' for the utility of testing for *H. pylori* in dyspeptic patients since populations not only differ in rates of *H. pylori* infection but also in the virulence of whatever strains happen to be present. In places where peptic ulcer disease due to *H. pylori* is still relatively common, 'test and treat' may still be a perfectly valid therapeutic option. Such favorable results are far less likely in most North American populations. ■

Pharmacology Update

Human Papillomavirus Quadrivalent (types 6, 11, 16, 18) Recombinant Vaccine (Gardasil®)

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

Dr. Elliott is Chair, Formulary Committee, Northern California Kaiser Permanente; Assistant Clinical Professor of Medicine, University of California, San Francisco; Dr. Chan is Pharmacy Quality and Outcomes Manager, Kaiser Permanente, Oakland, CA.

Drs. Chan and Elliott report no financial relationships to this field of study.

THE FDA HAS LICENSED THE FIRST VACCINE TO PREVENT cancer due to human papillomaviruses (HPV)

types 6, 11, 16, and 18, the most common subtypes of this prevalent virus. The vaccine represents the first vaccine approved for the prevention of cancer. The quadrivalent vaccine is marketed by Merck & Co. as Gardasil®.

Indications

HPV vaccine is indicated in girls and women (age 9-26 yrs) for the prevention of cervical cancer, genital warts, and precancerous or dysplastic lesions (cervical adenocarcinoma in situ (AIS), cervical intraepithelial neoplasia (CIN) grade 2 and 3, vulvar intraepithelial neoplasia (VIN) grade 2 and 3, vaginal intraepithelial neoplasia (VaIN) grade 2 and 3 and cervical intraepithelial neoplasia grade 1.¹

Dosage

0.5 mL is administered intramuscularly in 3 separate doses over 6 months (0, 2, 6 months).

Potential Advantages

The vaccine has demonstrated effectiveness in preventing HPV infection, cervical dysplasia, and external genital lesions related to the 4 types of HPV.¹⁻³ Studies were not long enough (~ 2 yrs) for cervical cancer to develop.⁴

Potential Disadvantages

The vaccine is not effective treatment for individuals who have already been infected with HPV (ie, PCR or seropositive) and does not protect against HPV types not included in the vaccine. The duration of immunity beyond 2 years has not been established. The most common adverse events are local injection site reactions—pain (84%), swelling (25%), erythema (25%), and fever (10%).¹

Comments

The HPV vaccine is comprised of virus-like particles (VLP) derived from the L1 capsid protein of HPV types 6, 11, 16, 18 using recombinant techniques. Each dose (0.5 mL) contains 20 µg, 40 µg, 40 µg, and 20 µg of VLPs respectively. The efficacy of HPV vaccine was established in four studies with 3 involving all four HPV types 6, 11, 16, and 18 (n ~ 18,000). Subjects were nonpregnant women ages 16-23. Combined efficacy in preventing AIS, CIN 1, 2, or 3 were 95.2% (95% CI, 87.2%-98.7%) and 98.9% (95% CI, 93.7%-100%) for genital warts in individuals who received all 3 doses and were PCR or seronegative at baseline and one month after the last dose.¹ For those who received at least one dose, were HPV-

naïve at baseline and 1 month after the first dose, the efficacies were 93.7% (95% CI, 87.7%-97.2%) and 93.4% (95% CI, 87.0%-97.0%) respectively. For the general population (HPV-naïve and nonnaive) under the same conditions, efficacies dropped to 46.4% (95% CI, 35.2%-55.7%) and 68.5% (95% CI, 57.5%-77.0%). The vaccine is only effective against types in the vaccine to which the patient is naïve. The vaccine appears to be as effective in young women and adolescents based on immune response. The vaccine is generally well tolerated with local injection reactions most frequently reported. The estimated cost for Gardasil is \$360 per person.

Clinical Implications

HPV is a common infection among sexually active women as up to 70% of sexually active women may become infected in their lifetime.⁵ The American Cancer Society estimates that in 2006 there will be about 9,710 new cases of cervical cancer and about 3,700 will die from the disease.⁶ HPV types 16 and 18 causes approximately 70% of cervical cancers and types 6 and 11, 90% of genital warts.⁴ The vaccine is most effective when administered to HPV-naïve individuals (eg, before start of sexual activity). The Advisory Committee on Immunization Practices (ACIP) recommends HPV vaccine for females at age 11 to 12 years of age.⁷ Catch up vaccination is also recommended for females 13 through 18 years of age who have not been previously vaccinated or who have not completed the full series. The vaccine does not protect against less common HPV types not included in the vaccine. Therefore routine and regular pap screening must not be ignored. ■

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CME Questions

9. *Helicobacter pylori* assessment with eradication of *H. pylori*-positive dyspeptic patients provides:
 - a. a potentially cost effective approach to the management of the dyspeptic patient
 - b. unequivocal reduction in subsequent gastric malignancy in treated patients.
 - c. no risk of subsequent systemic infections with antibiotic resistant organisms.
 - d. definite reductions in post-treatment reflux symptoms.
 - e. far better symptom resolution than was achieved in the PPI-only treatment group.
10. Which of the following strategies is the most cost effective for diagnosing deep vein thrombosis in a suspected 60-year-old patient?
 - a. Observe the patient with a low clinical risk, and order a venous ultrasound if the clinical exam becomes more suggestive.
 - b. Order a D-dimer test and if negative, observe the patient.
 - c. Order a D-dimer test and if positive, order an ultrasound.
 - d. If a D-dimer test is negative in a high risk patient, order an ultrasound and discharge the patient if it is negative.
11. Which of the following is *not* one of the Centor clinical criteria for assessment of pharyngitis:
 - a. tonsillar exudate
 - b. presence of cough
 - c. tender cervical lymph nodes
 - d. fever >100.4°
12. Physical activity in older people:
 - a. has no effect on mortality
 - b. can reduce mortality, but only if performed at high intensity
 - c. increases mortality
 - d. reduces mortality regardless of intensity
 - e. increases mortality if done at extreme intensity

CME Objectives

The objectives of *Internal Medicine Alert* are:

- to describe new findings in differential diagnosis and treatment of various diseases;
- to describe controversies, advantages, and disadvantages of those advances; and
- to describe cost-effective treatment regimens.

Answers: 9 (a); 10 (c); 11 (b); 12 (d)

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Hair Growth With Finasteride: Not Just More, but More Better!

MALE PATTERN BALDNESS IS A result of the impact of dihydrotestosterone (DHT) upon scalp hair follicles which results in a progressive miniaturization of follicles leading to thinner, shorter hairs in genetically susceptible men. Scalp biopsy has shown that susceptible men have higher levels of cutaneous DHT, more cutaneous 5-alpha-reductase (the hormone responsible for converting testosterone to DHT), and more androgen receptors than comparator groups.

Finasteride is a 5-alpha-reductase inhibitor (5ARI), which prevents production of DHT from testosterone. In this trial, subjects were given standard oral doses of finasteride (1 mg/d) or placebo for 4 years.

Active treatment produced a significant effect upon hair weight and hair count. For instance, by week #192, hair weight had increased by 21.6% in the treatment group, but had decreased by 24.5% in the placebo group, for a net increase of 46% compared to placebo. Finasteride has a favorable impact both upon the number of scalp hairs and their size. ■

Price VH, et al. *J Am Acad Derm* 2006;55:71-74.

Prevalence of Diabetic Neuropathy

THE RELEVANCE OF DIABETIC peripheral neuropathy (DPN), and its commonplace sequela of dia-

betic peripheral neuropathic pain (DPNP) has recently been highlighted by an American Diabetes Association survey that indicates a distressingly low level of patient awareness of this disorder or its importance. Since diabetes remains the number 1 cause of non-traumatic limb loss in the United States, and DPN is the most common antecedent, it is critical to heighten clinician attention to identification and management of persons with DPN or DPNP. Epidemiologic prevalence data may help to drive clinician awareness.

This cross-sectional survey of a population in South Wales, United Kingdom incorporated both a postal survey and neurologic examination to define the presence of DPN and DPNP. Of 326 diabetic persons who responded to the postal survey that they had "burning, aching, or tenderness in your legs or feet," evaluation by a neurologist indicated that DPNP was the etiology in 19% of the cases. In persons with DPNP, the vast majority (80%) reported the degree of pain as moderate to severe. Persons with DPNP demonstrated a poorer quality of life than persons with non-neuropathic pain.

The authors comment that extrapolating these data to the diabetic population of the United Kingdom, as many as a half million persons suffer DPNP, most of whom endure pain of moderate or greater intensity. To date, in this population only approximately half of DPNP sufferers have sought treatment. ■

Davies M, et al. *Diabetes Care* 2006;29:1518-1522

What is the Best Way to 'Predict' Diabetes: IFG, IGT, or A1c?

THE AMERICAN DIABETES ASSOCIATION (ADA) does *not* advocate use of the A1c for diagnosing diabetes. Rather, they suggest use of fasting or random glucose, or oral glucose tolerance testing (GTT). Most commonly, the diagnosis is made by means of the fasting or random measurement, since GTT is more cumbersome, expensive, and less convenient. Other authors have suggested that A1c might be a reasonable way to diagnose diabetes, since we only intervene with treatment when the A1c is above a particular threshold (> 7.0, according to the ADA). The ADA points out that although there *is* a national standard test for A1c, laboratories are *not* required to use it; we are in a similar state with A1c to where we used to be with the Pro-time for Coumadin monitoring: it varied from hospital to hospital. Then came the INR, so that now the results are standardized across all hospitals. We do not yet enjoy a similar universal standardization of A1c. Additionally, the A1c appears to be less sensitive to very early abnormalities of glucose as detected by IFG or IGT.

The DESIR study provided data on 2,720 men and women who were defined as being 'at-risk' on the basis of an elevated fasting glucose. These individuals also had A1c measured and were followed for 6 years.

A1c was less sensitive and less specific than fasting glucose for predicting diabetes. If some circumstance prevents patients from obtaining a fasting glucose measurement, A1c provides a second-best predictive value. ■

Droumaguet C, et al. *Diabetes Care* 2006;29:1619-1625.