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Financial Disclosure:
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.

In Search of the Healthy Diet

ABSTRACT & COMMENTARY

By Joseph E. Scherger, MD, MPH

Clinical Professor, University of California, San Diego

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

Synopsis: *Three diets were studied replacing saturated fats with 1) a carbohydrate-rich diet, 2) a protein-rich diet, and 3) a diet rich in unsaturated fat (predominately monounsaturated fat). All 3 diets lowered blood pressure, improved serum lipids and reduced calculated coronary heart disease risk. Diets rich in protein or unsaturated fat were better than the high carbohydrate diet in the overall calculations, although the protein rich diet resulted in lower HDL cholesterol levels.*

Source: Appel LJ, et al. Effects of protein, monounsaturated fat, and carbohydrate intake on blood pressure and serum lipids: results of the OmniHeart randomized trial. *JAMA*. 2005;294:2455-2464.

THIS STUDY WAS CONDUCTED BY THE OMNIHEART COLLABORAtive Research Group based at Johns Hopkins University. This group followed up on the research which led to the Dietary Approaches to Stop Hypertension (DASH diet), which is now widely used for the dietary prevention and treatment of hypertension.[1] The 3 diets studied were modifications of the DASH diet, varying the amount of carbohydrate, protein and unsaturated fat.

This OmniHeart Trial used a crossover design with 164 individuals with either prehypertension or stage 1 hypertension. The study participants consisted of 45% women, 55% African Americans, and 79% were overweight or obese. The basic DASH diet was modified to contain 58% carbohydrate, 25% protein (half from plant sources) or 37% unsaturated fat intake using olive oil, canola oil, safflower oil, nuts, and seeds. Each diet was ingested for 6 weeks and was designed to keep weight constant.

All 3 diets resulted in a modest drop (2-4 mm Hg) in blood pressure and LDL cholesterol (3-7 mg/dL). The high carbohydrate diet fared similar to the regular DASH diet. The diets high in protein and unsaturated fat had an additional slight reduction of blood pressure (1-2 mm Hg) and LDL cholesterol (about 2 mg/dL). The high pro-

VOLUME 28 • NUMBER 6 • MARCH 29, 2006 • PAGES 41-48

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tein diet had a slight decrease in HDL cholesterol (about 2 mg/dL) and was associated with reduced physical activity, reduced appetite, and bloating.

COMMENTARY

What to eat to be healthy remains mired in controversy. Nathan Pritikin and Dean Ornish demonstrated the benefits of reducing fat intake to 10% of the diet, but very few people are willing to stay on such a dietary program for the long haul. Moreover, Pritikin and Ornish failed to appreciate the health benefits of the monounsaturated and polyunsaturated oils. Atkins started a counterrevolution with the low-carbohydrate, high-protein pathway to weight loss. This works for some by reducing appetite and overall calories. Simple sugars drive hunger and protein seems to reduce it in some people. However, the long-term health benefits of a high-protein diet, especially from animal sources, are highly questionable. Next comes the Mediterranean diet with its healthy oils and even moderate alcohol intake to reduce cardiovascular risk. The Europeans seems to be able to ingest this in moderation but Americans love large portions and have an epidemic of overweight and obesity. What are we to do?

This study adds some interesting knowledge to the dietary equation. The DASH diet, with its lower sodium, higher potassium and calcium, does reduce blood pressure and has a modest benefit on serum lipids. Advocates of Pritikin and Ornish criticize this diet as still much too high in fat (27%) which will not only fail to reduce atherosclerosis but also will continue its progression. However, the DASH diet is easily followed and is an improvement over the way most American eat. This study refines the knowledge of the DASH diet by confirming the benefits of the unsaturated oils, at least with lowering blood pressure and LDL cholesterol, albeit very modestly. No actual cardiac outcomes were part of this brief study of a small group of subjects. Higher protein intake also improved blood pressure and LDL cholesterol, but with a price of lowering HDL cholesterol and reduced physical activity. We all know physical activity may be even more important than nutrition in reducing cardiovascular risk.

How should we interpret these findings and use them in daily practice? Our patients vary greatly in what they like to eat. One diet has limited clinical usefulness in practice because only a subgroup of patients will follow it. We benefit by having multiple dietary pathways to improving cardiovascular risk. By keeping a 2-week food diary on our patients, we gain an understanding of how they like to eat. The "grazers" eat all day and the "carnivores" eat like a lion—one big meal. Using the principles of the DASH diet (low sodium, more vegetables, and adequate calcium), we can adjust a person's diet with respect to complex carbohydrates, proteins and healthy fats according to culture and personal preference.

Being a Dean Ornish fan, I am much more aggressive in my recommendations for reducing overall fat intake. Reducing body weight through healthy eating and increased physical activity is the most important clinical intervention we can make today with our patients. This study shows that our tool kit for dietary recommendations has options. ■

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Internal Medicine Alert, ISSN 0195-315X, is published twice monthly by American Health Consultants, 3525 Piedmont Road., NE, Building. 6, Suite 400, Atlanta, GA 30305.

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GST Registration Number: R128870672.

Periodicals postage paid at Atlanta, GA.

POSTMASTER: Send address changes to ***Internal Medicine Alert***, P.O. Box 740059, Atlanta, GA 30374.

Back issues: $21. Missing issues will be fulfilled by Customer Service free of charge when contacted within one month of the missing issue's date.

This is an educational publication designed to present scientific information and opinion to health professionals, to stimulate thought, and further investigation. It does not provide advice regarding medical diagnosis or treatment for any individual case. It is not intended for use by the layman.

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Subscription Prices

United States
1 year *with* free AMA Category 1 credits: $289
(Student/Resident rate: $125).

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This CME activity is intended for the internist/family physician. It is in effect for 36 months from the date of the publication.

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PDE5 Inhibition: New Drug for Raynaud Disease?

ABSTRACT & COMMENTARY

By Allan J. Wilke, MD

Residency Program Director, Associate Professor of Family Medicine, University of Alabama at Birmingham School of Medicine—Huntsville Regional Medical Campus

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

Synopsis: *Add vardenafil to the list of phosphodiesterase type 5 inhibitors with promise in the treatment of Raynaud disease.*

Source: Caglayan E, et al. Phosphodiesterase type 5 inhibition is a novel therapeutic option in Raynaud disease. *Arch Intern Med*. 2006;166:231-233.

In an open-label pilot study, 40 patients (37 women) with Raynaud disease (RD) took vardenafil (Levitra®) 10 mg twice daily for 2 weeks. Their average age was 49 years. Twelve of them smoked cigarettes, but all abstained from smoking for at least 12 hours before testing. Seven had primary RD (no history or signs of a connective tissue disease, normal nail fold capillaries, and no autoantibodies). All calcium channel blockers, nitrates, and any other vasodilators were discontinued for at least one week before inclusion into the study. Primary outcomes were: blood flow in the index finger at 24°C and at 4°C ("cold exposure test" [CET]) one hour after taking the first dose and repeated after 2 weeks of treatment; nail fold capillary microscopy; the Raynaud condition score (RCS) that measures frequency, total daily duration, and severity of RD attacks; and the patient's daily impression of difficulty with RD on a 0 (no difficulty) to 10 (very severe) scale.

Statistically significant blood flow improvement was demonstrated at 1 hour and at 2 weeks at both temperatures. The most dramatic improvement was noted during the CET. There was no change in capillary microscopy, as expected. At baseline the average RCS was 5.05; at 2 weeks it had dropped to 3.54, which was also statistically significant. Patients experienced a modest reduction in blood pressure, but no serious adverse events were noted. Side effects commonly associated with phosphodiesterase type 5 (DPE5) inhibitors (headache, flushing, dyspepsia, rhinorrhea, and visual abnormalities) occurred in a minority of patients.

COMMENTARY

Raynaud disease (also termed Raynaud's phenomenon) has a prevalence of 3 to 5% (up to 30% in young women). It is primary when there are no signs or symptoms of a systemic connective tissue disease, such as scleroderma or lupus erythematosus. Classically, it appears as discoloration of the fingers or toes in the white, then blue, then red pattern over time, accompanied by pain or numbness. One patient in eight with primary RD will eventually develop an inflammatory rheumatic disease.[1] Women are 3 to 5 times more frequently affected than men. Management involves avoidance of cold temperatures, tobacco smoke, and vasoconstrictors, and use of calcium channel blockers (eg, nifedipine) and sympathetic nervous system inhibitors (eg, prazosin). Angiotensin II, serotonin, and thromboxane A2 have been implicated in some cases of RD, and losarten,[2] fluoxetine,[3] and low-dose aspirin have also been studied and prescribed. Cyclic intravenous iloprost (another vasodilator) was efficacious in the treatment of Raynaud's phenomenon in patients with systemic sclerosis and led to a marked improvement in the quality of life.[4]

We've all seen the movie where the classically trained pianist journeys to the big city to seek fame and fortune, only to be disappointed and ending up playing honky tonks. Then, one night, the impresario wanders in, listens as the pianist plays Chopin's *Polonaise in A-flat Major, Op. 53*, and exclaims, "Hey, this kid's got talent!" He plays Carnegie Hall and the rest is history. This is the storyline of the phosphodiesterase type 5 inhibitors. Originally developed as a treatment for hypertension and angina, sildenafil (Viagra®) was marketed as a treatment for erectile dysfunction. Subsequently, it has been shown to be useful in the treatment of pulmonary hypertension[5] and is marketed for same under the trade name Revatio®. Now is appears that we can add RD to list of diseases that respond to DPE5 inhibitors. Sildenafil was shown to be effective and well-tolerated in a small double-blinded, placebo-controlled study of patients with Raynaud's phenomenon.[6] A patient who had RD and had failed sildenafil did respond to tadalafil (Cialis®).[7]

Am I ready to begin using vardenafil in the treatment of RD? Not based on this study. Because of its design (open-labeled, not randomized, not placebo-controlled, only 2 weeks long, undefined patient selection, inclusion, and exclusion criteria), the best that can be said, and echoed by its authors, is that the results are intriguing and a proper study is warranted. ■

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meta-analysis of the frequency, rates, and predictors of transition to secondary diseases. *Arch Intern Med*. 1998;158:595-600.
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Troponin vs CKMB in ACS

ABSTRACT & COMMENTARY

By Michael H. Crawford, MD

Professor of Medicine, Chief of Clinical Cardiology, University of California, San Francisco

Dr. Crawford is on the speaker's bureau for Pfizer.

Synopsis: *Among patients with NSTE ACS, an elevated troponin level identifies patients at increased acute risk regardless of CK-MB status, but an isolated CK-MB+ status has limited prognostic value.*

Source: Newby LK, et al. Frequency and Clinical Implications of Discordant Creatine Kinase-MB and Troponin Measurements in Acute Coronary Syndromes. *J Am Coll Cardiol*. 2006;47:312-318.

CARDIAC BIOMARKER TESTING IS PART OF THE standard approach to evaluating patients with suspected acute coronary syndromes (ACS). Although troponin has become the diagnostic standard for myocardial infarction (MI), CKMB is often tested as well. Thus, Newby and colleagues evaluated the use of dual marker testing in patients with non-ST elevation ACS in the CRUSADE quality improvement initiative database. The end point chosen was in-hospital mortality. They specifically focused on the significance of discordant results of troponin and CKMB, which occurred in 28% of the 29,357 patients who had both measured. Most patients had concordant cardiac marker values; 12% were CKMB negative and troponin (Tn) negative and 60% were CKMB+/Tn+. CKMB+/ Tn- occurred in 10%; CKMB-/ Tn+ occurred in 18%. Hospital mortality was highest in the concordant positive (CKMB+/Tn+) patients at 5.9% and lowest in the concordant negative patients at 2.7%. Hospital mortality in the discordant patients was 3.0% in the CKMB+/Tn- patients and 4.5% in the CKMB-/Tn+ patients. Baseline characteristics showed that Tn+ patients were older, had more evidence of vascular disease, and more often had heart failure. After adjustment for baseline characteristic differences, troponin was more strongly associated with mortality than CKMB (chi square 23 for troponin and 8 for CKMB). Hospital therapy was similar for all cardiac marker groupings. Newby et al concluded that in patients with non-ST elevation ACS, an elevated troponin is associated with an increased risk of death regardless of the CKMB value, but an elevated CKMB alone is of little prognostic value.

COMMENTARY

The major conclusion of this study is that an elevated troponin value defines the highest risk patients among non-ST elevation ACS patients who are admitted. However, all the patients in this database were treated similarly, despite their troponin values. For example, those who were CKMB- and Tn- were most likely to have an early cardiac catheterization approach as compared to either group with discordant results. Newby et al argue that cardiac biomarker results should be used to direct the most aggressive therapy to the highest risk patients, those who were troponin positive. They believe CKMB adds little to the troponin results, yet most centers do both in ACS patients. Should CKMB be eliminated? Perhaps it should in the triage of ACS patients, but it may be useful later to estimate infarct size in selected patients.

Why are we not responding more aggressively to an elevated troponin? Perhaps because of troponin desensitization. We are used to seeing elevated troponins in many hospitalized patients. We are annoyed by consultation requests to see terminally ill non-cardiac patients with slight troponin elevations. Thus, in ACS patients where an elevated troponin is of value, we may not react appropriately anymore. Also, troponin assays have been a moving target; troponin T, then I; changes in cutoff values; test inaccuracies. In this study, they used each center's test and values;

there was no core laboratory. So, Newby et al note that as more centers convert to the latest troponin I system there could be changes in this ongoing database. Finally, it was pointed out that these results may not apply to lower risk patients who are not hospitalized, but held in chest pain observation units. ■

A Normal Temperature May Not Be What We Were Taught

ABSTRACT & COMMENTARY

By Mary Elina Ferris, MD

Clinical Associate Professor, University of Southern California

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

Synopsis: *Mean oral temperatures decline with age, ranging from 97.3ºF at 6 am to 97.8ºF at 10 pm in persons older than 65 years. The majority of both nursing home and community elderly have normal mean temperatures below 98.6ºF.*

Source: Gomolin IH, et al. Older is colder: temperature range and variation in older people. *J Am Geriatr Soc*. 2005;53:2170-2172.

Oral temperatures for 100 nursing home residents were measured on 3 consecutive days using a single digital electronic thermometer, and once during mid-day office visits for 50 community dwellers. Nursing home residents all had their measurements on the same days at 3 times: 6 AM, 4 PM, and 10 PM, and had not taken antipyretics, nor taken anything by mouth for 30 minutes before the reading. Average age was 80.7 years (range, 65-98 years old); 111 were women and 39 men. No statistical differences were present between the two measurement sites or genders. Although the individual range of measurements was 94.0ºF to 99.6ºF, the variability of the mean for each time period was less than 0.82ºF. Mean oral temperatures declined with age, from 98.2ºF for age 65-74 years old to 97.4ºF for age 85 years and older.

■ COMMENTARY

This simple yet important study confirms that the majority of healthy elderly persons have normal oral temperatures lower than the usually accepted 98.6ºF, ranging from 98.2ºF down to 97.4ºF. Geriatric specialists have suggested that recognition of fevers in this group should start at 99-100ºF, and should especially be compared to the baseline established for that particular patient, since we know the normal reading can decline with advancing age.[1] The maxim that older patients have "atypical presentations of disease" may actually represent our ignorance of their normal baseline measurements.

In fact, the accepted normal temperature of 98.6ºF may not be accurate for younger persons either. Previous studies have shown that 98.2ºF is a more accurate mean oral temperature in healthy adults aged 40 years or younger, with a variability of 0.9ºF.[2] There are also clear diurnal variations of temperature, with lowest temperatures at 6 AM and highest at 4-6 PM. As we accumulate more specific data to adjust our expectations of normal values, we should be able to assess developing diseases more accurately in the future. ■

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An Upgraded Blood Test That Identifies Tuberculous Infection

By Stan Deresinski, MD, FACP

Synopsis: *The CDC recommends that* QuantiFERON®-TB Gold (QFT-G) *may be used in all circumstances in which the TST is currently used, including contact investigations, evaluation of recent immigrants, and sequential-testing surveillance programs for infection control (eg, those for health-care workers).*

Source: Mazurek GH, et al. Guidelines for Using the QuantiFERON®-TB Gold Test for Detecting *Mycobacterium tuberculosis* Infection, United States. *MMWR Recomm Rep*. 2005;54(RR15):49-55. Erratum in: *MMWR Morb Mortal Wkly Rep*. 2005;54:1288.

Tuberculin skin testing is a crude procedure, fraught with potential error at every step, from application to interpretation, and requires 2 visits to a health care provider. Its use has persisted, nonetheless, because

it remained, until recently, the only means of detection of latent infection with *Mycobacterium tuberculosis*. The introduction of an in vitro test, QuantiFERON, several years ago did provide an alternative, but it suffered from the same problems of cross-reactivity with other mycobacteria, especially BCG, as did the PPD skin test. An advanced and much improved version of this test, the QuantiFERON®-TB Gold (QFT-G) test was approved by the US FDA in May of this year, and has replaced the older version which is no longer available.

The QFT-G test utilizes an ELISA test to quantify IFN- release in fresh, heparinized, whole blood incubated with mixtures of synthetic peptides representing 2 proteins of *M. tuberculosis*, culture filtrate protein-10 (CFP-10) and early secretory antigenic target-6 (ESAT-6). These antigens are absent from BCG vaccine strains, as well as from most non-tuberculous mycobacteria with the exception of the photochromogens, *M. kansasii* and *M. szulgai*, and the scotochromogen, *M. marinum*. This relative antigenic selectivity allows improved specificity of QFT-G relative to the discontinued QFT or to PPD skin testing. Of particular importance is that QFT-G results are not affected by prior BCG vaccination; its specificity in BCG-vaccinated individuals has been reported to be 96% to 98%, which compares very favorably to PPD skin testing with a specificity reported to be 49%. At the same time, it appears to have good sensitivity, reported in patients with culture-positive active tuberculosis to be similar to that of PPD skin testing, at approximately 80%.

An important drawback to the use of QFT-G is that incubation with the test antigens (which continues for 16-24 hours) must be initiated within 12 hours of phlebotomy. This requires relatively close proximity to the laboratory performing the test. The performance of the test in immunocompromised patients, such as those with AIDS, has not been evaluated, but its sensitivity is likely to be reduced, as is true for PPD skin testing. QFT-G, of course, in contrast to PPD skin testing, produces no boosting effect—which may be a good or a bad thing, depending on your point of view and circumstance.

The CDC states that the QFT-G test can be used in all circumstances in which PPD skin testing is currently utilized. These include contact investigation, evaluation of recent immigrants with a history of BCG vaccination (in whom QFT-G would appear to have particular value), and screening of health care workers and other undergoing serial screening. In each of these circumstances, the QFT-G may replace the skin test; there is no reason to follow a positive QFT-G with a PPD skin test. ■

Pharmacology Update

Insulin Human Inhalation Powder (Exubera®)

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 APPROVED THE FIRST NON-INJECTABLE insulin for the treatment of type 1 and type 2 diabetes. Marketed under the trade name Exubera®, the new insulin product is a dry powder inhalation delivery system that uses the vascular system of the alveoli to deliver insulin into the blood stream. Exubera® is licensed from Nektar Therapeutics and will be marketed by Pfizer Labs.

Indications

Inhaled insulin powder is indicated for the treatment of adult patients with type 1 and type 2 diabetes mellitus. For type 1 patients inhaled insulin should be used with a longer-acting insulin.[1]

Dosage

The administration timing of inhaled insulin (INH) is similar to injectable short-acting insulin (ie, immediately before meals and no more than 10 minutes prior). A 1 mg blister of inhaled insulin is approximately equivalent to 3 IU of injected regular human insulin. A 3 mg blister corresponds to 8 IU and 6 mg to 16 IU of regular insulin. Initial pre-meal dose may be calculated by multiplying the body weight in kg by 0.05. The product is rounded down to the nearest whole milligram number.[1]

INH is supplied as 1 mg and 3 mg blisters.

Potential Advantages

Inhaled insulin provides a non-invasive delivery of insulin. Compared to the injection, inhaled insulin had greater acceptance in terms of convenience and patient satisfaction.[2,3] INH is rapidly absorbed and is independent of BMI.[1]

Potential Disadvantages

INH is contraindicated in patients who smoke or who have discontinued smoking < 6 months prior. Systemic exposure to insulin is significantly greater in smokers than non-smokers. Absorption is reduced by 20-30% in patients

exposed to passive cigarette smoke. INH is not recommended in patients with underlying lung disease.[1] Higher frequencies of cough and increase in insulin serum antibodies have been associated with INH.[2-5] INH has been associated with a decline in pulmonary function specifically FEV_1 and carbon monoxide diffusing capacity.[1] A decline in FEV_1 from baseline of 20% occurred in 1.5% of patients compared to 1.3% for the comparator group. A decline of 20% in DLCO occurred in 5.1% of the INH group compared to 3.6% for the comparator group. Pulmonary function should be performed before initiation of therapy, after 6 months, and annually thereafter.[1]

In patients who need basal insulin, INH does not eliminate this requirement. The long-term effect on insulin on lung structure and function is not known.

Comments

Inhaled insulin is delivered in small particles (1-5 m) and absorbed via the alveolar capillary bed by trancytosis. INH is absorbed at a more rapid rate than subcutaneous (SQ) insulin. Maximum serum concentration is 24 minutes for INH vs 106 minutes for SQ insulin.[7] The efficacy of INH compared to SQ regular insulin was determined in 2 phase III studies in type 1 diabetics (n = 663) and 1 study in type 2 diabetics (n = 299). These noninferiority studies were powered to detect a treatment difference in HbA1c of 0.5%.[6] No significant differences in change in HbA1c were observed between treatments. A greater decrease in fasting blood glucose was seen with INH.[2,3,8] Type 2 patients on SQ insulin can be switched to INH while maintaining HbA1c levels.[7] INH can be effectively added to, or substituted for, oral therapy or in patients inadequately controlled on diet or oral regimens.[8,9] Overall risk of hypoglycemia was similar between groups although a higher rate of severe hypoglycemia was reported with INH in one study.[4] Patient satisfaction and quality of life favored INH. The clinical relevance of insulin antibodies is not clear, as these do not appear to impair postprandial glucose tolerance, affect the pharmacodynamics of insulin, or affect tolerability.[5] The cost of INH was not available at the time of this review.

Clinical Implications

INH provides a noninvasive delivery of insulin. Since the long-term effects of INH are not known, subcutaneous insulin remains the preferred route of administration. ■

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CME Questions

12. Choose the correct statement. Patients with Raynaud disease who took vardenafil:

a. experienced incapacitating side effects.
b. had marked drops in blood pressure.
c. noted improved capillary microscopy.
d. more frequently had primary RD.
e. had improvement in their symptoms at two weeks.

13. Which of the following oral temperatures for a healthy 85-year-old man is closest to the actual mean found in community dwellers?

a. 98.6ºF
b. 98.0ºF
c. 97.4ºF
d. 96.8ºF
e. 96.2ºF

Answers: 12 (e); 13 (c)

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.

By Louis Kuritzky, MD, Clinical Assistant Professor, University of Florida, Gainesville
Dr. Kuritzky is a consultant for GlaxoSmithKline and is on the speaker's bureau of GlaxoSmithKline, 3M, Wyeth-Ayerst, Pfizer, Novartis, Bristol-Myers Squibb, AstraZeneca, Jones Pharma, and Boehringer Ingelheim.

Ethnic and Racial Differences in the Smoking-Related Risk of Lung Cancer

ALTHOUGH CIGARETTE SMOKING IS the primary risk factor for lung cancer (LCA), with similar amounts of smoking exposure some groups demonstrate greater incidence of LCA than others. To gain insight into LCA susceptibility, an analysis of data from the Multiethnic Cohort Study stratified smokers (n = 183,813) by number of cigarettes smoked, gender, and ethnicity (African American, Japanese-American, Latino, Native Hawaiian, and Caucasian). Three tiers of smoking intensity were selected: 10 or less, 11-20, and 30 or greater cigarettes per day.

For the lowest tertile of smoking intensity, African Americans and Native Hawaiians had a three-fold greater risk of LCA than Japanese Americans or Latinos, and more than double the risk of Caucasians. At intermediate levels of smoking intensity, the African American/Hawaiian population risk was still more than double that of Latino/Japanese Americans. At the highest levels of smoking, risks were similar between all ethnicities, and were only modestly influenced by gender. Although the explanation for differences between LCA risk amongst different ethnicities is not fully clear, it is recognized that, for instance, Blacks have higher levels of cotinine (a primary nicotine metabolite) than others who smoke the same number of cigarettes, suggesting a difference in metabolism, greater environmental exposure, different smoking technique, or some combination of similar factors. ■

Haiman CA, et al. N Engl J Med. 2006;354:333-342.

Neuropathy Among the Diabetes Control and Complications Trial Cohort 8 Years After Trial Completion

NEUROPATHY IS ONE OF THE 3 CARdinal microvascular complications of diabetes that have been show to be favorably impacted by tight glucose control. At the conclusion of the Diabetes Control and Complications Trial (DCCT), neuropathy was reduced by approximately one-third in the tight control group vs conventional treatment. Study subjects from both treatment arms were encouraged to participate in tight control from that point onward, since better control was associated with numerous favorable outcomes.

Eight years after DCCT completion 1,257 of the original 1,441 participants were re-examined for neuropathy. Neuropathy was assessed by symptoms alone or by the Michigan Neuropathy Screening Instrument (MNSI). Even though the overall level of glycemic control amongst the 2 groups was quite similar over the 8 year hiatus since DCCT conclusion, there remained a statistically significant lesser prevalence of neuropathy in the group originally assigned to tight control. Overall, the prevalence of neuropathy according to the MNSI was 64% less in the prior tight control group. Lower extremity amputations were similar in both groups.

These data support the concept that early intensive treatment of diabetes may have long-lasting impact. Eight years after participation in a 6.5 year (mean) intensive treatment trial, subjects achieving lower levels of A1c continue to enjoy lesser prevalence of neuropathy. ■

Martin CL, et al. Diabetes Care. 2006;29:340-344.

Saw Palmetto for Benign Prostatic Hyperplasia

BENIGN PROSTATIC HYPERPLASIA (BPH) is the most common neoplastic condition in aging men. Alpha blockers (ABL) such as alfuzosin, doxazosin, tamsulosin, and terazosin provide substantial symptomatic relief, but are not disease-modifying (ie, they do not alter outcomes such as need for surgical intervention or acute urinary retention). Alpha reductase inhibitors such as dutasteride and finasteride are disease modifying, but do not provide prompt symptomatic relief. Many men and their clinicians look to alternative therapies such as saw palmetto (SAW) for treatment, rather than rely upon the above traditional methods. Small studies, some with design flaws, have suggested beneficial effects for men with BPH using SAW. The study by Bent follows rigorous methodology to clarify the effectiveness of SAW for both subjective (eg, quality of life) and objective (eg, prostate size, urinary flow rate, PSA) parameters.

Men older than age 49 (n = 225) with moderate-to-severe BPH were randomly assigned to SAW (160 mg b.i.d.) or placebo and followed for 1 year. To 'cut to the chase,' SAW was not superior to placebo for any measured end point. The evidence-based role of SAW for treatment of BPH is tenuous. ■

Bent S, et al. N Engl J Med. 2006;354:557-566.