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INSIDE

The Nose Knows . . .

ABSTRACT & COMMENTARY

Synopsis: *Patients with unexplained chronic fatigue and bodily pain are more likely to have rhinosinusitis symptoms than are people in the general population.*

Source: Chester AC. *Arch Intern Med*. 2003;163:1832-1836.

THIS PAPER IS A STUDY OF CONSECUTIVE PATIENTS YOUNGER THAN 41 who presented for a general physical examination. Chester, an internist, did a history, physical examination, complete blood count, sedimentation rate, thyroxine level, chemistry panel, rapid plasma reagin test, and urinalysis. Patients older than 30 had a chest radiograph.

Unexplained chronic fatigue was defined as chronic fatigue, a continuing troublesome tiredness, or lack of energy for longer than 2 months that was not a normal response to excessive physical or mental demands and not due to a physical or mental illness. Only 6 of the patients with this condition were taking medications other than oral contraceptives. Unexplained chronic bodily pain was defined as widespread musculoskeletal pain for longer than 1 month from no apparent cause. Symptoms needed to be constant or recurrent, present for longer than 1 month, and be problematic (the example given was that "sore throats" had to be frequent and severe enough to be troublesome). Symptoms of chronic rhinosinusitis were adapted from the *American Academy of Otolaryngology-Head and Neck Surgery Task Force Report*.[1]

The total sample included 297 patients (45% women) with a mean age of 30.3 years. They were well educated, white, and middle class. There were 65 patients with unexplained chronic fatigue, and Chester diagnosed 15 of these with chronic fatigue syndrome. There were 33 patients with bodily pain and most of them (n = 26) had unexplained chronic fatigue. Thirty eight of the patients had explained chronic fatigue, and 13 had explained acute fatigue.

Chester compared the 65 patients with unexplained chronic fatigue to 232 patients without this symptom (controls). There were no significant differences in age, body mass index (BMI), laboratory findings, marital status, or educational level between the fatigued

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and the control group. However, both women (60% vs 42%) and smokers (26% vs 13%) were more likely to be in the unexplained chronic fatigue group, as were people with gastrointestinal symptoms, DSM-IV symptoms (58% vs 38%), a lifetime history of psychiatric care (62% vs 42%), and sleep disturbance (26% vs 8%). Patients with unexplained chronic fatigue also had lower recumbent blood pressures (SBP, 120.8 vs 125.3 mm Hg) and more rapid recumbent heart rates (70.2 vs 66.7 beats/min). Those with unexplained chronic fatigue were significantly more likely than were controls to have these rhinosinusitis symptoms: facial pressure, heavy headedness, nasal obstruction, frontal headache, postnasal drip, sore throat, and cervical node tenderness.

In the subset of those patients with unexplained chronic fatigue whom Chester diagnosed with chronic fatigue syndrome (n = 15), similar increases in rhinosinusitis symptoms were noted, but there were also more symptoms of depression (73% vs 38%), sleep disturbance (47% vs 8%), and a lifetime history of psychiatric care (73% vs 42%) in the chronic fatigue syndrome patients than in the controls.

In the 38 patients who had explained fatigue, the prevalence of gastrointestinal complaints, sleep disturbances, and depression were similar that that of the patients with unexplained chronic fatigue; however, most symptoms of rhinosinusitis were less common in the patients with explained fatigue than in those with unexplained fatigue.

The patients with bodily pain (n = 33) had no important differences in sociodemographic factors, laboratory findings, or physical findings compared with controls, but they, too, were more likely to have the symptoms of rhinosinusitis investigated in this study. They were also more likely to have psychiatric symptoms.

None of the patient groups was more likely to have a history of pollen allergy than was the control group.

COMMENT BY BARBARA A. PHILLIPS, MD, MSPH

There are lots of things wrong with this paper. Chief among them is the finding that cigarette smoking is more prevalent in those with unexplained chronic fatigue than it is in controls; cigarette smoking is associated with depression,[2] snoring and sleep apnea,[3] sinusitis,[4] and general sleep disturbance.[5] Another problem is that there are no objective differences between groups except for heart rate and blood pressure; the data were gathered by Chester in an oral interview and could well be biased.

But smoking was not more common in those with bodily pain than in controls, yet those with bodily pain had more nasal symptoms. And the prevalence of the nonspecific complaints of gastrointestinal problems, sleep disturbances, and depression were similar in the patients who had explained fatigue as in the patients with unexplained chronic fatigue, despite the fact that most symptoms of rhinosinusitis were less common in patients with explained fatigue.

Chester notes that otolaryngologists have observed this relationship between fatigue, pain, and nasal symptoms previously. Patients with rhinosinusitis are likely to have fatigue, and the degree of fatigue correlates with severity of nasal symptoms.[6] Further, those with chronic rhinosinusitis score lower in quality of life than an older population with medical problems that would be considered by most of us to be more significant.[7]

Fatigue and bodily pain are common and troublesome complaints in the internist's office, and the differential diagnosis and evaluation of these symptoms are com-

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plex. This preliminary paper suggests that nasal symptoms are at least as common as are the gastrointestinal, sleep, and psychiatric problems associated with complaints of fatigue and bodily pain. The good news is that several studies suggest that sinus surgery may improve fatigue and bodily pain.[8-10]

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Endoscopic Therapy in Patients Receiving Omeprazole for Bleeding Ulcers with Nonbleeding Visible Vessels or Adherent Clots

ABSTRACT & COMMENTARY

Synopsis: *There are arguments about the optimal treatment for ulcers with nonbleeding visible vessels and adherent clots. This study showed that the combination of endoscopic hemostasis with IV proton pump inhibitor therapy is superior to PPI alone in management of such patients.*

Source: Sung JJ, et al. *Ann Intern Med*. 2003;139:237-243.

GI HEMORRHAGE IS A DREADED COMPLICATION OF ulcer disease, whether idiopathic, *Helicobacter pylori* related, or due to NSAIDs. Most physicians medically treat GI bleeding with acid suppression. Proton pump inhibitors (PPI) are used in this setting with increasing frequency. In the United States, IV pantoprazole (Protonix™) is the PPI available for this purpose. Elsewhere in the world, IV omeprazole is often used. Gastroenterologists often perform urgent endoscopy in patients presenting with GI hemorrhage, and they commonly treat bleeding vessels with local injection or thermal therapy. Use of endoscopic hemostasis in nonbleeding vessels or for ulcers with adherent clots has not been widely accepted. Several articles suggest that PPI therapy can decrease ulcer rebleeding in this setting. This study of 156 patients with bleeding ulcers with adherent clots or visible vessels compared IV omeprazole alone to IV omeprazole plus endoscopic hemostasis using a heater probe and injection of diluted epinephrine. Sham endoscopy involved only gentle irrigation of the ulcer site without other manipulation. Nine of 54 patients receiving omeprazole alone had recurrent bleeding compared to none of 63 treated with PPI plus endoscopic hemostasis. Adherent clots without visible vessels were less likely to bleed than all ulcers with visible vessels.

COMMENT BY MALCOLM ROBINSON, MD, FACP, FACG

Data continue to accumulate that support aggressive acid suppression in the setting of gastrointestinal hemorrhage due to ulcer disease. It now seems clear that more ulcer patients than previously thought could benefit from aggressive endoscopic therapeutic intervention. The dose of IV omeprazole used in this study was 80 mg by bolus, followed by the constant infusion of 8 mg/hour. Similar dose requirements exist for pantoprazole, the only PPI that is currently available in an intravenous form in the United States. Prompt gastroenterology consultation appears to be highly appropriate in patients presenting with upper GI hemorrhage.

Life Can be Less Risky!

ABSTRACT & COMMENTARY

Synopsis: *Eighty-seven percent or more of patients with fatal or nonfatal myocardial infarction (MI) have major risk factors prior to the event.*

Source: Greenland P, et al. *JAMA*. 2003;290:891-897.

IT HAS BEEN FREQUENTLY STATED THAT CORONARY heart disease (CHD) occurs in the absence of major risk factors in as many as 50% of patients. The purpose of this paper was to determine the frequency of exposure to major risk factors in patients with fatal or nonfatal myocardial infarction.

Three prospective cohort studies were included: the Chicago Heart Association Detection Project in Indus-

try, with a population of 35,642 men and women aged 18-59 years; screens for the Multiple Risk Factor Intervention Trial, including 347,978 men aged 35-57 years; and a population-based sample of 3295 men and women aged 34-59 years from the Framingham Heart Study (FHS). Follow-up lasted 21-30 years.

Fatal CHD in all cohorts and nonfatal MI in the FHS, compared by exposure to major CHD risk factors, defined as total cholesterol of at least 240 mg/dL, systolic blood pressure of at least 140 mm Hg, diastolic blood pressure of at least 90 mm Hg, cigarette smoking, and diabetes. Participants were stratified by age and sex (18-39 vs 40-59 years)

For fatal CHD (n = 20,995), exposure to at least 1 major risk factor ranged from 87% to 100%. Among those aged 40-59 years at baseline with fatal CHD (n = 19263), exposure to at least 1 major risk factor ranged from 87% to 94%. For nonfatal MI, prior exposure was documented in 92% (n = 167) of men 40-59 years at baseline and in 87% of women in this age group.

It was concluded that antecedent CHD major risk factor exposures were very common among those who developed CHD, emphasizing the importance of considering all major risk factors in CHD risk estimation and in attempting to prevent clinical CHD. The results challenge claims that CHD events commonly occur in persons without at least 1 major risk factor.

COMMENT BY RALPH R. HALL, MD, FACP

Greenland and colleagues carried out a secondary analysis by changing the cholesterol levels to > 200 mg/dL and the blood pressure criteria to 120/80 mm Hg. The prevalence of risk factors remained at 87% or higher.

If this study involving 386,915 subjects doesn't convince us about the risk factor prevalence in CHD, an additional article in the same issue of *JAMA* by Khot et al, evaluating the same 4 risk factors in 14 international randomized clinical trials with 122,458 subjects, reached the same conclusions.[1]

A large number of subjects who had risk factors did not have MI. The reasons for this are probably varied. Some may have been protected by high levels of high density lipoproteins or life style interventions or died with stroke or cancer.

Khot et al note that "much attention has recently focused on the identification of genetic factors that play a role in the development of CHD. Although genetic differences may explain an individual's propensity to develop CHD in the setting of conventional risk factors, it is doubtful that the population-wide prevalence of CHD is explained by genetic factors. Epidemiological studies have shown that the risk of CHD in populations is largely dependent on the prevalence of conventional risk factors and other environmental factors such as diet.[2,3] Furthermore, the prevalence can vary as the environmental conditions change over short periods, as seen in Japanese migration studies."[4]

The implications for these studies are immense. The authors of these papers note that 2 studies have shown that lack of hypertension, hyperlipidemia, and cigarette smoking was associated with a 77% to 90% reduction in cardiovascular mortality.[5,6] There have been numerous trials demonstrating the decreased morbidity and mortality following treatment of elevated cholesterol levels. The Anglo-Scandinavian Cardiac Outcomes Trial (ASCOT)[4] of high-risk hypertensive subjects without evidence of CHD demonstrated a 36% reduction in death and MI in only 3.3 years.

Hackam and Anand in the same issue of *JAMA* evaluate other risk factors that are associated with CHD. They conclude that the optimal use of C-reactive protein, homocysteine, lipoprotein (α), and fibrinogen in routine screening remains to be determined.[7]

The message is clear. Treating the 4 major risk factors will dramatically reduce morbidity, mortality and the huge monetary drain on the health care budget. ■

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Azithromycin as Single-Drug Therapy for Community-Acquired Pneumonia

ABSTRACT & COMMENTARY

Synopsis: *Azithromycin is an effective, single-drug therapy for mild-to-moderate community-acquired pneumonia.*

Source: Feldman RB, et al. *Arch Intern Med*. 2003;163: 1718-1726.

To determine whether azithromycin alone (without an additional ß-lactam antibacterial agent)

is an effective treatment for patients with mild-to-moderately severe community-acquired pneumonia, Feldman and associates performed this retrospective cohort study of patients hospitalized at the West Los Angeles Healthcare Center over a 3.5-year period ending in mid-2001.

Eligible patients included those admitted to the general medical ward with clinical symptoms and signs of pneumonia, as well as radiographic demonstration of pulmonary infiltrates that were not previously present and that appeared within the first 2 days of hospitalization. Excluded were patients immunosuppressed by virtue of HIV infection, neutropenia, malignancy, or medication, as well as patients with hospital-acquired pneumonia, mycobacterial infection, or other explanations for the pulmonary infiltrate. Patients transferred from other hospitals or hospitalized within the previous 2 weeks were also excluded. Patients who were initially admitted to the general medical ward but then transferred to the intensive care unit within 24 hours were assumed to have severe pneumonia and to have been misclassified for the purposes of this study and were not included in the analysis.

A total of 442 patients' records remained after the exclusion criteria were applied. The majority were white, but approximately 30% were black and 10% were Hispanic. Average age was mid-to-late 60s. As expected in a VA patient series, about 95% were male, and nearly half were current smokers.

All patients were assigned a pneumonia severity index score,[1] a scoring system using age, coexisting medical conditions, abnormalities of mentation and vital signs upon admission to the hospital, and laboratory and radiographic findings. Statistically, patients in classes I and II have a predicted mortality of < 1%, while patients in class III have a predicted mortality of < 4%. Patients in classes IV and V have predicted probability of death of 4-10% and > 10%, respectively.

In this VA study, patients were grouped according to the initial antibiotic regimen received (excluding the first dose of antibiotic usually given in the emergency department). During the time of this study, recommended empiric therapy for patients with less-than-severe pneumonia was azithromycin as monotherapy. As a result, the largest group of patients (221—exactly half) received azithromycin initially; 29% received an alternate American Thoracic Society (ATS)-recommended regimen,[2] and 21% received an initial regimen different from the ATS-recommended guidelines. (Inexplicably, identities of antibiotics received by these non-azithromycin groups were not specified.)

The groups were comparable with respect to age and other demographic features. Pneumonia severity index scores among the 3 groups were similar.

Patients receiving azithromycin as the initial therapy fulfilled early discharge criteria sooner and length of stay was shorter than in patients in the other 2 groups. Need to transfer to the intensive care unit and in-hospital mortality—markers for progressive disease—were similar in all 3 groups.

Streptococcus pneumoniae was the most frequent presumed pathogen, comprising 41% of all isolates from sputum, other respiratory tract sites, and blood. Eighty percent of *S pneumoniae* isolates were erythromycin-susceptible. Outcomes were similar irrespective of erythromycin susceptibility among these isolates.

In summary, Feldman et al concluded that azithromycin as single-drug therapy for hospitalized patients with mild-to-moderate community-acquired pneumonia was equivalent to other ATS-recommended regimens.

COMMENT BY JERRY D. SMILACK, MD

The literature on community-acquired pneumonia is vast. A quick Medline search found 985 articles on the subject in the English language medical literature over the last 5 years. Comparison of results is confounded by such methodologic differences as definitions of pneumonia, case entry criteria, measurement of outcome, institutional differences in quality of care, etc. Efforts to standardize medical therapy have advanced considerably in recent years by publication of guidelines by the Infectious Diseases Society of America,[3] the American Thoracic Society,[2] the Canadian Infectious Diseases Society and Canadian Thoracic Society,[4] and the Drug-Resistant *Streptococcus pneumoniae* Therapeutic Working Group.[5] In general, for the hospitalized patient not requiring intensive care, most guidelines call for a ß-lactam, such as a third-generation cephalosporin or a ß-lactam/ß-lactamase inhibitor combination, plus a macrolide, or monotherapy with an enhanced-activity fluoroquinolone. The ATS guidelines, on the other hand, offer several options for patients with no underlying cardiopulmonary disease or modifying risk factors: azithromycin or an antipneumococcal fluoroquinolone as monotherapy, or a combination of doxycycline and a ß-lactam.

The present VA study retrospectively analyzed the outcomes of patients admitted with a diagnosis of community-acquired pneumonia. Because hospital routine at the time called for azithromycin monotherapy, half of the patients received that regimen from the outset. However, since treating physicians were apparently not compelled to follow recommended treatment guidelines, other regimens were also used.

Feldman et al found that patients treated with azithromycin generally fared as well as patients treated with other ATS-recommended and nonrecommended regimens. They had shorter lengths of stay, met clinical stability and discharge criteria more quickly, and had equal or lesser need to return to the emergency room or require readmission following hospital discharge than the comparator patient groups.

Although Feldman et al state that the treatment groups were almost entirely comparable, it appears to this reviewer that patients treated with azithromycin alone were "less sick" overall than those in the group receiving other ATS-recommended regimens or those treated with non-ATS recommended regimens. For example, the azithromycin group had lower pneumonia severity scores (although differences just escaped statistical significance); over 55% were in classes I and II, whereas 43% and 42% of patients in the other 2 treatment groups were in these lowest severity index classes. Additional support for the notion that the azithromycin group might not have appeared to the treating physicians to be as ill was the fact that patients in this group were less likely to have blood cultures drawn and to have arterial O_2 assessment performed upon admission. In addition, patients admitted from a skilled nursing facility were more likely to receive non-ATS-recommended treatment, perhaps because the treating physicians felt they may be "sicker." Questions about comparability of the groups weaken the conclusions of this study.

Other randomized studies, both retrospective[6] and prospective,[7] have shown similar results even though details concerning methods of selection, analysis, and outcome were somewhat different. After reviewing all of these studies, one could conclude that patients hospitalized for community-acquired pneumonia, particularly in the absence of such significant risk factors as serious underlying disease, advanced age, recent nursing home exposure, and recent hospitalization or antibiotic exposure, can safely and effectively be treated with azithromycin as monotherapy. Of course, this begs the question: Could these patients be treated as outpatients? If so, all of the expert guidelines agree that either a macrolide or doxycycline, among other alternatives, is appropriate therapy. ■

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Pharmacology Update

Vardenafil Tablets—Levitra

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

VARDENAFIL HAS BEEN APPROVED FOR THE TREATment of erectile dysfunction (ED) in men. The drug is the second oral type 5 phosphodiestase (PDE5) inhibitor approved for this indication along with sildenafil (Viagra). Vardenafil is manufactured by Bayer Corporation in Europe and will be distributed by GlaxoSmithKline under the trade name "Levitra." It is expected to be heavily promoted in this lucrative market.

Indications

Vardenafil is approved for the treatment of erectile dysfunction in men.

Dosage

The recommended dose is 10 mg taken approximately 60 minutes before sexual activity. The dose may be increased to 20 mg or reduced to 5 mg depending on effectiveness, side effects, or interacting drugs. Vardenafil may be taken without regard to meals. No dose adjustment is required in patients with renal impairment or mild hepatic impairment. The dose should be reduced to 5 mg in patients with moderate hepatic impairment.[1] The dose should be reduced if concomitant medications include potent CYP3A4 inhibitors.

Potential Advantages

Vardenafil is more selective for the type 5-phosphodiesterase inhibitor and is more potent on a mg basis. In animal models, vardenafil produced an increase in intracavernosal pressure faster, with a higher magnitude, and with longer duration then sildenafil.[2]

Potential Disadvantages

The most common side effects are headache (15% vs 4% for placebo), flushing (11% vs 1%), rhinitis (9% vs 3%), and dyspepsia (4% vs 1%).[1] Similar to sildenafil, the drug should not be used concomitantly with nitrates or alpha blockers since the combination may lead to hypotension and syncope. Vardenafil should also be avoided in men with prolonged QT interval syndrome because of the risk of arrhythmia.

Comments

Vardenafil is the second PDE5 inhibitor to be approved for erectile dysfunction. It appears to be more selective and more potent than sildenafil. It has been studied in 4 major double-blind, randomized, placebo-controlled, fixed-dose, multicenter studies involving 2431 study subjects.[1] Efficacy has been shown in subjects with diabetes and after radical prostatectomy.[1,3] Efficacy is generally assessed by Erectile Function Doman score of the International Index of Erectile Function domain score, rates of vaginal penetration, and successful intercourse. Similar to sildenafil, vardenafil is well tolerated, and side effects appeared to be similar and both have a median peak plasma concentration at 60 minutes.[1,5] The PDE5 inhibitors even have similar QTc effects.[4] Precautions for use and potential drug interactions are similar for these drugs. Vardenafil is priced at $9.63 per tablet (all strengths) compared to $8.10 for sildenafil.

Clinical Implications

Vardenafil provides the first competitor for sildenafil since its launch in 1998. While vardenafil appears to be more selective and more potent, no clear clinical advantage has been demonstration, as there have not been any published comparative studies. Some have suggested that vardenafil may be more effective in difficult-to-treat erectile dysfunction in diabetics;[3] however, that remains to be established. ■

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CME Questions

13. Compared to controls, patients with unexplained chronic fatigue and body pain are:

a. more likely to have pollen allergies.
b. more likely to be obese.
c. more likely to have rhinosinusitis.
d. more likely to have bradycardia.
e. more likely to be married.

14. Which one of the following questions is *false*?

a. Changing the threshold for intervention to lower levels for hypertension and cholesterol did not lower the number of persons with risk factors who had MI or death.
b. The environment remains more important than genetics in predicting CHD events.
c. Hypertensive patients without evidence of CHD receive little benefit from the treatment of their hypertension.
d. Diet may play a major role in preventing or correcting risk factors.

15. Optimal therapy for GI hemorrhage from ulcers with a visible vessel or adherent clot should involve:

a. injection of dilute epinephrine around the apparent source of bleeding.
b. thermal treatment of the bleeding ulcer (eg, using a heater probe).
c. high dose intravenous PPI therapy.
d. combined therapy with a, b, and c.
e. high-dose H2 receptor antagonist therapy intravenously.
f. sucralfate (Carafate™) administration as an oral suspension.

Answers: 13 (c); 14 (c); 15 (d)

Readers are Invited. . .

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By Louis Kuritzky, MD

Insulin 70/30 Mix Plus Metformin vs Triple Oral Therapy in Type 2 Diabetes

PATIENT PREFERENCES OFTEN DIRECT the use of multiple oral agents in an attempt to control DM2, in an effort to avoid using insulin. Trial data to date have not provided specific guidance about which agent(s) should be preferred to achieve glucose control. The UKPDS trial has indicated that sulfonylurea, metformin, and insulin are all effective tools to control glucose and reduce microvascular end points. Which combination of agents might provide the best outcomes remains indeterminate.

This 6-month study (n = 188) compared different treatment avenues after dual oral therapy no longer was effective in controlling glucose in DM2: adding a third oral agent, or switching to an insulin + metformin combination to achieve an A1C < 7%, using maximal doses of oral agents or insulin.

Insulin was administered as a 70/30 mix twice daily (two-thirds of the total daily dose in the morning). The oral agents were insulin secretagogues, thiazolidinediones, and metformin. Baseline A1C was approximately 9.6 in both groups.

Although there was a statistically significant difference in A1C favoring the insulin group in the initial few weeks of the trial, by the close of the trial, there was no statistically significant difference (final A1C, 7.66-7.70). Lipid changes (LDL and triglycerides) were significantly more favorable in the insulin/metformin group, as was the daily cost of therapy ($3.20 vs $10.20). Severe hypoglycemia occurred in only 1 patient (in the insulin group). Despite an aggressive dose-escalation protocol, only one-third of patients in either group achieved the goal of A1C < 7%. Though insulin-based treatment was less costly, successful control was achieved equally well with either regimen. ■

Schwartz S, et al. Diabetes Care. 2003;26:2238-2243.

ARB and ACE-I in Diabetic Nephropathy

IT HAS BEEN CONSISTENTLY DEMONstrated that treatment of albuminuria in diabetics with either an ACE inhibitor (ACEI) or angiotensin II receptor blocker (ARB) produces reductions in albuminuria, delay in decline of renal function, and improvements in survival. Data on combination therapies (eg, ACE + spironolactone, ACE + ARB) is only beginning to accrue. This randomized crossover trial compared albuminuria in diabetic patients treated with maximal daily doses of ACEI alone (enalapril 40 mg, lisinopril 40 mg, or captopril 150 mg) vs maximal ACEI plus ARB (candesartan 16 mg/d) for 8 weeks in 20 diabetic men and women.

Adding ARB to ACEI resulted in a statistically significant reduction in albuminuria by 28% when compared with ACEI treatment alone. There was no correlation between other variables such as age, BMI, degree of albuminuria, plasma renin, cholesterol, ambulatory blood pressure, or salt intake. Even in as brief a period of time as 8 weeks, combination blockade of the renin-angiotensin-aldosterone system with ACEI + ARB provided superior renoprotection to ACEI alone. ■

Rossing K, et al. Diabetes Care. 2003; 26:2268-2274.

Low-Glycemic Index Diets and Diabetes

THE EFFECT OF LIFESTYLE MODULAtion in diabetes is sometimes overshadowed by the favorable effect of pharmacotherapy, despite the data indicating for instance that diet and exercise are more efficacious in prevention of diabetes than medication. Glycemic index is a measurement of the glycemic effect of a food, recognizing that 2 foods with the same overall amount of carbohydrate may have as much as a 5-fold difference in glucose level achieved. Observational data have suggested that it is the glycemic index of carbohydrate, rather than the total amount, that is associated with both development of diabetes and cardiovascular consequences. Unfortunately, prospective trials of low glycemic index foods have produced conflicting results. Major consensus groups differ on whether low glycemic index foods should be preferred.

This meta-analysis reviewed 14 randomized controlled trials (356 subjects) ranging in duration from 2 weeks to 1 year. A low glycemic index diet provided a statistically significant 0.4 lower A1C than "conventional" diet; similarly, fructosamine (a marker of mean glucose exposure over a 2-3 week period, as opposed to the 3 months exposure for A1C) was more favorable in the low glycemic index group. These data suggest that if clinicians were to use a low glycemic index diet in their diabetic patients, within 10 weeks time the patient might enjoy as much as a 0.4 improvement in A1C. ■

Brand-Miller J, et al. Diabetes Care. 2003;26:2261-2267.

In Future Issues: Oral Anticoagulation on Stroke Severity in Atrial Fibrillation