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What's Best for the Breast?

ABSTRACT & COMMENTARY

Source: Velicer CM, et al. *JAMA*. 2004;291:827-835.

Synopsis: *Use of antibiotics is associated with increased risk of breast cancer and death from breast cancer in a dose-dependent way.*

THE STUDY POPULATION WAS DRAWN FROM MEMBERS OF GROUP Health Cooperative (GHC), a large nonprofit health plan in Washington State. Cases were 2266 women with primary invasive breast cancer who had been enrolled in the plan for at least 1 year. Controls were 7953 age-matched women who were also drawn from the GHC plan. Data on antibiotic use came from the GHC pharmacy. Information about other breast cancer risk factors came from GHC breast cancer surveillance questionnaires and other sources. Women who had used either tetracycline or a macrolide for at least 50 days for acne or rosacea were compared to those who had used these antibiotics for respiratory tract infections, to determine if underlying hormonal conditions (present in acne) could contribute to increased risk

There was an association between antibiotic use and the risks both of breast cancer and of breast cancer deaths in a dose-dependent way. Compared with women who had never taken antibiotics, the adjusted Relative Risks (RR) and confidence intervals for breast cancer increased with the number of days of lifetime antibiotic use as follows: 0 days, RR, 1; 1-50 days, RR, 1.45 (1.24-1.69); 51-100 days, RR, 1.53 (1.28-1.83);. 101-500 days, RR, 1.68 (1.42-2.00); 501-1000 days, RR, 2.14 (1.6-2.88). > 1000 days, RR 2.07 (RR, 1.48-2.89). This was highly statistically significant, of course. This increased risk was observed for all antibiotic classes, and was not substantially changed by controlling for other risk factors. When the analysis was restricted to women who had filled at least 1 antibiotic prescription, an increased risk was still present. However, in the sub study of 136 women who took at least 50 days' worth of tetracycline or a macrolide for acne or for rosacea, compared with 65 women who took these antibiotics for respiratory tract infections, there was no increased risk of breast cancer for those who took it for "dermatologic" reasons, compared with those who took it for respiratory tract infections.

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There were some other interesting differences between cases and controls in this study: patients with breast cancer tended to be educated beyond high school, to have more health care visits, to be premenopausal, and to have used either oral contraceptives or more than 26 hormone replacement prescriptions. They also were more likely to have had menarche before age 11, to have had their first birth after the age of 30, to have a higher body mass index, to have a first degree family relative with breast cancer, and to have a higher mammography breast density.

COMMENT BY BARBARA A. PHILLIPS, MD, MSPH

If you need a compelling argument to use the next time a patient requests unwarranted antibiotics, this is it! This article received some attention in the lay press, and many of your patients will have heard about it and will be looking to you for reinforcement. Of course, heart disease is the leading cause of death in post-adolescent people in this country. But patients tend to focus more on cancer. If you are a woman and you don't smoke, the cancer you are most likely to get is breast cancer. While we have made great strides in early detection and reduced mortality from breast cancer, our female patients appropriately still fear it. In this study, any antibiotic use increased the risk of breast cancer.

The accompanying editorial[1] elaborates on a couple of possible mechanisms suggested by Velicer and colleagues. These are that antibiotics might reduce the ability of gut microbes to metabolize phytochemicals and that antibiotics might stimulate production of prostaglandin E2, which is implicated in breast cancer.[2] It is also possible that some of the increased risk of breast cancer could have resulted from the increased likelihood of upper respiratory tract infections in women who smoked. Smoking is a well-established risk factor for breast cancer,[3] and it is possible that cigarette smokers were more likely to receive antibiotics in this study. I did not find any evidence that controlled for smoking in this study.

The bottom line for us and for our patients is that this study is one more piece of evidence for the increasingly compelling case against unwarranted antibiotics.

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Tough Love for Low Back Pain

ABSTRACT & COMMENTARY

Synopsis: *Graded activity can return a patient to full employment faster than usual care.*

Source: Staal JB, et al. *Ann Intern Med.*. 2004;140:77-84.

THE LIFETIME PREVALENCE OF LOW BACK PAIN (LBP) is 58-84% with a point prevalence of 4-33%.[1] It ranks fifth in physician visits.[2] The American Productivity Audit revealed that in a 2-week period 3.20% of US employees were absent from work due to back pain, sec-

ond only to headache at 5.43%.[3] Into this arena strides Staal and colleagues from the Netherlands with a single-blind, randomized, controlled trial of a graded activity intervention for LBP. The study was performed at KLM Royal Dutch Airline's occupational health services center at Schiphol Airport in Amsterdam and funded by the Dutch Health Insurance Executive Council.

Nonspecific graded activity interventions have several components. The foundation is the concept that pain behaviors (lying around, whining, and missing work) are subject to operant conditioning (ie, these are learned behaviors) and that recovery from pain is subject to unlearning the behaviors. A second, and equally important, concept is that pain does not necessarily mean harm. Exercise is the nemesis of pain behavior. Patients are encouraged to exercise, even if it hurts, because improvement in function, not pain relief, is the primary goal. Operationally, the physiotherapist puts the patient through his paces for 1 hour twice weekly. During each session the patient does a combination of common exercises. These exercises are aerobic (cycling or rowing), floor abdominal sit-ups, dynamic back extension, leg-press, latissimus pull-down, and standing from a low chair. Individually tailored exercises mimic the patient's work; in this study, that could be lifting and moving suitcases. In the first 3 sessions, the patient does each exercise to his limit of pain tolerance. These limits are then averaged, and the averages become the baseline for future sessions. Together, the patient and the therapist decide at what level the exercises must be done at the end of therapy. The patient decides on a return-to-work date. Then an exercise quota is established; at each session the bar is set a little higher. The patient exercises to the quota, even if it is painful.

In this study, 134 KLM employees were randomized to 2 groups that were stratified by work type and level of pain. An occupational physician made the first determination whether a worker who was absent with LBP was eligible for inclusion into the study. These people were then referred to a research assistant who determined whether they met the inclusion (full or partial work absence secondary to nonspecific LBP with symptoms > 4 weeks) and exclusion criteria (LBP with radiculopathy below the knee, heart disease precluding exercise, consideration of legal action, or pregnancy). The control group received usual care, which consisted of guidance about work-related problems and barriers to return to work and advise on ergonomics and prevention from the occupational physician. The intervention group received usual care plus graded activity. The outcomes of interest were number of days absent from work due to LBP, functional status, and pain.

The researchers chose a difference of 5 days of work absence between the control and intervention groups as clinically and economically significant (the reduction in days absent pays for the cost of the intervention) and used this to calculate how many participants they would need to show statistical significance. That number was 70.

There were 67 workers in both groups. The groups were well matched. The workers' average age was in the late 30s, and men made up greater than 90%. The various work categories (baggage handlers, maintenance, cargo, cockpit, and passenger services) were evenly distributed between to the 2 groups. In both groups the workers were absent from work for an average of 6 weeks before randomization. After randomization, the workers in the graded activity group were absent 58 days vs 87 days for the usual care group. This was statistically significant. The workers in both groups returned to work at essentially the same rate up to 50 days; thereafter, the graded activity group returned in greater frequency. Both groups experienced improvement in pain and functional status with a nonsignificant trend in favor of the graded activity group.

COMMENT BY ALLAN J. WILKE, MD

Methodologically, this study raises some questions. Acute low back pain is usually self-limited with most people recovering and returning to work within 1 month.[4] These workers were off for 6 weeks even before entering the study. Were they more severely injured? Or could it be that the Netherlands's disability system that pays workers full salary for the first year of absence encourages a slow return to work? The occupational physician made the first cut. What interior criteria did that physician use to select eligible participants? Were the workers who were not referred to the research assistant in some way different than the workers who were? Although their power calculations determined that they needed 70 participants in each group to show a 5-day difference, they had only 67. Because they were able to demonstrate a 29-day difference, the results were still significant.

Economically, this type of intervention makes a lot of sense, but when a patient presents to me complaining of back pain, the first thing out of his mouth is not, "Gee, doc, get me back to work!" The patient sees me looking for pain relief. In the long run, though, pain relief without return to work is an unsatisfactory outcome. Treatment for LBP takes many forms, some effective, others not, and still others harmful. A recent meta-analysis found that massage is effective for back pain, but spinal manipulation was not any more effec-

tive than conventional therapy, and studies of acupuncture are so poor as to make evaluation of its effectiveness unclear.[5] Muscle relaxants reduce pain, decrease muscle tension, and increase mobility, but drowsiness, dizziness, and dependency are common.[6] Back exercises are not effective for acute LBP, but may allow people with chronic LBP to resume normal daily activities and work.[7] Nonsteroidal anti-inflammatory drugs are effective for short-term relief in patients with acute LBP; there is no NSAID clearly more effective than another.[8] Bed rest is not effective and may delay recovery. Simply advising patients to stay active and to continue ordinary activities[9] and telling them "hurt does not mean harm" [10] may be the easiest method to get them back to work. However, the US Preventive Health Services Task Force "concludes that the evidence is insufficient to recommend for or against the routine use of interventions to prevent low back pain in adults in primary care settings."[11] ■

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Subclinical Thyroid Disease

ABSTRACT & COMMENTARY

Synopsis: *Data supporting associations of subclinical thyroid disease with symptoms or adverse clinical outcomes or benefits of treatment are few.*

Source: Surks MI, et al. *JAMA*. 2004;291:228-238.

A NATIONAL GROUP OF 13 EXPERTS PARTICIPATED IN A consensus conference sponsored by The Endocrine Society to evaluate the literature on subclinical thyroid disease in order to address the question of treatment. This effort was stimulated by the obvious differences in conclusions and recommendations regarding this clinical problem in the medical literature. The literature was evaluated according to the evidence-based standards established by the US Preventive Services Task Force. The results of this exercise can be presented as answers to a series of questions:

What is the definition of subclinical hypothyroidism?

- A TSH above the upper limit of the reference range, 0.45-4.5 mIU/L, when free T4 is normal;
- Other causes have been ruled out: thyroid medication adjustments, recent illness.

What is the definition of subclinical hyperthyroidism?

- A TSH below the lower limit of the reference range when free T4 and T3 are normal; usually nondetectable to 0.40 mIU/L;
- Other causes have been ruled out: overadministration of thyroid medication, pregnancy, recent medications (especially glucocorticoids or dopamine).

What is the prevalence of subclinical thyroid disease?

- Subclinical hypothyroidism is present in 4-8.5% of US adults, increases with age, is less common in blacks, and is present in up to 20% of women older than age 60. About 2-5% will progress each year to overt hypothyroidism;
- Subclinical hyperthyroidism is less common, occurring in about 2% of the US population without known thyroid disease. It is more common in women and blacks. Progression to overt hyperthyroidism is essentially limited to those individuals with TSH levels lower than 0.1 mIU/L.

What are the consequences of subclinical hypothyroidism?

Possible consequences include progression to overt hypothyroidism, atherosclerosis, cardiac dysfunction, elevated total cholesterol and LDL-cholesterol, and neuropsychiatric symptoms. None of these risks have been definitively established by appropriate clinical trials, although sufficient evidence exists to be concerned. Similar reservations exist regarding treatment. Nevertheless, the panel recommended treatment if the TSH is elevated and the free T4 is below the range of 0.8-2.0 ng/dL. Support for treatment increased with rising levels of TSH, and treatment for a TSH above 10 mIU/L carries a reasonable prospect for improvement in symptoms and the lipid profile. The panel recommended follow-up evaluation every 6-12 months when the TSH is 4.5-10 mIU/L, unless symptomatic complaints indicate a need for treatment.

There is evidence to suggest that subclinical hypothyroidism carries risks for fetus and mother during pregnancy. TSH levels should be measured every 6-8 weeks during pregnancy and maintained within the normal range.

What are the consequences of subclinical hyperthyroidism?

Possible consequences include progression to overt hyperthyroidism, atrial fibrillation, cardiac problems, reduced bone density and fractures, and neuropsychiatric symptoms. Good evidence indicates an increase in atrial fibrillation, especially in older women, when the TSH is less than 0.1 mIU/L, and suggestive with levels of 0.1-4.5 mIU/L. Treatment lowers the risk of this problem. The panel recommended treatment for TSH levels less than 0.1 mIU/L, especially to avoid bone loss and atrial fibrillation in elderly women or in those at increased risk for osteoporosis and heart disease. With TSH levels 0.1-4.5 mIU/L, treatment is indicated only in older individuals to avoid cardiac complications.

■ COMMENT BY LEON SPEROFF, MD

The recommendations of this expert consensus panel are handicapped by the ultra-conservative position these exercises ultimately embrace. The influence of the "evidence-based movement" proves to be an inhibitory force in the exercise of clinical judgment. I would argue that this process provides little assistance for the clinician who, when all is said and done, is left with making a clinical decision for the individual patient. But then that is as it should be. If these decisions were clear-cut, reached by simply following an algorithm, there would be no need for clinicians experienced in the art and science of medicine.

For example, the panel recommended against population screening for thyroid disease, even in women planning to become pregnant. The diagnosis of subclinical thyroid disease is a laboratory diagnosis, and it seems to me that the relatively inexpensive measurement of TSH is warranted to screen our patients as they age, to make sure thyroid medication is given in the right dose and to avoid fetal and maternal consequences in pregnancy.

A simplified conclusion is possible: Confirm abnormal levels of TSH, adding a measurement of free T4 if hypothyroid and both free T4 and free T3 if hyperthyroid. Treat patients with TSH levels higher than 10 mIU/L or lower than 0.1 mIU/L. Follow those patients every 6-12 months with levels in the midrange of abnormal because in some cases, the values return to normal. Remember that it takes 8 weeks for the laboratory values to stabilize after changes in thyroid medication. In patients with subclinical hypothyroidism, it is worthwhile to measure thyroid antibodies; the presence of thyroid antibodies increases the risk of overt hypothyroidism at the rate of approximately 20% per year and increases the risk of miscarriage. During pregnancy, treatment should be guided by TSH values, obtained every 2-3 months.

A good reason to treat subclinical hypothyroidism is to avoid the development of a goiter. Furthermore, some patients in retrospect (after treatment) recognize improved physical and mental well-being. Patients with subclinical hypothyroidism have alterations in energy metabolism in skeletal muscle.[1] An improvement in impaired cognitive function and emotional behavior has been documented with thyroxine treatment of subclinical hypothyroidism.[2] Patients with an abnormal cholesterol-lipoprotein profile can show a rapid improvement with thyroxine treatment.[3-5] About 10% of elderly women have subclinical hypothyroidism, a strong risk factor for coronary heart disease.[6]

TSH values below 0.1 mIU/L are regarded as nondetectable, and patients with overt hyperthyroidism usually have undetectable TSH. Subclinical hyperthyroidism is half as common in older people as subclinical hypothyroidism (excluding the most common cause, treatment with excessive doses of thyroxine). Keep in mind that the dose of thyroxine required to treat hypothyroidism declines with age (because of the decrease in metabolic clearance with age); all patients being treated with thyroid hormone should have their TSH levels assessed every year. Atrial fibrillation is a common cardiovascular problem associated with subclinical hyperthyroidism.[7] If subclinical hyperthyroidism persists, it should be treated, especially in postmenopausal women, because of the cardiac complications and the loss of bone associated with excess thyroid hormone.[8] TSH levels that are low but not undetectable (0.1-0.5 mIU/L) need not be treated, but TSH measurement is warranted every 6 months. Progression to overt hyperthyroidism is uncommon.

Although an increased prevalence of antithyroid antibodies and antinuclear antibodies has been observed in women with recurrent pregnancy loss, their relevance is uncertain because neither predicts subsequent pregnancy outcome, and there is no logical and proven effective treatment to offer.[9-11] Tests to detect antinuclear and antithyroid antibodies have no clinical use in euthyroid women with recurrent pregnancy loss.

Risk of pregnancy loss may be increased for women with uncorrected overt or even subclinical hypothyroidism.[12] Mild or subclinical disease generally has not been considered as having important clinical consequences.[13,14] However, the results of a study of pregnancy outcomes in women with hypothyroidism challenge that notion. The incidence of pregnancy loss was very

low in treated hypothyroid women having normal thyroid indices but markedly increased in women with elevated thyroid-stimulating hormone (TSH) levels, including both women with untreated subclinical disease and those with overt disease who received inadequate exogenous thyroid hormone replacement.[12] These observations suggest that subclinical hypothyroidism may not be entirely benign and further justify earlier recommendations to include TSH screening in the evaluation of women with recurrent pregnancy loss. ■

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Pharmacology Update

Bevacizumab Injection (Avastin)

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

THE FDA HAS APPROVED THE FIRST ANTINEOPLASTIC that acts by the inhibiting the formation of new blood vessels in tumors. Genentech's bevacizumab, which is approved for the treatment of metastatic colorectal cancer, is a recombinant monoclonal antibody that binds vascular endothelial cell growth factor (VEGF). VEGF is believed to be one of the more important factors responsible for normal as well as abnormal angiogenesis.[1] Bevacizumab is marketed by Genentech as Avastin.

Indications

Bevacizumab is approved for use in combination with intravenous 5-fluorouracil-based chemotherapy as first-line treatment of patients with metastatic carcinoma of the colon or rectum.[2]

Dosage

The recommended dose is 5 mg/kg once every 14 days until disease progression. The drug is administered as an intravenous infusion over 90 minutes. If the first infusion is well tolerated, the second infusion may be given over 60 minutes. If the 60-minute infusion is well tolerated, then subsequent infusion may be given over 30 minutes. A minimum of 28 days should elapse following major surgery and surgical incisions are completely healed before the initiation of bevacizumab therapy.[2]

Bevacizumab is available as 100 mg (4 mL) and 400 mg (16 mL) single-use vials.

Potential Advantages

The addition of bevacizumab (5 mg/kg) to a regimen of 5-fluorouracil and leucovorin (5-FU/LV) improved time to disease progression and response rate compared to 5-FU/LV alone.[2,3] The median time to progression was 9 months vs 5.2 months (P = .005).[2,3] Response rates were 40% vs 17% respectively (P = .029). The addition of bevacizumab to irinotecan/5-FU/LV also showed improvement in time to disease progression (10.6 vs 6.4 months; $P < .001$) and response rate (45% vs 35%; $P < .001$).[2]

Potential Disadvantages

Common serious side effects include GI hemorrhage (19-24%), hypertension (23-34%), epistaxis (32-35%), proteinuria (36%), and thromboembolic events (6-9%).[2,3] Less common and serious side effects include gastrointestinal perforation and wound dehiscence.[2]

Comments

Bevacizumab is the first drug to affect angiogenesis. This is based on an anti-VEGF mechanism. VEGF is a cytokine that binds to receptors on the vascular endothelium and results in endothelial cell migration and proliferation, and protects against endothelial cell apoptosis.[4] The approval for the treatment of colorectal cancer was based on two clinical trials with time to progression and response rate as primary efficacy end points. One

involved adding bevacizumab to 5FU/LV (n = 104) and the other to irinotecan (IFL) and 5FU/LV (n = 813). Both studies showed improved response rate and time to progression. The difference in time to progression is about 4 months. Overall survival was longer with bevacizumab, IFL and 5FU/LV compared to IFL and 5FU/LV (20.3 months vs 15.6 months; $P < .001$). However, overall survival was not significantly different in the bevacizumab 5FU/LV study. Side effects include thromboembolic events (eg, deep vein thrombosis), hypertension, proteinuria, and epistaxis. Bevacizumab has been reported to prolong the time to progression in patients with metastatic renal-cell cancer.[5] The median time to survival was 4.8 months compared to 2.5 months for placebo. Bevacizumab is also being evaluated in other tumors such as non-small cell lung, prostate, and breast cancers. Wholesale cost for one month of therapy ranges from $3300-$4400, depending on the weight of the patient.

Clinical Implications

Colorectal cancer is the third leading cause of cancer death worldwide.[6] Treatment for metastatic colorectal cancer has generally involved irinotecan with 5-fluorouracil and leucovorin or oxaliplatin with 5-fluorouracil and leucovorin. Introduction of bevacizumab provides another treatment option. Other novel therapies are on the horizon. Another monoclonal antibody, cetuximab, selective for epidermal growth factor receptor is also being evaluated for colorectal cancer.[7]

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CME Questions

12. Regarding antibiotic use and breast cancer risk, which of the following is true?

a. The risks both of breast cancer and of breast cancer death increase in a dose-dependent way with the number of days of antibiotic use, regardless of antibiotic class or indication.
b. The risks of breast cancer but not of breast cancer death increase in a dose-dependent way with the number of days of antibiotic use, regardless of antibiotic class or indication.
c. The risks of breast cancer but not of breast cancer death increase in a dose-dependent way with the number of days of antibiotic use, except for tetracyclines.
d. The risks of breast cancer and of breast cancer deaths increase in a dose-dependent way with the number of days of antibiotic use, except when antibiotics are prescribed for respiratory tract infections.
e. The risks of breast cancer but not of breast cancer deaths increases in a dose-dependent way with the number of days of antibiotic use, especially when antibiotics are prescribed for acne or for rosacea.

13. Choose the one correct answer. Graded activity for low back pain resulted in:

a. decreased pain.
b. a more rapid return to work.
c. increased functional status.
d. all of the above
e. none of the above

14. The following statements are true regarding subclinical thyroid disease except:

a. The screening test for thyroid disease is the full battery of thyroid tests.
b. A decision to treat can be based on the degree of abnormality in the level of the TSH measurement.
c. A decision to treat is influenced by the degree of risk the individual patient has for the consequences.
d. A TSH assessment is the best guide to proper treatment.

Answers: 12 (a); 13 (d); 14 (a)

By Louis Kuritzky, MD

Migraine and Subclinical Brain Lesions

The data on the relationship between migraine and other vascular events such as stroke have been conflicting, although in some populations (such as young women smokers who suffer migraine with aura) the adverse association is more clear-cut. Because such a high proportion of women, and a not-insubstantial population of men suffer migraine, any important association with other major morbidities becomes epidemiologically compelling.

Using MRI scans in a population of migraine sufferers without history of prior stroke or TIA, infarcts and white matter lesions were defined, all by the same neuroradiologist who was blinded to the clinical data about the patients (n = 435, inclusive of 140 controls). Most patients (71%) were female, the mean age was 48 years, and patients were equally divided between migraine with and without aura.

Although the absolute number of infarcts demonstrated only a trend towards being more frequent in migraneurs, it was the posterior circulation infarcts which were markedly more common (7-fold increase in migraine population vs controls), an effect which was even more exaggerated in the migraine with aura category (odds ratio = 13.7). In the total unselected population, no difference in white matter lesions between migraine sufferers and controls was discerned; however women migraneurs had an increased odds ratio (OR = 2.1) for white matter lesions compared to controls.

None of these patients had any prior evidence of cerebral ischemic events. The relationship between migraine and increased risk of cerebral ischemia prompts consideration of whether more vigorous prevention of migraine might reduce risk of subsequent tissue damage. ■

Kruit MC, et al. JAMA. 2004;291: 427-434.

Memantine Treatment in Alzheimer Disease

Memantine (MEM) is the first clinically available NMDA receptor antagonist with demonstrated clinical efficacy and an acceptable adverse event profile for persons with Alzheimer disease (ALZ). Cholinesterase inhibitors like donepezil (DON) might work in a complementary fashion, hence this MEM + DON trial.

Subjects with ALZ (n = 404) who had been on a stable dose of DON for at least 6 months, and were free of known secondary etiologies for dementia, were randomized in a double-blind fashion to MEM titrated from 5 mg/d up to 20 mg/d (administered as 10 mg b.i.d.) for 6 months, vs placebo. DON was continued in both the placebo and the MEM treatment arm.

Changes in cognitive function, functional capacity, and global outcome were measured throughout the trial, the primary outcome being based upon scores on the Severe Impairment Battery and Activities of Daily Living Inventory.

There was a statistically significant positive effect of MEM when added to DON, complemented with a very favorable adverse effect profile: more patients in the placebo group withdrew due to adverse events than in the MEM group. Only headache and confusion were more common in the MEM group, both of which occurred in less than 10% of recipients. In addition to being useful as ALZ monotherapy, there may be additional clinical benefits from combining MEM with DON in ALZ therapy. ■

Tariot PN, et al. JAMA. 2004;291: 317-324.

PPG in Type 2 DM

Tight control of type 2 diabetes (DM2) has been proven to reduce microvascular complications. Use of the hemoglobin A1c to assess long-term control is standard, but for modulation of treatment, timed specimens (eg, fasting, 1-2 hours postprandial) obtained by patient self-monitoring of blood glucose are often the information clinicians use to make choices about therapy modification.

Unless instructed otherwise, most DM2 patients are 1-4 hours postprandial at the time of an office visit. El-Kebbi, et al, investigated whether casual glucose levels obtained at the office visit might function as an adequate barometer of glucose control to help modify treatment.

Established DM2 patients (n = 1827) at the Grady Diabetes Clinic (Atlanta) underwent simultaneous A1c and casual glucose measurement during their regular visit. The correlation between casual glucose measurement and A1c was strong (correlation coefficient = 0.63). The presence of a casual glucose > 150 predicted an A1c > 7.0 with a sensitivity of 78% (positive predictive value = 80%).

El-Kebbi and colleagues suggest that a casual plasma glucose greater than 150 mg/dL may serve as a surrogate for A1c; results above this level should prompt an intensification of therapy. ■

El-Kebbi IM, et al. Diabetes Care. 2004;27:335-339.

In Future Issues: When Should I Order a BNP?